Central Administration of Pharmaceutical Care
General Administration For Drug Utilization and pharmacy Practice

Egyptian National Antimicrobial Formulary

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Preface

The Egyptian Antimicrobial Drug Formulary is published under the authority of the General Administration of Drug Utilization and Pharmacy Practice, Central Administration of Pharmaceutical Care, Egyptian Drug Authority. It has been discussed within the National Rational Antimicrobial Use Committee

The Egyptian Drug Formulary aims to provide pharmacists and other healthcare professionals with accessible reliable information about the available medications in the Egyptian database for making the right clinical decisions.

The Egyptian Drug Formulary is a guide that should be interpreted in light of professional knowledge. The developers work to ensure that the information is as accurate and up-to-date as possible at the date of publication but knowledge and best practice change regularly. No responsibility on the work team for errors or omissions.

Egyptian Antimicrobial drug formulary manual

The Egyptian Antimicrobial Drug Formulary contains a list of medicines that are registered in the Egyptian database. It is designed as drug monographs classified pharmacologically and arranged alphabetically. There is a pharmacologically classified drug index at the beginning of the document and another alphabetically classified index at the end of the document.

Egyptian drug formulary presents detailed practical information for health care providers about each medicine.

Each monograph includes:

1. Generic name
2. Dosage form/strengths available in Egypt from the EDA database
3. Route of administration
4. Pharmacological category and ATC code
5. Indications: labeled indications
6. For antibiotics: includes category from AWaRe list:
   - Acess: This group includes antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups.
   - Watch: This group includes antibiotic classes with higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine and/or antibiotics at relatively high risk of selection of bacterial resistance. These medicines should be prioritized as key targets of stewardship programs and monitoring.

- Reserve: This group includes antibiotics and antibiotic classes that should be reserved for the treatment of confirmed or suspected infections due to multi-drug-resistant organisms. Reserve group antibiotics should be treated as “last resort” options.

7. Dosage regimens for adults and children
8. Dosage adjustments if needed.
9. Contraindications
10. Adverse drug reaction
11. Monitoring parameters
12. Drug Interactions: that imply avoidance or considering modifications.
13. Pregnancy and lactation
14. Administration: detailed administration information for all routes [parenteral (preparation concentrations, compatibility with diluents, infusion rate, precautions during administration), Oral (food correlation)].
    Refer to the manufacturer PIL (Patient Information Leaflet) if there are other specific considerations.
15. Warnings/Precautions
16. Storage:
    - For reconstituted vials, apply mentioned storage conditions only if prepared in aseptic techniques and ISO-controlled conditions according to USP standards, otherwise discard immediately if not used.
    - USP develops standards for compounding medications to help ensure the patient benefit and reduce risks such as contamination, infection, or incorrect dosing.
      Refer to manufacturer PIL (Patient Information Leaflet) and SPC (Summary of product characteristics) if there are other specific consideraions.

Acknowledgment

Great efforts of work, research and dedication have been exerted for the development of "The Egyptian Drug Formulary". It would not be ever possible except with the devotion and dedication of many experts and affiliated organizations in this field.

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Disclaimer

Any information about drugs contained within this formulary is general in nature, and does not cover all data on the medicines mentioned. The Content is not intended as medical advice for individual problems or for evaluating the risks and benefits of taking a particular drug. Refer to the product insert if there are specific considerations. Authors of the Content disclaim all responsibility for any consequence, directly or indirectly, of the use and application of any of the content on this formulary.

Contributors

Chief editor

Dr. Nesma Atef
Head of Egyptian Drug Formulary unit at Drug Utilization and Pharmacy Practice General Administration-EDA

Editorial Board

Dr. Shimaa Nasr
Head of Rational Drug Use unit at Drug Utilization and Pharmacy Practice General Administration-EDA

Dr. Eman Zakaria
Head of National drug lists unit at Drug Utilization and Pharmacy Practice General Administration-EDA

Dr. Abeer Elbehairy
Head of Pharmacy development administration at Drug Utilization and Pharmacy Practice General Administration-EDA

Dr. Lobna Sami
Head of Pharmaceutical care initiative unit, at Drug Utilization and Pharmacy Practice General Administration-EDA

Members of the National Rational Antimicrobial Use Committee (Ordered Alphabetically)

Dr. Ahmed Motawea
Chief of medical supply dept.
Armed Forces Medical Services Authority

Prof. Dr. Hossam Arafa
Consultant of the General Authority of Healthcare (GAH Representative)

Dr. Asaad Sadek
Acting Director IPC General Directorate
(MOHP Representative)

Prof. Dr. Maha Abdel Aziz El-touny
Prof. Internal medicine ASU.
IPC consultant Ministry of Interior

Dr. Elizabeth Tayler
Senior technical officer-AMR Consultant at WHO Country Office

Dr. Mohammed Abdelfattah
Head of the central administration for preventive affairs (MOHP Representative)

Dr. Eman Nadim
Clinical pharmacist at the central administration for unified procurement
(The Egyptian Authority for unified procurement Representative)

Prof. Dr. Nirmeen Ahmed Sabry
Professor of clinical pharmacy
Cairo University
Medication management consultant

Prof. Dr. Ghada Esmail
Prof. of Clinical Pathology (Microbiology) at Faculty of Medicine Ain Shams University.
Head of IPC University Hospitals
(University Hospitals representative)

Dr. Omar Abdel Aziz
World Health Organization Technical Officer – Surveillance, Preparedness, and Response

Dr. Ghada Ali Younis
Former General Manager of the Drug Utilization and Pharmacy Practice General Administration at the Egyptian Drug Authority.

Dr. Sherif Kamal
Chief pharmacist
Clinical pharmacy programs director
Children's cancer hospital Egypt

Dr. Hema Soliman
Quality and Patient Safety Consultant
(GAHAR Representative)

Dr. Shereen Abdel Gawad
Head of Pharmaceutical Care Central Administration – Head of National Rational Antimicrobial Use Committee-EDA.

List of Contents (Pharmacologically)

Aminoglycosides

1. Amikacin

Generic Name	Amikacin
Dosage form/strengths	Vial 100mg, 250mg, 500mg, 1000mg
Route of administration	IV, IM
Pharmacologic category	Antibiotic, Aminoglycoside ATC: J01GB06
Indications	**Serious infections**: Treatment of serious infections (eg, bone infections, respiratory tract infections, endocarditis, septicemia) due to gram-negative organisms
Dosage Regimen	Individualization is critical because of the low therapeutic index. In underweight and nonobese patients, use total body weight (TBW) instead of ideal body weight. For obese patients (ie, TBW >1.25 × IBW), use 40% adjusted body weight ([0.4 × (TBW - IBW)] + IBW) for initial weight-based dosing **Therapeutic drug monitoring**: Monitoring of serum concentrations is recommended to ensure efficacy and avoid toxicity, particularly in critically ill patients with serious infections or in disease states known to significantly alter aminoglycoside pharmacokinetics (eg, cystic fibrosis, burns, major surgery). Timing and frequency of concentration monitoring are individualized based on dosing and monitoring strategy **Dosing: Adult** **Usual dosage range**: Injectable aminoglycoside dosing is highly variable and dependent on several factors. Maximum doses are: IM, IV: 5 mg/kg every 8 hours or 7.5 mg/kg every 12 hours. Target peak concentration depends on the indication, site of infection, and minimum inhibitory concentration (MIC) of the pathogen; in general, adjust dose to achieve the peak of 20 to 40 mg/L. Target trough concentrations should be <8 mg/L; the ideal target trough is 1 to 4 mg/L. **Note**: Some clinicians suggest a daily dose of 15 to 20 mg/kg once daily for patients with normal renal function. **Dosing: Pediatric** General dosing, severe, susceptible infections: Infants, Children, and Adolescents: IM, IV: 15-20 mg/kg/day divided every 12 or 8 hours or 15 to 20 mg/kg/dose every 24 hours.
Dosage adjustment	• **Dosing: Renal impairment Adult:**

CrCl	If the usual indication-specific dose is 7.5 mg/kg every 12 hours or 5 mg/kg every 8 hours
≥60 mL/minute	No dosage adjustment necessary.
40 to <60 mL/minute	5 to 7.5 mg/kg every 12 hours.
20 to <40 mL/minute	5 to 7.5 mg/kg every 24 hours.

Serum concentrations of the drug should be monitored in dialysis patients and dosage adjusted to maintain desired serum concentrations.

	• **Dosing: Altered Kidney Function: Pediatric** Infants, Children, and Adolescents: IM, IV: **Note:** Renally adjusted dose recommendations are based on doses of 5 to 7.5 mg/kg/dose every 8 hours: GFR >50 mL/minute/1.73 m^2: No adjustment is required. GFR 30 to 50 mL/minute/1.73 m^2: Administer every 12 to 18 hours. GFR 10 to 29 mL/minute/1.73 m^2: Administer every 18 to 24 hours. GFR <10 mL/minute/1.73 m^2: Administer every 48 to 72 hours. Intermittent hemodialysis: 5 mg/kg/dose; readjust dose as indicated by serum concentrations. Peritoneal dialysis (PD): 5 mg/kg/dose; readjust dose as indicated by serum concentrations. Continuous renal replacement therapy (CRRT): 7.5 mg/kg/dose every 12 hours, monitor serum concentrations. • **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to amikacin, other aminoglycosides, or any component of the formulation
Adverse Drug Reactions	**Frequency not defined:** **Nervous system**: Neurotoxicity (including muscle twitching, numbness, seizure, tingling of skin) **Otic**: Auditory ototoxicity, vestibular ototoxicity **Renal**: Nephrotoxicity **Respiratory**: Respiratory paralysis
Monitoring Parameters	• Urinalysis, BUN, serum creatinine, appropriately timed peak and trough concentrations, vital signs, temperature, weight, hearing parameters • Initial and periodic peak and trough plasma drug levels should be determined, particularly in critically ill patients with serious infections or in disease states known to significantly alter aminoglycoside pharmacokinetics (eg, cystic fibrosis, burns, or major surgery). • Close monitoring of aminoglycoside levels in case of combination therapy with penicillin and aminoglycoside is needed in patients with significant renal impairment **Reference Range** Traditional dosing: Target concentrations: Peak: 20 to 40 mg/L; trough: <8 mg/L (ideal target 1 to 4 mg/L) Timing of serum samples: Draw peak 30 minutes after completion of 30-minute infusion or at 1 hour following initiation of infusion or IM injection; draw trough within 30 minutes prior to next dose
Drug Interactions	• **Risk X: Avoid combination** Aminoglycosides Ataluren BCG (Intravesical) Bacitracin (Systemic) Cholera Vaccine Cisplatin Foscarnet Mannitol Mecamylamine Methoxyflurane Netilmicin (Ophthalmic) Polymyxin B • **Risk D: Consider therapy modification** Bacillus clausii Colistimethate Sodium Picosulfate Typhoid Vaccine Vancomycin
Pregnancy and Lactation	**Pregnancy risk factor D.** A decision should be made to discontinue breastfeeding or discontinue the drug, taking into account the importance of the drug to the mother. Patients with multidrug-resistant tuberculosis and a sputum smear-positive test should avoid breastfeeding when possible The effects on the nursing infant are unknown. -Breastfed infants should be monitored for antibiotic-associated colitis, diarrhea, and/or

	candidiasis.
Administration	Administration: **IM** injection in large muscle mass. Administration: **IV** Infuse over 30 to 60 minutes. In infants, infusion over 1 to 2 hours is recommended. **Preparation for Administration**: For intravenous administration, dilute in a compatible solution (eg, NS, D_5W) to a final concentration of 0.25 to 5 mg/mL Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • **Hypersensitivity*:*** Cross-sensitivity to other aminoglycosides may occur**.** • **Nephrotoxicity**: [US Boxed Warning]: May cause nephrotoxicity; usual risk factors include preexisting renal impairment, concomitant nephrotoxic medications, advanced age and dehydration. Discontinue treatment if signs of nephrotoxicity occur; renal damage is usually reversible. • **Neuromuscular blockade and respiratory paralysis*:*** [US Boxed Warning]: May cause neuromuscular blockade and respiratory paralysis; especially when given soon after anesthesia or muscle relaxants. • **Neurotoxicity*:*** [US Boxed Warning]: May cause neurotoxicity; usual risk factors include preexisting renal impairment, concomitant neuro-/nephrotoxic medications, advanced age and dehydration. Ototoxicity is proportional to the amount of drug given and the duration of treatment. Tinnitus or vertigo may be indications of vestibular injury and impending bilateral irreversible damage. Discontinue treatment if signs of ototoxicity occur. • **Superinfection*:*** Prolonged use ***Disease-related concerns:*** • **Hearing impairment:** Use with caution in patients with preexisting vertigo, tinnitus, or hearing loss. • **Hypocalcemia:** Use with caution in patients with hypocalcemia. • **Neuromuscular disorders:** Use with caution in patients with neuromuscular disorders, including myasthenia gravis or parkinsonism. • **Renal impairment:** Use with caution in patients with preexisting renal insufficiency; dosage modification required. **Concurrent drug therapy issues:** • **Neurotoxic and/or nephrotoxic drugs: [US Boxed Warning]:** Avoid concomitant or sequential use of other neurotoxic and/or nephrotoxic drugs (eg, bacitracin, cisplatin, amphotericin B, paromomycin, polymyxin B, colistin, vancomycin, other aminoglycosides). • **Potent diuretics: [US Boxed Warning]:** Avoid concomitant use with potent diuretics (eg, ethacrynic acid, furosemide) since diuretics themselves may cause ototoxicity and may enhance aminoglycoside toxicity. **Dosage form specific issues:** • **Sulfites:** May contain sulfites which may cause allergic reactions **Other warnings/precautions:** • **Surgical irrigation:** Irreversible deafness, renal failure, and death due to neuromuscular blockade have been reported following use of aminoglycosides as surgical irrigation
Storage	Store intact vials at 20°C to 25°C. Following admixture, amikacin is stable for 24 hours at room temperature, 60 days at 4°C, or 30 days at -15°C. Previously refrigerated solutions are stable for 24 hours at 25°C. Refer to manufacturer PIL if there are specific considerations.

2. Gentamicin

Access Group

Generic Name	Gentamicin
Dosage form/strengths	Ampoule 20mg, 40mg, 80mg Topical cream or ointment 0.1%, 0.3% Eye/ear Drops 0.3%, 5mg/ml, Eye/ Ear Ointment: 3mg/gm, 5mg/gm
Route of administration	*IV, IM, Topical, Opthalmic*
Pharmacologic category	Antibiotic, Aminoglycoside Systemic ATC: J01GB03 Ophthalmic ATC: S01AA11 Topical: D06AX07
Indications	**IV, IM: Serious infections:** Treatment of serious infections (eg, sepsis, meningitis, urinary tract infections, respiratory tract infections, peritonitis, bone infections, skin and soft tissue infections) caused by susceptible strains Treatment of infective endocarditis caused by enterococci, in combination with other antibiotics. **Dermatologic infections**: Topical treatment of superficial dermatologic infections **Ophthalmic infections:** Topical treatment of ocular bacterial infections, including conjunctivitis, keratitis, keratoconjunctivitis, corneal ulcers, blepharitis, blepharoconjunctivitis, acute meibomianitis, and dacryocystitis
Dosage Regimen	**Note:** Aminoglycoside dosing weight: For obese patients (ie, TBW >1.25 x IBW), use 40% adjusted body weight ([0.4 x {TBW-IBW}] + IBW) for initial weight-based dosing. **Therapeutic drug monitoring:** Monitoring of serum concentrations is recommended to ensure efficacy and avoid toxicity. **Note:** High-dose, extended-interval dosing is generally preferred for treatment of gram-negative infections. Conventional/traditional dosing is typically used for synergy dosing or non-CNS, gram-positive infections. **Dosing: Adult** ***Gram-negative infections*:** Conventional dosing: **IV, IM**: 3 to 5 mg/kg/day in divided doses every 8 hours High-dose extended-interval dosing (once-daily dosing): **IV:** 5 to 7 mg/kg once daily; use with caution in patients with CrCl <40 mL/minute *Synergy dosing for non-CNS gram-positive infections*: **IV, IM:** 3 mg/kg/day in 1 to 3 divided doses in combination with a gram-positive active agent **Endocarditis, treatment:** *Enterococcus spp. (native or prosthetic valve, without high-level gentamicin resistance)*: **IV, IM:** 1 mg/kg every 8 hours as part of an appropriate combination regimen. **Urinary tract infection, complicated (pyelonephritis or urinary tract infection with systemic signs/symptoms) (alternative agent):**

	Inpatients: **IV, IM:** 5 mg/kg once daily. Switch to an appropriate oral regimen once symptoms improve, if culture and susceptibility results allow. Total duration of therapy ranges from 5 to 14 days and depends on clinical response and the antimicrobial chosen to complete the regimen. *Outpatients:* **IV, IM:** 5 mg/kg once, followed by 5 to 14 days of appropriate oral therapy **Meningitis, bacterial:** *Enterococcus spp.*: **IV:** 5 mg/kg/day in 1 or 3 divided doses; give as part of an appropriate combination regimen and individualize duration based on clinical response *Listeria monocytogenes*: **IV:** 5 mg/kg/day in 3 divided doses in combination with ampicillin or penicillin. Gentamicin is given until clinical improvement **Dosing: Pediatric** **IV or IM:** **Premature or full-term neonates ≤1 week of age**: 2.5 mg/kg every 12 hours ***Conventional dosing****:* Infants, Children, and Adolescents: IM, IV: 2 to 2.5 mg/kg/dose every 8 hours **Endocarditis, treatment:** Synergy dosing (eg, gram-positive bacteria): Children and Adolescents: IV: 3 to 6 mg/kg/day divided every 8 hours; use in combination with other antibiotics dependent on pathogen and source of infection (ie, valve type). Treatment dosing (eg, gram-negative bacteria): Children and Adolescents: IV: 7.5 mg/kg/day divided every 8 hours; use in combination with other antibiotics **Intra-abdominal infection, complicated:** Infants, Children, and Adolescents: IV: 3 to 7.5 mg/kg/**day** divided every 8 to 24 hours; use in combination with other antibiotics **Surgical prophylaxis:** Infants, Children, and Adolescents: IV: 2.5 mg/kg as a single dose; administer within 60 minutes prior to surgical incision with or without other antibiotics (procedure dependent) **Urinary tract infection (UTI):** *Conventional dosing:* Infants, Children, and Adolescents: IV: 7.5 mg/kg/**day** divided every 8 hours until clinical improvement and ability to oral intake; complete course with oral antibiotics; duration should be individualized based upon age, severity, and degree of urinary tract involvement **Dermatologic infections: Adult/pediatric**: Topical: Apply 3 to 4 times daily to affected area **Ophthalmic infections: Adult/pediatric:** Ophthalmic: Ointment: Instill (1.25 cm) 2 to 3 times daily Solution: Instill 1 to 2 drops every 4 hours, up to 2 drops every hour for severe infections
Dosage adjustment	**Dosing: Renal Impairment: Adult** **High-dose, extended-interval dosing:** **Note:** Use with caution in patients with CrCl <40 mL/minute; high-dose, extended-interval dosing may still be considered, especially in patients with severe sepsis/shock or those infected with multidrug-resistant gram-negative organisms (expert opinion). **IV:** Initial dose: 5 to 7 mg/kg. Subsequent doses and frequency of administration should be determined based on therapeutic drug monitoring; regimens may vary. The following recommendations may serve as a general guideline after the initial dose: CrCl ≥60 mL/minute: **IV:** Administer every 24 hours; adjust dose and/or interval based on gentamicin serum concentrations. CrCl 40 to <60 mL/minute: **IV:** Administer every 36 hours; adjust dose and/or interval based on gentamicin serum concentrations. CrCl 20 to <40 mL/minute: **IV:** Administer every 48 hours; adjust dose and/or interval based on gentamicin serum concentrations.

	CrCl <20 mL/minute: **IV:** Administer usual dose once, then determine subsequent dose and interval based on serum concentration monitoring. **Conventional/traditional dosing:** Regimens may vary based on individualized pharmacokinetic calculations and pharmacodynamic targets; also refer to institutional-specific policies. **Note:** The following recommendations are expert opinion and based on a usual dosage range of 3 to 5 mg/kg/day: CrCl ≥60 mL/minute: **IM, IV:** No dosage adjustment necessary. CrCl ≥40 to <60 mL/minute: **IM, IV:** Administer usual dose every 12 hours; adjust dose and/or interval based on gentamicin serum concentrations. CrCl 20 to <40 mL/minute: **IM, IV:** Administer usual dose every 24 hours; adjust dose and/or interval based on gentamicin serum concentrations. CrCl <20 mL/minute: **IM, IV:** Administer usual dose every 36 to 48 hours; adjust dose and/or interval based on gentamicin serum concentrations. **Dosing: Renal Impairment: Pediatric** Parenteral: **Note:** Gentamicin serum concentrations should be monitored in patients with kidney impairment; following the initial dose, subsequent doses may be determined based on therapeutic monitoring. Infants, Children, and Adolescents: IM, IV: The following adjustments have been recommended: **Note:** Renaly adjusted dose recommendations are based on doses of 2.5 mg/kg/dose every 8 hours: GFR >50 mL/minute/1.73 m^2: No dosage adjustment necessary. GFR 30 to 50 mL/minute/1.73 m^2: Administer every 12 to 18 hours. GFR 10 to 29 mL/minute/1.73 m^2: Administer every 18 to 24 hours. GFR <10 mL/minute/1.73 m^2: Administer every 48 to 72 hours. Intermittent hemodialysis: 2 mg/kg/dose; readjust dose as indicated by serum concentration. Peritoneal dialysis (PD): 2 mg/kg/dose; readjust dose as indicated by serum concentration. Continuous renal replacement therapy (CRRT): 2 to 2.5 mg/kg/dose every 12 to 24 hours, monitor serum concentrations. **Dosing: Hepatic Impairment:** No dosage adjustment is needed
Contra-indications	Hypersensitivity to gentamicin, other aminoglycosides, or any component of the formulation
Adverse Drug Reactions	**Frequency not defined.** **Cardiovascular**: Edema, hypertension, hypotension, phlebitis, thrombophlebitis **Central nervous system**: Abnormal gait, ataxia, brain disease, confusion, depression, dizziness, drowsiness, headache, lethargy, myasthenia, numbness, paresthesia, peripheral neuropathy, pseudomotor cerebri, seizure, vertigo **Dermatologic**: Alopecia, erythema, pruritus, skin rash, urticaria **Endocrine & metabolic**: Hypocalcemia, hypokalemia, hypomagnesemia, hyponatremia, weight loss **Gastrointestinal**: Anorexia, *Clostridioides difficile*-associated diarrhea, decreased appetite, enterocolitis, nausea, sialorrhea, stomatitis, vomiting **Genitourinary**: Casts in urine (hyaline, granular), Fanconi-like syndrome (infants and adults; high dose, prolonged course), oliguria, proteinuria **Hematologic & oncologic**: Agranulocytosis, anemia, eosinophilia, granulocytopenia, leukopenia, purpura, reticulocytopenia, reticulocytosis, splenomegaly, thrombocytopenia **Hepatic**: Hepatomegaly, increased liver enzymes Hypersensitivity: Anaphylaxis, anaphylactoid reaction, hypersensitivity reaction

	Local: Injection site reaction, pain at injection site **Neuromuscular & skeletal:** Arthralgia, muscle cramps, muscle fatigue (myasthenia gravis-like syndrome), muscle twitching, tremor, weakness **Ophthalmic**: Visual disturbance **Otic**: Auditory impairment, hearing loss (associated with persistently increased serum concentrations; early toxicity usually affects high-pitched sound), tinnitus **Renal**: Decreased creatinine clearance, decreased urine specific gravity, increased blood urea nitrogen, increased serum creatinine, polyuria, renal failure (high trough serum concentrations), renal tubular necrosis **Respiratory**: Dyspnea, laryngeal edema, pulmonary fibrosis, respiratory depression Miscellaneous: Fever
Monitoring Parameters	• Urinalysis, urine output, BUN, serum creatinine, plasma gentamicin levels (as appropriate to dosing method). Levels are typically obtained before and after the third dose in conventional dosing. Hearing should be tested before, during, and after treatment; particularly in those at risk for ototoxicity or who will be receiving prolonged therapy (>2 weeks) • Close monitoring of aminoglycoside levels is warranted in case of combination therapy with penicillin derivatives. **Reference range: Conventional dosing:** Timing of serum samples: Draw peak 30 minutes after the 30-minute infusion has been completed or 1 hour after IM injection; draw trough immediately before the next dose is due. **Therapeutic levels:** **Peak:** Sepsis, pneumonia, and other serious infections (including life-threatening infections): 7 to 10 mcg/mL Urinary tract infections, including pyelonephritis: 4 to 6 mcg/mL Synergy against gram-positive organisms: 3 to 4 mcg/mL **Trough:** Gram-negative infections: <2 mcg/mL (ideal target <1 mcg/mL) Synergy against gram-positive organisms: <1 mcg/mL Obtain drug levels after the third dose unless renal dysfunction/toxicity suspected
Drug Interactions	• ***Risk X: Avoid combination*** Agalsidase Alfa Aminoglycosides Ataluren Bacitracin (Systemic) BCG (Intravesical) Cholera Vaccine Cisplatin Foscarnet Mannitol (Systemic) Mecamylamine Methoxyflurane Netilmicin (Ophthalmic) Polymyxin B • ***Risk D: Consider therapy modification*** Agalsidase Beta Bacillus clausii Colistimethate Sodium Picosulfate Typhoid Vaccine Vancomycin • ***Risk C: Monitor therapy*** Amphotericin B Arbekacin Bisphosphonate Derivatives Botulinum Toxin-Containing Products Capreomycin Carboplatin Cardiac Glycosides Cephalosporins Cyclosporine Cyclizine Distigmine Lactobacillus And Estriol Loop Diuretics Neuromuscular-Blocking Agents Nonsteroidal Anti-Inflammatory Agents Oxatomide Penicillins Tacrolimus (systemic) Tenofovir Products

Pregnancy and Lactation	**Pregnancy risk factor D** Aminoglycosides may cause fetal harm if administered to a pregnant woman. The World Health Organization (WHO) considers gentamicin to be compatible with breastfeeding. Infants should be monitored for thrush and diarrhea
Administration	**IM:** Administer undiluted. Gentamicin in NS is not intended for IM administration.; in paralyzed patients, suggest the IV route. **IV:** Administer as a diluted solution by slow intermittent infusion over 30 to 120 minutes; usual infusion time is 30 to 60 minutes; consider longer infusion time (60 to 120 minutes) with high doses. Shorter infusion times (≤5 minutes) have been reported in pediatric patients, including preterm and term neonates, receiving ≤4 mg/kg/dose. Avoid infusing concomitantly with penicillins or cephalosporins if feasible; Consult drug interactions database for more information. **Preparation for Administration:** IV: May dilute in NS or D5W. In adults, dilution in 50 to 200 mL is recommended; the concentration of the pediatric-specific product is 10 mg/mL. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity: Cross-sensitivity to other aminoglycosides may occur. • Nephrotoxicity: [US Boxed Warning]: May cause nephrotoxicity; usual risk factors include preexisting renal impairment, concomitant nephrotoxic medications, advanced age and dehydration. Discontinue treatment if signs of nephrotoxicity occur; renal damage is usually reversible. • Neuromuscular blockade and respiratory paralysis: especially when given soon after anesthesia or neuromuscular blockers. • Neurotoxicity: **May cause neurotoxicity;** usual risk factors include preexisting renal impairment, concomitant neuro-/nephrotoxic medications, advanced age and dehydration. Tinnitus or vertigo may be indications of vestibular injury and impending bilateral irreversible damage. Discontinue treatment if signs of ototoxicity occur. • Superinfection: Prolonged use. • Corneal healing: May delay corneal healing in ophthalmic administration. ***Disease-related concerns:*** • Electrolyte abnormalities: Use with caution in patients with hypocalcemia, hypokalemia, or hypomagnesemia. • Hearing impairment: Use with caution in patients with preexisting vertigo, tinnitus, or hearing loss. • Neuromuscular disorders: Use with caution in patients with neuromuscular disorders, including myasthenia gravis. • Renal impairment: Use with caution in patients with preexisting renal insufficiency; dosage modification is required. ***Special populations:*** • Pregnancy: Aminoglycosides may cause fetal harm if administered to a pregnant woman. ***Concurrent drug therapy issues:*** • Neurotoxic and/or nephrotoxic drugs: [US Boxed Warning]: Avoid concomitant or sequential use of other neurotoxic and/or nephrotoxic drugs (eg, cisplatin, polymyxin B, colistin, vancomycin, other aminoglycosides). • Potent diuretics: Avoid concomitant use with potent diuretics (eg, ethacrynic acid, furosemide) since diuretics themselves may cause ototoxicity and may enhance aminoglycoside toxicity. ***Other warnings/precautions:*** • Long-term use: Risk of toxicity is increased; additional monitoring may be required with long-term use. • Surgical irrigation: May be almost completely systemically absorbed after local irrigation

	and/or topical application (except to the urinary bladder) during surgical procedures. Consider potential for nephrotoxicity, neuromuscular blockade, ototoxicity, and respiratory paralysis.
Storage	• Intact vials: Store at 20°C to 25°C. Protect from freezing. • IV infusion solutions mixed in NS or D5W are stable for 48 hours at room temperature and refrigeration. • Cream/ Ointments: Store at controlled room temperature of 20°C to 25°C • Refer to manufacturer PIL if there are specific considerations.

3. Neomycin

Watch Group

Generic name	Neomycin
Dosage form/strengths	Tablets 350.000 I. U, 500 mg Ophthalmic and topical preparations in combinations
Route of administration	Oral
Pharmacologic category	Ammonium Detoxicant; Antibiotic, Aminoglycoside ATC: A07AA01
Indications	**Hepatic coma (portal-systemic encephalopathy):** Adjunctive therapy in hepatic coma. **Surgical (perioperative) prophylaxis:** Adjunctive therapy as part of a regimen for the suppression of the normal bacterial bowel flora (eg, preoperative bowel preparation)
Dosage Regimen	**Oral:** **Dosing: Adult** To minimize risk of toxicity, use lowest possible dosage and shortest duration of therapy. Closely monitor patients for aminoglycoside toxicity. Treatment duration >2 weeks is *not* recommended. **Surgical (perioperative) prophylaxis:** Oral: 1 g at 19, 18 and 9 hours before the time of surgery as an adjunct to mechanical cleansing of the intestine, followed by an appropriate IV antibiotic prophylaxis regimen. **Hepatic encephalopathy:** 4 to 12 g daily divided every 4 to 6 hours for 5 to 6 days **Chronic hepatic insufficiency:** 4 g daily **Dosing: Pediatric** **General Pediatric Dosage** If neomycin is considered necessary in children <18 years of age, duration of therapy should not exceed 2 weeks. **Hepatic Encephalopathy** Children: 50-100 mg/kg daily given in 4 divided doses for ≤7 days. Prior to initiation of neomycin, withdraw protein from the diet and avoid diuretics; incrementally return protein back to the diet during treatment. Monitor closely; give supportive therapy (including blood products) as indicated **Preoperative intestinal antisepsis:** Infants, Children, and Adolescents: Oral: 15 mg/kg/dose for 3 doses administered over 10 hours the day before surgery; maximum dose: 1,000 mg/dose; used in combination with other oral antimicrobial (eg, erythromycin or metronidazole) and with/or without adjunct to mechanical cleansing of the intestine
Dosage adjustment	**Dosing: Renal Impairment:** Dosage reduction or discontinuation of therapy should be considered if a patient develops renal insufficiency. The risk of nephro- and/or ototoxicity is increased in patients with renal impairment. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed. Caution in severe cases.
Contra-indications	Hypersensitivity to the neomycin or any component of the formulation; intestinal obstruction; patients with inflammatory or ulcerative GI disease. Patients with a history of hypersensitivity or serious toxic reactions to other aminoglycosides may have a cross-sensitivity to neomycin.
Adverse Drug Reactions	**>10%:** Central nervous system: Sore mouth Gastrointestinal: Anorectal pain, diarrhea, mouth irritation, nausea, rectal irritation, vomiting

Monitoring Parameters	Serum creatinine/BUN at baseline and periodically during chronic therapy; audiometry in symptomatic patients
Drug Interactions	***Risk X: Avoid combination*** Aminoglycosides Ataluren Bacitracin BCG (Intravesical) Cholera Vaccine Cisplatin Foscarnet Mannitol Mecamylamine Methoxyflurane Netilmicin (Ophthalmic) Polymyxin B Sorafenib ***Risk D: Consider therapy modification*** Bacillus clausii Sodium Picosulfate Colistimethate Typhoid Vaccine Vancomycin
Pregnancy and Lactation	**Pregnancy Risk Factor D** It is not known if neomycin is excreted into breast milk. Due to the potential for serious adverse reactions in the nursing infant, It is recommended a decision be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of treatment to the mother. As a class, aminoglycosides are expected to be poorly distributed into breast milk, limiting systemic exposure to a nursing infant. In general, modification of bowel flora may occur with any antibiotic exposure
Administration	Oral: Administer without regard to meals; for preoperative intestinal antisepsis, administer at prescribed dosing times. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Systemic:*** ***Concerns related to adverse effects:*** • Hypersensitivity: Cross-sensitivity to other aminoglycosides may occur. • Malabsorption: Small amounts of neomycin are absorbed through intact intestinal mucosa; increases in fecal bile acid excretion and reduction of intestinal lactase activity may occur. Oral doses of >12 g/day produce malabsorption of fats, nitrogen, cholesterol, carotene, glucose, xylose, lactose, sodium, calcium, cyanocobalamin and iron. • Nephrotoxicity: **[US Boxed Warning]: May cause nephrotoxicity;** usual risk factors include preexisting renal impairment, concomitant nephrotoxic medications, advanced age and dehydration. Discontinue treatment if signs of nephrotoxicity occur; renal damage is usually reversible. • Neuromuscular blockade and respiratory paralysis: **[US Boxed Warning]: May cause neuromuscular blockade and respiratory paralysis;** especially when given soon after anesthesia or muscle relaxants. • Neurotoxicity: **[US Boxed Warning]: May cause neurotoxicity;** symptoms also include numbness, skin tingling, muscle twitching and seizures. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Hearing impairment: Use with caution in patients with preexisting vertigo, tinnitus, or hearing loss. • Neuromuscular disorders: Use with caution in patients with neuromuscular disorders, including myasthenia gravis and Parkinson's disease. • Renal impairment: Use with caution in patients with preexisting renal insufficiency; dosage modification required. ***Concurrent drug therapy issues:*** • Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information. ***other warnings/precautions:*** • Parenteral administration: More toxic than other aminoglycosides when given

	parenterally; **do not administer parenterally.** • Surgical irrigation: **Do not use as surgical irrigation** due to significant systemic absorption of the drug.
Storage	Store at 20ºC to 25ºC Refer to manufacturer PIL if there are specific considerations.

4. Streptomycin

Watch Group

Generic Name	Streptomycin
Dosage form/strengths	Vial (or Powder for injection): 1gm
Route of administration	IM Or oral in combinations
Pharmacologic category	Antibiotic, Aminoglycoside; Antitubercular Agent ATC: Parentral: J01GA01 Oral: A07AA04
Indications	**Tuberculosis**: Treatment of tuberculosis, in combination with other appropriate antituberculosis agents, when the primary agents are contraindicated because of toxicity or intolerance. **Nontuberculosis infections:** Treatment of infections caused by susceptible bacteria that are not amenable to therapy with less potentially toxic agents.
Dosage Regimen	**Dosing: Adult** **Aminoglycoside dosing weight:** For underweight patients (ie, total body weight [TBW] < ideal body weight [IBW]), calculate the dose based on TBW. For obese patients (ie, TBW > 1.25 × IBW), calculate the dose based on 40% adjusted body weight (IBW + [0.4 × (TBW-IBW)]). **Therapeutic drug monitoring:** Monitoring of serum concentrations is recommended to ensure efficacy and avoid toxicity; confirm availability of rapid streptomycin serum concentrations. Timing and frequency of concentration monitoring are individualized based on dosing and monitoring strategy **Note** IV is offlabel use **Usual dosage range: IM, IV:** 15 to 30 mg/kg/day or 1 to 2 g daily **Indication-specific dosing:** **Brucellosis: IM, IV:** 1 g once daily in combination with doxycycline. Duration depends on extent of disease; streptomycin is usually given for the first 14 to 21 days of therapy, followed by doxycycline monotherapy **Endocarditis (alternate agent):** *Enterococcus spp. (native or prosthetic valve, susceptible to penicillin and streptomycin/resistant to gentamicin):* **IM, IV:** 7.5 mg/kg every 12 hours in combination with ampicillin or penicillin **Plague: IM:** 1 g every 12 hours for 7 to 14 days and for at least a few days after clinical resolution **Tuberculosis (alternative agent): IM, IV:** 15 mg/kg once daily **or** 25 mg/kg 3 times weekly **Tularemia (alternative agent): IM:** 1 g twice daily for ≥10 days depending on severity **Pediatric Patients** **General Dosage for Infants and Children** **IM** 20–40 mg/kg daily given in divided doses every 6–12 hours, maximum dose: 1,000 mg/dose; maximum daily dose: 2,000 mg/day. maximum daily dose: 2,000 mg/day
Dosage adjustment	**Dosing: Renal Impairment: Adult** The following adjustments have been recommended:

	CrCl more than 50 mL/minute: Administer the dose every 24 hours. CrCl 10 to 50 mL/minute: Administer the dose every 24 to 72 hours. CrCl less than 10 mL/minute: Administer the dose every 72 to 96 hours. ATS/CDC/IDSA: **Tuberculosis:** CrCl ≥30 mL/minute: No dosage adjustment is necessary. CrCl <30 mL/minute: 15 mg/kg/dose 2 to 3 times weekly. ESRD on IHD: 15 mg/kg/dose 2 to 3 times weekly. Give after dialysis if given on day of dialysis**.** **Dosing: Renal Impairment: Pediatric** **Infants, Children, and Adolescents: Note:** Renally adjusted dose recommendations are based on doses of 20 to 40 mg/kg/day every 24 hours. Monitor serum concentrations. GFR 30 to 50 mL/minute/1.73 m^2: Administer 7.5 mg/kg/dose every 24 hours GFR 10 to 29 mL/minute/1.73 m^2: Administer 7.5 mg/kg/dose every 48 hours GFR <10 mL/minute/1.73 m^2: Administer 7.5 mg/kg/dose every 72 to 96 hours Intermittent hemodialysis (IHD): Administer 7.5 mg/kg/dose every 72 to 96 hours Peritoneal dialysis (PD): Administer 7.5 mg/kg/dose every 72 to 96 hours **Dosing: Hepatic Impairment:** There are no dosage adjustments needed **Dosing: Geriatric** Dose reductions are recommended in patients >60 years of age.
Contra-indications	Hypersensitivity to streptomycin, other aminoglycosides, or any component of the formulation
Adverse Drug Reactions	**Frequency not defined.** Cardiovascular: Hypotension Central nervous system: Drug fever, facial paresthesia, headache, neurotoxicity Dermatologic: Exfoliative dermatitis, skin rash, urticaria Gastrointestinal: Nausea, vomiting Genitourinary: Azotemia, nephrotoxicity Hematologic & oncologic: Eosinophilia, hemolytic anemia, leukopenia, pancytopenia, thrombocytopenia Hypersensitivity: Anaphylaxis, angioedema Neuromuscular & skeletal: Arthralgia, tremor, weakness Ophthalmic: Amblyopia Otic: Auditory ototoxicity, vestibular ototoxicity Respiratory: Dyspnea
Monitoring Parameters	Baseline and periodic hearing tests (audiograms), clinical assessment for vertigo and tinnitus, BUN, creatinine, serum electrolytes; serum drug concentrations should be monitored in all patients
Drug Interactions	***Risk X: Avoid combination*** Aminoglycosides Ataluren Bacitracin (Systemic) BCG (Intravesical) Cholera Vaccine Foscarnet Mannitol Mecamylamine Methoxyflurane Netilmicin (Ophthalmic) Polymyxin B Cisplatin ***Risk D: Consider therapy modification*** Bacillus clausii Typhoid Vaccine Sodium Picosulfate Colistimethate Vancomycin
Pregnancy and Lactation	**Pregnancy Risk Factor** D Aminoglycosides have poor oral bioavailability, which may limit systemic absorption via

	breast milk. Streptomycin is considered compatible with breastfeeding. In general, antibiotics that are present in breast milk may cause non-dose-related modification of bowel flora. Monitor infants for GI disturbances, such as thrush and diarrhea
Administration	**Administration:** Parenteral: IM: Inject deep IM into a large muscle mass; rotate injection sites IV (off-label route): After further dilution, infuse over 30 to 60 minutes **Preparation for Administration:** **IM:** Reconstitute vial with 4.2 mL, 3.2 mL, or 1.8 mL sterile water for injection (SWFI) to yield a final concentration of ~ 200 mg/mL, 250 mg/mL, or 400 mg/mL, respectively **IV:** Further dilute dose to concentration of 5 to 10 mg/mL in D5W or NS Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Neuromuscular blockade and respiratory paralysis: **[US Boxed Warning]: May cause neuromuscular blockade and respiratory paralysis; especially when given soon after anesthesia or muscle relaxants.** • Neurotoxicity: **[US Boxed Warning]: May cause neurotoxicity, including disturbances of vestibular and cochlear function, optic nerve dysfunction, peripheral neuritis, arachnoiditis, and encephalopathy;** usual risk factors include pre-existing renal impairment, concomitant neuro-/nephrotoxic medications. Ototoxicity is proportional to the amount of drug given and the duration of treatment. Tinnitus or vertigo may be indications of vestibular injury and impending bilateral irreversible damage. Baseline and periodic caloric stimulation and audiometric tests are recommended with prolonged therapy. Discontinue treatment if signs of ototoxicity occur. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Hearing impairment: Use with caution in patients with pre-existing vertigo, tinnitus, or hearing loss. • Neuromuscular disorders: Use with caution in patients with neuromuscular disorders, including myasthenia gravis. • Renal impairment: **[US Boxed Warning]: May cause nephrotoxicity.** Use with caution in patients with renal impairment; dose adjustment is necessary in patients with renal impairment and/or nitrogen retention. Monitor renal function closely; peak serum concentrations should not surpass 20 to 25 mcg/mL in patients with renal impairment. ***Concurrent drug therapy issues:*** • Neurotoxic and/or nephrotoxic drugs: **[US Boxed Warning]: Avoid concomitant or sequential use with other neurotoxic and/or nephrotoxic drugs (eg, neomycin, kanamycin, gentamicin, paromomycin, polymyxin B, colistin, tobramycin, cyclosporine).** ***Dosage form specific issues:*** • Sulfite sensitivity: Some formulations may contain sodium metabisulfite; may cause allergic reactions including anaphylaxis or asthma exacerbations (some life-threatening) in susceptible patients. ***Other warnings/precautions:*** • Appropriate use: **[US Boxed Warning]: Parenteral form should be used only where appropriate audiometric and laboratory testing facilities are available.** IM injections should be administered in a large muscle well within the body to avoid peripheral nerve damage and local skin reactions

Storage	Store intact vials at 20°C to 25°C. Protect from light. Reconstituted solution remains stable for 24 hours at room temperature. Exposure to light causes darkening of solution without apparent loss of potency. Refer to manufacturer PIL if there are specific considerations.

5. Tobramycin

Watch Group

Generic Name	Tobramycin
Dosage form/strengths	Ophthalmic ointment 0.3% (3 mg/gm) Ophthalmic solution 0.3% Inhalation Solution 300 mg/5ml
Route of administration	Ophthalmic, Inhalation
Pharmacologic category	Antibiotic, Aminoglycoside Ophthalmic ATC: S01AA12 Inhalation ATC: J01GB01
Indications	**Inhalation:** **Cystic fibrosis:** Management of cystic fibrosis in adults and pediatric patients ≥6 years of age with *Pseudomonas aeruginosa*. **Ophthalmic**: Ocular infections: Treatment of external infections of the eye and its adnexa caused by susceptible bacteria.
Dosage Regimen	**Inhalation:** **Dosing: Adult** **Cystic fibrosis:** Inhalation: 300 mg every 12 hours (do not administer doses <6 hours apart); administer in repeated cycles of 28 days on drug followed by 28 days off drug. **Dosing: Pediatric** **Eradication of new or initial *Pseudomonas aeruginosa* airway culture in patients with cystic fibrosis:** Limited data available: Infants ≥6 months, Children, and Adolescents: Inhalation: 300 mg every 12 hours for 28 days. ***Pseudomonas aeruginosa* colonization; chronic lung maintenance:** *Patients with cystic fibrosis:* Children and Adolescents (limited data in children <6 years): Inhalation: 300 mg every 12 hours; administer in repeated cycles of 28 days on drug followed by 28 days off drug **Ophthalmic**: **Dosing: Adult, Pediatric** **Ocular infections:** Ophthalmic: **Ointment**: Apply half-inch ribbon into affected eye(s) 2 or 3 times daily for mild to moderate infections; for severe infections, apply every 3 to 4 hours until improvement (then reduce before discontinuation). **Solution**: Instill 1 to 2 drops into affected eye(s) every 4 hours for mild to moderate infections; for severe infections, instill 2 drops every hour until improvement (then reduce prior to discontinuation).
Dosage adjustment	**Dosing: Renal Impairment: Adult** It is recommended either maintain the standard dose and increase the interval between doses or decrease the dose while maintaining every 8-hour dosing interval. should be individualized **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments needed

Contra-indications	Hypersensitivity to tobramycin, other aminoglycosides, or any component of the formulation
Adverse Drug Reactions	**Inhalation:** **>10%:** Central nervous system: Voice disorder (4% to 14%), headache (11%) Respiratory: Cough (31%), rhinitis (11% to 35%), pulmonary disease (30% to 34%; includes pulmonary or cystic fibrosis exacerbations), reduced forced expiratory volume (1% to 31%), discoloration of sputum (21%), productive cough (18% to 20%), rales (6% to 19%), dyspnea (12% to 16%), decreased lung function (7% to 16%), oropharyngeal pain (11% to 14%), hemoptysis (12% to 13%), pharyngolaryngeal pain (3%) Miscellaneous: Fever (12% to 16%) **1% to 10%:** Cardiovascular: Chest discomfort (3% to 7%) Central nervous system: Malaise (6%) Dermatologic: Skin rash (2%) Gastrointestinal: Nausea (8% to 10%), dysgeusia (<1%), vomiting (6%), diarrhea (2% to 4%) Hematologic & oncologic: Increased erythrocyte sedimentation rate (8%), eosinophilia (2%), increased serum immunoglobulins (2%) Neuromuscular & skeletal: Musculoskeletal chest pain (<1% to 5%), myalgia (≤5%) Otic: Hypoacusis (powder: 10%), tinnitus (2% to 3%), deafness (≤1%; including unilateral deafness, reported as mild to moderate hearing loss or increased hearing loss) Respiratory: Upper respiratory tract infection (7% to 9%), nasal congestion (7% to 8%), wheezing (5% to 7%), throat irritation (2% to 5%), bronchospasm (≤1% to 5%), laryngitis (≤5%) bronchitis (3%), epistaxis (2% to 3%), tonsillitis (2%)
Monitoring Parameters	Monitor serum tobramycin concentrations in patients with a known history of auditory dysfunction, renal dysfunction, and/or concomitant use of nephrotoxic drugs. One hour after inhalation, serum concentrations of 1 to 2 mcg/mL have been observed. Urinalysis, urine output, BUN, serum creatinine, peak, and trough plasma tobramycin levels. Levels are typically obtained after the third dose in conventional dosing. Be alert to ototoxicity; hearing should be tested before and during treatment
Drug Interactions	***Risk X: Avoid combination*:** Mannitol (Systemic): May enhance the nephrotoxic effect of Tobramycin (Oral Inhalation).
Pregnancy and Lactation	**Pregnancy Category** D The amount of tobramycin available systemically following topical application of the ophthalmic drops is undetectable Systemic absorption following oral inhalation is expected to be low compared to IV administration. Infants should be monitored for loose or bloody stools and candidiasis. The amount of tobramycin available systemically following topical application of the ophthalmic drops is undetectable. If ophthalmic agents are needed in lactating women, the minimum effective dose should be used to decrease systemic absorption
Administration	**Administration: Inhalation** To be orally inhaled over ~15 minutes. If multiple different nebulizer treatments are required, administer bronchodilator first, followed by chest physiotherapy, any other nebulized medications, and then tobramycin last. Do not mix with other nebulizer medications. **Administration: Ophthalmic** For topical ophthalmic use only; not for injection into the eye. Contact lenses should not be worn during treatment of ophthalmic infections. Avoid contact of tube or bottle tip with skin or eye.

	Ointment: Apply into conjunctival sac(s) of eye; the patient should look downward before closing eye **Solution**: Apply gentle pressure to lacrimal sac during and immediately following instillation (1 minute) or instruct patient to gently close eyelid after administration, to decrease systemic absorption of ophthalmic drops Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Inhalation:*** ***Concerns related to adverse effects:*** • Bronchospasm: Bronchospasm may occur; bronchospasm or wheezing should be treated appropriately if either arise. • Nephrotoxicity: Nephrotoxicity was not observed during tobramycin inhalation clinical studies, but has been associated with aminoglycosides. Patients with known or suspected renal dysfunction or taking concomitant nephrotoxic drugs should be closely monitored (renal function tests and serum tobramycin concentrations) as clinically indicated. If nephrotoxicity occurs, discontinue therapy until serum concentrations fall below 2 mcg/mL. • Neuromuscular disorders: Use with caution in patients with neuromuscular disorders, including myasthenia gravis and Parkinson's disease; neuromuscular blockade, respiratory failure, and prolonged respiratory paralysis may occur. Concomitant neuromuscular blocking agents may also increase the risk of prolonged respiratory paralysis. • Ototoxicity: Ototoxicity, as measured by complaints of hearing loss or tinnitus, has been reported. Tinnitus may be a sentinel symptom of ototoxicity, and therefore, the onset of this symptom warrants further investigation. Ototoxicity, manifested as both auditory and vestibular toxicity, has been reported with parenteral aminoglycosides. Vestibular toxicity may be manifested by vertigo, ataxia, or dizziness. Patients with known or suspected auditory or vestibular dysfunction should be closely monitored (audiometric evaluations and serum tobramycin concentrations). A baseline audiogram should be considered for patients at increased risk of auditory dysfunction. Use with caution in patients with preexisting vertigo, tinnitus, or hearing loss. **Ophthalmic:** ***Concerns related to adverse effects:*** • Hypersensitivity reactions: Sensitivity varying from local to generalized effects (eg, erythema, pruritus, urticaria, skin rash, anaphylaxis, anaphylactoid reaction, bullous reaction) to topically applied aminoglycosides and cross-sensitivity to other aminoglycosides antibiotics may occur; discontinue use if hypersensitivity develops. • Superinfection: Prolonged use may lead to overgrowth of nonsusceptible organisms, including fungi. If superinfection is suspected, institute appropriate alternative therapy. ***Special populations:*** • Contact lens wearers: Some products may contain benzalkonium chloride or benzododecinium bromide which may be absorbed by soft contact lenses; contact lenses should not be worn during treatment of ophthalmologic infections. ***Other warnings/precautions:*** • Appropriate use: For topical application to the eye only; not for injection. To avoid contamination, do not touch tip of container to any surface.
Storage	Inhalation: Store in original package at 25°C Ophthalmic: Store at 2°C to 25°C Refer to manufacturer PIL if there are specific considerations.

Anthelmintic

1. Albendazole

Generic Name	Albendazole
Dosage form/strengths	Suspension 200mg/5ml, 2 gm/100ml Tablets 400mg
Route of administration	*Oral*
Pharmacologic category	Anthelmintic ATC: P02CA03
Indications	Treatment of cystic hydatid disease of the liver, lung, and peritoneum caused by the larval form of the dog tapeworm, E. granulosus. Treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, T. solium.
Dosage Regimen	**Dosing: Adult** **Hydatid disease (*Echinococcus granulosis*, dog tapeworm): Oral:** <60 kg: 15 mg/kg/day in 2 divided doses (maximum: 800 mg/day). ≥60 kg: 800 mg/day in 2 divided doses. Duration: Optimal duration uncertain; 1 to 6 months based on clinical factors **Neurocysticercosis (*Taenia solium*, pork tapeworm), parenchymal disease: Oral:** 15 mg/kg/day in 2 divided doses (maximum: 1.2 g/day) for 10 to 14 days; may be repeated if persistent viable lesions on 6-month follow-up imaging. **Note:** Concomitant therapy with praziquantel is recommended if >2 viable cysts present. Initiate adjunctive corticosteroid therapy prior to initiation of albendazole. **Dosing: Pediatric** **Hydatid disease (*E. granulosus*, dog tapeworm):** Children and Adolescents: Oral: 5 to 7.5 mg/kg/dose twice daily for 1 to 6 months; maximum dose: 400 mg/dose **Neurocysticercosis (*T. solium*, pork tapeworm), parenchymal disease:** Children and Adolescents: Oral: 7.5 mg/kg/dose twice daily for 8 to 30 days; maximum dose: 600 mg/dose. **Note:** Patients should receive concurrent corticosteroid for the first week of albendazole therapy and anticonvulsant therapy as required.
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed. **Dosing: Hepatic Impairment:** Consider discontinuing therapy if hepatic enzymes increase to twice the ULN while on therapy.
Contra-indications	Hypersensitivity to albendazole, benzimidazoles, or any component of the formulation
Adverse Drug Reactions	**>10%:** Central nervous system: Headache (neurocysticercosis: 11%; hydatid: 1%) Hepatic: Increased liver enzymes (hydatid: 16%; neurocysticercosis: <1%) **1% to 10%:** Central nervous system: Increased intracranial pressure, dizziness, vertigo, meningism Dermatologic: Alopecia Gastrointestinal: Abdominal pain, nausea and vomiting Miscellaneous: Fever

Monitoring Parameters	LFTs and CBC with differential at start of each 28-day cycle and every 2 weeks during therapy (more frequent monitoring for patients with liver disease); pregnancy test Patients with neurocysticercosis: Ophthalmic exam for retinal lesions prior to therapy initiation; MRI every 6 months after completing therapy until resolution of cystic lesion
Drug Interactions	***Risk C: Monitor therapy*** Carbamazepine Grapefruit Juice Phenobarbital Phenytoin Ritonavir
Pregnancy and Lactation	**Pregnancy Category** C Use during the first trimester of pregnancy is not recommended. albendazole is generally considered compatible with breastfeeding
Administration	**Administration: Oral** Administer with a high-fat meal if treating a systemic infection (to increase absorption). Administration on an empty stomach may be appropriate for treating an intraluminal infection with no systemic involvement. If patients have difficulty swallowing, tablets may be crushed or chewed, then swallowed with a drink of water. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Bone marrow suppression: rare; use with caution in patients with hepatic impairment (more susceptible to hematologic toxicity). Discontinue therapy in all patients who develop clinically significant decreases in blood cell counts. • Transaminase elevations: Reversible elevations in hepatic enzymes have been reported. Patients with abnormal LFTs and hepatic echinococcosis are at an increased risk of hepatotoxicity. ***Disease-related concerns:*** • Neurocysticercosis: Appropriate use: Antiparasitic therapy may worsen symptoms of neurocysticercosis by inducing an inflammatory response; adjunctive corticosteroid therapy should be started before initiation of albendazole. Antiparasitic therapy should not be initiated in patients with untreated hydrocephalus, calcified lesions, or cysticercal encephalitis. Perform funduscopic exam prior to initiation of antiparasitic therapy to exclude intraocular cysticerci; antiparasitic therapy may lead to blindness in some cases with unsuspected intraocular parasites.
Storage	Store between 20°C and 25°C Refer to manufacturer PIL if there are specific considerations.

2. Diethylcarbamazine

Generic Name	Diethylcarbamazine
Dosage form/strengths	Tablets: 50mg, 100 mg
Route of administration	Oral
Pharmacologic category	Anthelmintic ATC: P02CB02
Indications	**Loiasis:** Treatment and prophylaxis of loiasis **Lymphatic filariasis:** Treatment of lymphatic filariasis
Dosage Regimen	**Loiasis:** Oral: Treatment: *CDC recommendations:* 8 to 10 mg/kg/day in 3 divided doses for 21 days; **Note:** For patients with microfilaria in the blood, some clinicians recommend the following dose-escalating regimen: 50 mg as a single dose on day 1; 50 mg 3 times daily on day 2; 100 mg 3 times daily on day 3; 9 mg/kg/day in 3 divided doses on day 4 to end of treatment course. Repeat courses of treatment may be needed to achieve cure Prophylaxis: 300 mg once weekly; continue as long as exposure occurs. **Lymphatic filariasis:** Oral: ***Oral*:** 6 mg/kg/day for 1 **or** 12 days (14 to 21 days in patients with tropical pulmonary eosinophilia); daily dose may be given as a single dose or in 3 divided doses. **Note:** For patients with microfilaria in the blood, some clinicians recommend the following dose-escalating regimen: 50 mg as a single dose on day 1; 50 mg 3 times daily on day 2; 100 mg 3 times daily on day 3; 6 mg/kg/day in 3 divided doses on day 4 to end of treatment course **Dosing: Pediatric** **Loiasis:** Children and Adolescents: Oral: 8 to 10 mg/kg/day in 3 divided doses for 21 days; patients with symptomatic loiasis and microfilarial loads ≥8,000 microfilariae/mL should receive apheresis or treatment with albendazole prior to treatment with diethylcarbamazine. For patients with microfilaria in the blood, some clinicians recommend starting with a lower dosage (eg, 50 mg/day) with gradual increase over 3 days to 9 mg/kg/day in 3 divided doses on day 4 to end of treatment course. **Lymphatic filariasis:** Oral: *CDC recommendations:* Children ≥18 months and Adolescents: 6 mg/kg/day as a single dose **or** 6 mg/kg/day in 3 divided doses for 12 days (14 to 21 days in patients with tropical pulmonary eosinophilia). For patients with microfilaria in the blood, some clinicians recommend starting with a lower dosage (eg 50 mg/day) with gradual increase over 3 days to 6 mg/kg/day in 3 divided doses on day 4 to end of treatment course.
Dosage adjustment	**Dosing: Altered Kidney Function: Adult** Reduce dose in moderate to severe impairment (no specific adjustment is provided)
Contra-indications	Patients with onchocerciasis
Adverse Drug Reactions	**Frequency not defined:** Cardiovascular: Collapse, orthostatic hypotension, tachycardia Central nervous system: Brain disease, coma, dizziness, drowsiness, encephalitis (allergic), fatigue, headache, lethargy, malaise, meningoencephalitis (helminthic), vertigo

	Dermatologic: Dermatitis, Mazzotti reaction, pruritus, urticaria Endocrine & metabolic: Adenitis Gastrointestinal: Abdominal pain, decreased appetite, diarrhea, nausea, vomiting Genitourinary: Proteinuria (may be reversible) Hematologic & oncologic: Lymphadenitis, lymphangitis Local: Skin edema Neuromuscular & skeletal: Arthralgia, myalgia Ophthalmic: Conjunctivitis, corneal edema, eye disease (inflammatory and degenerative changes of optic nerve and retina with prolonged use), eye pain, increased intraocular pressure, iridocyclitis, lacrimation, optic neuritis, photophobia, punctate keratitis, visual field defect Respiratory: Asthma, respiratory distress Miscellaneous: Fever
Monitoring Parameters	Renal function at baseline and periodically during treatment; in patients with loiasis, measure microfilarial load prior to treatment; patients with microfilarial loads ≥8,000 microfilariae/mL treated with albendazole to reduce microfilarial load should have close, frequent monitoring of microfilarial load to confirm reduction before initiation of treatment with diethylcarbamazine
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	Use of diethylcarbamazine during pregnancy is not recommended It is not known if diethylcarbamazine is present in breast milk; breastfeeding is not recommended.
Administration	Oral: Administer after meals Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Encephalopathy: When treating loiasis, encephalopathy (sometimes fatal), and other severe neurologic adverse reactions may occur; the risk is related to the microfilarial load. Microfilarial load must be tested prior to treatment. Use caution if microfilarial load >2,500 microfilariae/mL; patients with microfilarial loads ≥8,000 microfilariae/mL should have the load reduced through apheresis or treatment with albendazole before initiation of treatment with diethylcarbamazine. Corticosteroid use and/or slow dose escalation has **not** been shown to decrease the risk of fatal encephalopathy. • Inflammatory reactions: Use in patients with onchocerciasis may precipitate Mazzotti reaction (pruritus, fever, arthralgia). Inflammatory response occurring in the cornea and retina can result in permanent visual damage. Use is contraindicated in patients with onchocerciasis; possibility of co-infection with onchocerciasis should be excluded prior to initiation of treatment with diethylcarbamazine • Skin reactions: In patients treated for loiasis, some symptoms of loiasis (eg, Calabar swelling, pruritus) may increase briefly during treatment; concomitant use of antihistamines and corticosteroids during the first week of treatment may decrease these symptoms. ***Disease-related concerns:*** • Cardiac disorders: Use with caution in patients with cardiac disorders. • Renal impairment: Use with caution; dosage reduction recommended. ***Other warnings/precaution:*** • Alkaline urine: Elimination half-life is prolonged and AUC is increased in alkaline urine; dose reductions may be needed in patients with diets that promote urinary alkalinization
Storage	Store at room temperature. Refer to manufacturer PIL if there are specific considerations.

3. Ivermectin

Generic Name	Ivermectin
Dosage form/strengths	Tablet 3mg, 6mg Topical Lotion 5mg/gm, 10mg/1gm Topical cream 10mg/1gm
Route of administration	*Oral, Topical*
Pharmacologic category	Anthelmintic ATC: D11AX22 (Dermatologic) P02CF01 (Oral)
Indications	**Systemic:** **Onchocerciasis:** Treatment of onchocerciasis due to the immature form of *Onchocerca volvulus*. **Strongyloidiasis, intestinal:** Treatment of intestinal (eg, nondisseminated) strongyloidiasis due to *Strongyloides stercoralis*. **Topical**: **Head lice** (*Pediculus capitis)* (Sklice lotion): Treatment of head lice infestations in patients 6 months and older. **Rosacea** (cream): Treatment of inflammatory lesions of rosacea in adult patients.
Dosage Regimen	**Dosing: Children ≥15 kg, Adolescents and Adult** **Onchocerciasis:** Oral: 150 mcg/kg as a single dose; retreatment may be required every 3 to 12 months until asymptomatic **Strongyloidiasis, intestinal:** Oral: 200 mcg/kg/day for 1 to 2 days. **Topical**: **Rosacea**: Apply once daily. **Head lice:** Single dose use only
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed **Dosing: Hepatic Impairment:** Although not extensively studied, ivermectin plasma concentrations can be expected to increase significantly in patients with hepatic disease.
Contra-indications	Hypersensitivity to ivermectin or any component of the formulation
Major Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** **CNS effects** **Hypersensitivity reactions (delayed)** **Immunologic post-treatment reaction (Mazzoti reaction)** **≥10%:** Miscellaneous: Mazzotti reaction (associated with onchocerciasis: pruritus: 28%; fever: 23%; skin edema, papular rash, pustular rash, and urticaria: ≤23%; arthralgia and synovitis: ≤9%; lymphadenitis [axillary node: 4% to 11%, cervical node: 1% to 5%, inguinal node: 13% to 14%, other lymph node: 2% to 3%]) **1% to 10%:** Cardiovascular: Orthostatic hypotension (1%), peripheral edema (3%), tachycardia (4%) Dermatologic: Pruritus (associated with strongyloidiasis: 3%)

	Gastrointestinal: Diarrhea (2%), nausea (2%) Hematologic & oncologic: Decreased white blood cell count (3%), eosinophilia (3%), increased hemoglobin (1%) Hepatic: Increased serum alanine aminotransferase (2%), increased serum aspartate aminotransferase (2%) Hypersensitivity: Facial edema (1%) Nervous system: Dizziness (3%) Ophthalmic: Inflammation of limbus of eyes (5%), punctate cataract (2%) **Topical:** **1% to 10%:** Central nervous system: Localized burning (≤1%) Dermatologic: Skin irritation (≤1%)
Monitoring Parameters	Skin and eye microfilarial count, periodic ophthalmologic exams; follow up stool examinations
Drug Interactions	• ***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine • ***Risk D: Consider therapy modification*** Sodium Picosulfate, Typhoid Vaccine
Pregnancy and Lactation	Pregnancy category C Although use in pregnancy is likely low risk, other agents are currently recommended for the treatment of pediculosis pubis or scabies in pregnant patient. Ivermectin is present in breast milk. Although use is likely low risk, other agents are currently recommended for the treatment of pediculosis pubis or scabies in patients who are breastfeeding
Administration	Administer on an empty stomach with water. Some experts recommend administering with food to increase absorption. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Ivermectin may cause an immunologic post-treatment reaction, also known as a **Mazzoti reaction**, which is associated with **pruritus**, **skin rash**, **fever**, **fatigue**, lymphadenopathy, **arthralgia**, **tachycardia**, **hypotension** (including **orthostatic hypotension**), edema, and **abdominal pain**. Most cases have been reported in association with the treatment of onchocerciasis, but cases have also been reported in association with the treatment of other infections (eg, scabies). Symptoms are mostly mild and usually resolve in 4 days; however, cases of coma and death have been reported, although these deaths are often attributed to *Loa loa*-associated encephalopathy. Serious Mazzoti reactions are estimated to occur in 19% to 81% of patients exposed to ivermectin for the treatment of filarial parasites, which is disproportionality more than other antinematodal drugs. *Onset:* Varied; within 1 to 7 days of therapy initiation ***Special populations:*** • Immunocompromised patients: Repeated treatment may be required in immunocompromised patients (eg, HIV); control of extraintestinal strongyloidiasis may necessitate suppressive (once monthly) therapy. ***Other warnings/precautions:*** • Appropriate use: *Onchocerca volvulus:* Ivermectin has no activity against adult *O. volvulus* parasites. **Warnings: Additional Pediatric Considerations**

	Avoid use or use with extreme caution in pediatric patients <2 years or <15 kg; due to a less developed blood-brain barrier compared to older pediatric patients and an increased risk for CNS effects (ie, encephalopathy); monitor patients closely.
Storage	Store at temperatures below 30°C. Refer to manufacturer PIL if there are specific considerations.

4. Levamisole

Generic Name	Levamisole
Dosage form/strengths	**Syrup**: 0.8% (40mg/5ml) **Tablet**: 40mg
Route of administration	*Oral*
Pharmacologic category	Anthelmintic ATC: P02CE01
Indications	Treatment of ascariasis and mixed ascariasis/hookworm infections
Dosage Regimen	**Dosage Range** Oral: Infants, Children, and Adults: *Weight-based dosing*: 2.5 mg/kg (maximum: 150 mg/dose) as a single dose. *Age-based dosing*: 1 month to <1 year: 40 mg as a single dose. 1 to 7 years: 80 mg as a single dose. >7 years: 150 mg as a single dose
Dosage adjustment	No data available
Contra-indications	Hypersenesitivity to any component of the formulation.
Adverse Drug Reactions	Hematologic: (sometimes fatal) agranulocytosis, Leukopenia, thrombocytopenia Cardiovascular: edema and chest pain Dermatologic: include dermatitis, alopecia, pruritus and urticaria Gastrointestinal: nausea, diarrhea, vomiting, stomatitis, anorexia, abdominal pain and constipation. Flatulence and dyspepsia. Musculoskeletal arthralgia and myalgia Nervous system: dizziness, headache, paresthesia, taste perversion, an altered sense of smell Psychiatric: somnolence, depression, nervousness, insomnia, and anxiety. Confusion, hallucinations, impaired concentration, nightmares, and an encephalopathy-like syndrome Ocular side effects including blurred vision conjunctivitis, Periorbital edema Hepatic: Hyperbilirubinemia and increased alkaline phosphatase Renal: Renal failure, elevated serum creatinine rarely. Other: vaginal bleeding, anaphylaxis, Fever, Flu-like symptoms including fatigue, fever, rigors, myalgia, and malaise
Monitoring Parameters	No data available
Drug Interactions	• Albendazole: The bioavailability of Albendazole can be increased when combined with Levamisole. • Ivermectin: The bioavailability of Ivermectin can be increased when combined with Levamisole.
Pregnancy and Lactation	Pregnancy category C WHO recommends against breastfeeding with maternal levamisole therapy.
Administration	Take on an empty stomach. Refer to manufacturer PIL if there are specific considerations. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	No data available

Storage	Store at room temperature and keep away from moisture and sunlight Refer to manufacturer PIL if there are specific considerations.

5. Mebendazole

Generic Name	Mebendazole
Dosage form/strengths	Oral suspension: 100mg/5ml Tablets: 100mg, 500mg
Route of administration	*Oral*
Pharmacologic category	Anthelmintic ATC: P02CA01
Indications	Intestinal nematode infection: Treatment of patients ≥2 years of age with GI infections.
Dosage Regimen	***Dosing: Adult, Adolescents and children > 2 years*** ***Ancylostoma duodenale* or *Necator americanus* (hookworm) or Ascariasis (roundworm):** Oral: 100 mg twice daily for 3 days **or** 500 mg as a single dose. Repeat in 3 weeks if not cured with initial treatment. **Trichuriasis (whipworm):** Oral: 100 mg twice daily for 3 days; repeat in 3 weeks if not cured with initial treatment. **Enterobiasis (pinworm):** Oral: 100 mg as a single dose; repeat in 2 weeks
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed **Dosing: Hepatic Impairment:** Mebendazole undergoes extensive hepatic metabolism; use with caution as systemic exposure may be increased.
Contra-indications	Hypersensitivity to mebendazole or any component of the formulation
Adverse Drug Reactions	Gastrointestinal: Abdominal pain, anorexia, diarrhea, flatulence, nausea, vomiting Hepatic: Hepatitis
Monitoring Parameters	Periodic hematologic, hepatic, and renal function; check for helminth ova in feces within 3-4 weeks following the initial therapy
Drug Interactions	***Risk X: Avoid combination*** Metronidazole (Systemic)
Pregnancy and Lactation	**pregnancy category** C Mebendazole is poorly excreted into breastmilk and poorly absorbed orally. Reports on the use of mebendazole during breastfeeding have found no adverse reactions in breastfed infants.
Administration	Administer with or without food. Tablets may be chewed, swallowed whole, or crushed and mixed with food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Bone marrow suppression: Neutropenia and agranulocytosis have been reported with high doses and prolonged use. Monitor CBC if used at higher doses or for a prolonged duration. ***Disease-related concerns:*** • Hepatic impairment: Use with caution; systemic exposure may be increased. ***Special populations:*** • Pediatric: Experience with use in children <2 years of age is limited; convulsions have been reported postmarketing in pediatric patients <1 year.
Storage	Store at 20°C to 25°C. Refer to manufacturer PIL if there are specific considerations.

6. Niclosamide

Generic Name	Niclosamide
Dosage form/strengths	Chewable Tablets 500mg
Route of administration	*Oral*
Pharmacologic category	Anthelmintic ATC: P02DA01
Indications	**Tapeworm infections:** Treatment of intestinal tapeworm infections caused by Taenia saginata (beef tapeworm), Taenia solium (pork tapeworm), Diphyllobothrium latum (fish tapeworm), and Hymenolepis nana (dwarf tapeworm)
Dosage Regimen	**Dosing: Adult** • *Taenia saginata (beef tapeworm), Taenia solium (pork tapeworm), Diphyllobothrium latum (fish tapeworm):* 2 g as a single dose. • *Hymenolepis nana (dwarf tapeworm):* Initial: 2 g as a single dose on day 1, followed by 1 g/day for 6 days. **Dosing: Pediatric** *Taenia saginata (beef tapeworm), Taenia solium (pork tapeworm), Diphyllobothrium latum (fish tapeworm):* Children <2 years: 500 mg as a single dose. Children 2 to 6 years: 1 g as a single dose. Children >6 years and Adolescents: 2 g as a single dose. *Hymenolepis nana (dwarf tapeworm):* Children <2 years: Initial: 500 mg as a single dose on day 1, followed by 250 mg/day for 6 days. Children 2 to 6 years: Initial: 1 g as a single dose on day 1, followed by 500 mg/day for 6 days. Children >6 years and Adolescents: Initial: 2 g as a single dose on day 1, followed by 1 g/day for 6 days.
Dosage adjustment	**Dosing: Renal Impairment: Adult** There are no dosage adjustments needed. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to niclosamide or any component of the formulation
Adverse Drug Reactions	Gastrointestinal: Abdominal pain, nausea, retching other: Hypersensitivity reaction
Monitoring Parameters	Stool cultures
Drug Interactions	Alcohol (Ethyl): Niclosamide may increase the absorption of Alcohol (Ethyl).
Pregnancy and Lactation	**pregnancy category** B The World Health Organization (WHO) classifies niclosamide as compatible with breastfeeding, although data on the use of niclosamide during lactation are limited. The safety of niclosamide in children has not been established, although niclosamide is not thought to be systemically absorbed.
Administration	Chew or crush tablets into a fine pulp and swallow with a little water or disintegrate tablet in a little water; administer dose after breakfast. A strong saline laxative may be administered 2

	hours after the daily dose to aid in worm elimination (strongly recommended for pork tapeworm infections). Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness (eg, operating machinery or driving). ***Disease-related concerns:*** • Constipation: Restore regular bowel movements in patients who are constipated prior to niclosamide treatment. ***Other warnings/precautions:*** • Appropriate use: A strong saline laxative may be administered 2 hours after the daily dose to aid in worm elimination. The laxative is strongly recommended for pork tapeworm (*Taenia solium*) infections to decrease the risk of cysticercosis by rapid excretion of lower tapeworm segments containing ripe eggs.
Storage	Store below 25°C Refer to manufacturer PIL if there are specific considerations.

7. Praziquantel

Generic Name	Praziquantel
Dosage form/strengths	Tablet 600mg Suspension 1.8gm/15ml
Route of administration	Oral
Pharmacologic category	Anthelmintic ATC: P02BA01
Indications	**Helminths:** Treatment of infections in patients ≥1 year caused by the following: All species of *Schistosoma* and the liver flukes *Clonorchis sinensis*/*Opisthorchis viverrini*
Dosage Regimen	**Dosing: Adult** **Clonorchiasis/opisthorchiasis:** Oral: 25 mg/kg/dose 3 times daily for 1 to 2 days. **Schistosomiasis: Note:** Repeat treatment may be needed in 2 to 4 weeks to increase effectiveness. – *S. haematobium*, *Schistosoma intercalatum*, or *S. mansoni*: Oral: 40 mg/kg/day as a single dose or in 2 divided doses for 1 day. – *S. japonicum* or *S. mekongi:* Oral: 60 mg/kg/day in 2 -3 divided doses for 1 day. **Dosing: Pediatric** **Flukes:** Clonorchiasis; Opisthorchiasis: Children and Adolescents: Oral: 25 mg/kg/dose 3 times daily at 4- to 6-hour intervals for 1 to 2 days **Schistosomiasis (Bilharziasis):** **Note:** Repeat treatment may be needed in 2 to 4 weeks to increase effectiveness Children and Adolescents: Oral: 20 mg/kg/dose2- 3 times daily for 1 day
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary. **Dosing: Hepatic Impairment: Adult** Total drug exposure in moderate-to-severe impairment is increased. use with caution.
Contra-indications	Hypersensitivity to praziquantel or any component of the formulation; ocular cysticercosis; concomitant administration with strong cytochrome P450 (CYP450) inducers, such as rifampin
Adverse Drug Reactions	**Frequency not defined** Central nervous system: Dizziness, headache, malaise Dermatologic: Urticaria Gastrointestinal: Abdominal distress, nausea Miscellaneous: Fever
Monitoring Parameters	Liver function tests; monitor patients with cardiac irregularities during treatment; monitor for seizures; culture urine or feces for ova prior to instituting therapy
Drug Interactions	***Risk X: Avoid combination*** Conivaptan Fexinidazole Fusidic Acid (Systemic) Rifampin ***Risk D: Consider therapy modification*** Barbiturates (phenobarbital) Carbamazepine Corticosteroids Phenytoin Rifampicin St John's wort
Pregnancy and	**Pregnancy class B**

Lactation	Use during breastfeeding is considered acceptable.
Administration	Oral: Administer tablets with water during meals Tablets should be promptly swallowed whole (do not chew) to avoid bitter taste that may cause gagging or vomiting; tablets are scored and may be halved or quartered. Tablets may be crushed or disintegrated and mixed with semi-solid food or liquid (eg, orange juice, honey) to reduce the bitter taste; use within 1 hour of mixing. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Disease-related concerns:*** • Cardiac arrhythmias: Bradycardia, ectopic rhythms, ventricular fibrillation, and AV blocks have been observed with praziquantel administration. • Central nervous system effects: Praziquantel may exacerbate central nervous system pathology due to schistosomiasis, paragonimiasis, or *Taenia solium* cysticercosis. Assess whether the potential benefit justifies the potential risk in patients with a history of seizures and/or other signs of potential central nervous system involvement such as subcutaneous nodules suggestive of cysticercosis. • Hepatic impairment: Use with caution in patients with moderate to severe hepatic impairment; reduced liver drug metabolism may result in higher and longer lasting plasma concentrations of unmetabolized praziquantel. • Neurocysticercosis: Appropriate use: Antiparasitic therapy may worsen symptoms of neurocysticercosis by inducing an inflammatory response; adjunctive corticosteroid therapy should be started before initiation of antiparasitic therapy. Antiparasitic therapy should not be initiated in patients with untreated hydrocephalus, calcified lesions, or cysticercal encephalitis. Perform funduscopic exam prior to initiation of antiparasitic therapy to exclude intraocular cysticerci; antiparasitic therapy may lead to blindness in some cases with unsuspected intraocular parasites. • Schistosomiasis: Praziquantel may not be effective against migrating schistosomulae; observational data indicate that praziquantel treatment in the acute phase of the infection may not prevent progression from asymptomatic to acute schistosomiasis, or from asymptomatic/acute disease to chronic disease. In addition, use in patients with schistosomiasis may be associated with clinical deterioration such as paradoxical reactions or serum sickness Jarisch-Herxheimer-like reactions, which is a sudden inflammatory immune response likely caused by the release of schistosomal antigens. Such reactions typically occur during the acute disease phase, and may lead to life-threatening events such as respiratory failure, encephalopathy, papilledema, and/or cerebral vasculitis. ***Concurrent drug therapy issues:*** • Drug/drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Therapeutic levels of praziquantel may not be achieved with concurrent administration of strong inducers of cytochrome P450 (eg, rifampin); concurrent use is contraindicated. ***Other warnings/precautions:*** • Patient information: Patients should be instructed to not drive or operate machinery on the day of treatment and the day after treatment.
Storage	Store below 30°C Refer to manufacturer PIL if there are specific considerations.

8. Pyrantel

Generic Name	Pyrantel
Dosage form/strengths	Oral Suspension: 250 mg/5ml
Route of administration	Oral
Pharmacologic category	Anthelmintic ATC: P02CC01
Indications	**Enterobiasis (pinworm):** Treatment of pinworms caused by *Enterobius vermicularis*
Dosage Regimen	**Dosing Adult and pediatrics:** **Enterobiasis (pinworm):** Oral: 11 mg/kg (maximum: 1 g/dose) as a single dose; repeat dose in 2 weeks to prevent reinfection. **Note:** It is recommended to treat the entire household to prevent reinfection
Dosage adjustment	**Dosing: Altered Kidney Function:** There are no dosage adjustments needed **Dosing: Hepatic Impairment:** Use with caution.
Contra-indications	Hypersensitivity to pyrantel or any component of the formulation
Adverse Drug Reactions	Central nervous system: Dizziness, headache Gastrointestinal: Abdominal cramps, diarrhea, nausea, vomiting
Monitoring Parameters	Stool for presence of eggs, worms, and occult blood
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	Pregnancy **category C**. No information is available on the use of pyrantel pamoate during breastfeeding. It is poorly absorbed orally, so excretion into breastmilk and absorption by the breastfed infant is unlikely.
Administration	**Administration: Oral** May be administered without regard to meals; may be taken with water, milk, or fruit juice. The use of a laxative is not required prior to, during, or after use. Suspension: Shake well before use. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Disease-related concerns:*** • Hepatic impairment: Use with caution in patients with hepatic impairment. ***Dosage form specific issues:*** • Benzyl alcohol and derivatives: Some dosage forms may contain sodium benzoate/benzoic acid;which is a metabolite of benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates. • Phenylalanine: Some products may contain phenylalanine. ***Other warnings/precautions:*** • Household contacts: Since pinworm infections are easily spread to others, treat all family members in close contact with the patient.
Storage	Store at 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.

9. Triclabendazole

Generic Name	Triclabendazole
Dosage form/strengths	Scored Tablets 250mg
Route of administration	Oral
Pharmacologic category	Anthelmintic ATC: P02BX04
Indications	**Fascioliasis:** Treatment of fascioliasis in patients ≥6 years of age
Dosage Regimen	**Fascioliasis dosing: Children ≥6 years, Adolescents and Adult** Oral: 10 mg/kg every 12 hours for 2 doses **Note:** Round dose up to the nearest half (125 mg) or whole tablet (250 mg).
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments have not been studied **Dosing: Hepatic Impairment:** There are no dosage adjustments have not been studied
Contra-indications	Hypersensitivity to triclabendazole, other benzimidazoles, or any component of formulation
Adverse Drug Reactions	**>10%:** Central nervous system: Headache (14%) Dermatologic: Hyperhidrosis (25%), urticaria (11%) Gastrointestinal: Abdominal pain (93%), decreased appetite (18%), nausea (18%) **1% to 10%:** Dermatologic: Pruritus (4%) Gastrointestinal: Diarrhea (7%), vomiting (7%) Hepatic: Increased serum bilirubin (7%), increased serum aspartate aminotransferase (5%), increased serum alkaline phosphatase (4%), increased serum alanine aminotransferase (3%) Neuromuscular & skeletal: Musculoskeletal chest pain (4%)
Monitoring Parameters	Monitor ECG in patients with a history of known or suspected QT prolongation or when used with concomitant QTc-prolonging drugs.
Drug Interactions	***Risk C: Monitor therapy*** Haloperidol QT-prolonging Agents (Highest Risk)
Pregnancy and Lactation	Adverse events were not observed in animal reproduction studies. Human data is limited. Lactation: Limited data. Because of protein binding of the drug and metabolites, exposure of the breastfed infant is likely to be low.
Administration	**Oral**: Administer with food and water; tablet may be swallowed whole, divided in half, or crushed and sprinkled over a small amount of applesauce; administer within 4 hours; round dose up to the nearest whole or half tablet. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hepatic toxicity: Transient increases in liver enzymes and total bilirubin have been reported in patients receiving triclabendazole. • QTc Prolongation: Transient QTc interval prolongation has been observed in animals; monitor ECG in patients with a history of known or suspected QTc prolongation or when used with concomitant QTc-prolonging drugs.
Storage	Store below 30°C in the original container. Refer to manufacturer PIL if there are specific considerations.

Antifungal

1. Amphotericin B

Generic Name	Amphotericin B
Dosage form/strengths	Vial 50 mg/15ml
Route of administration	IV
Pharmacologic category	Antifungal Agent, Parenteral ATC: J02AA01
Indications	**Fungal infection, invasive:** Treatment of patients with progressive, potentially life-threatening fungal infections **Leishmaniasis**
Dosage Regimen	**Adult**: • ***Test dose:*** *A test dose of 1 mg in 20 mL D5W administered over 20 to 30 minutes may be considered.* • ***Usual dosage range: IV:*** 0.5 to 1 mg/kg/day (range: 0.3 to 1.5 mg/kg/day); maximum dose: 1.5 mg/kg/day. **Note:** Lipid-based formulations of amphotericin B are generally preferred for treatment of systemic infections because they demonstrate comparable efficacy and better tolerability • *Duration of therapy* depends on the initial severity of the infection and the clinical response of the patient. In some infections, a satisfactory response is only obtained after several months of continuous treatment **Pediatrics**: Infants, Children, and Adolescents • **Test dose:** Infants, Children, and Adolescents: IV: 0.1 mg/kg/dose to a maximum of 1 mg; infuse over 20 to 60 minutes; • Initial test dose: 0.25-0.5 mg/kg/dose to a maximum of 1 mg; infuse over 20 to 60 minutes; gradually increase daily, usually in 0.25 mg/kg increments (except in critically ill patients) until the desired daily dose is reached (maximum daily dose: 1.5 mg/kg/day); • Maintenance dose: 0.25 to 1 mg/kg/dose once daily; doses up to 1.5 mg/kg/day may be used for rapidly progressing disease for short-term use; once therapy has been established; amphotericin B may be administered on an every-other-day basis at 1 to 1.5 mg/kg/dose in some cases
Dosage adjustment	**Dosing: Renal Impairment: Adult, Pediatric** **Altered kidney function: IV:** No dosage adjustment necessary for any degree of kidney impairment (only 2% to 5% excreted in biologically active form). However, a dosage interval of 24 to 36 hours has been recommended in patients with a GFR < 10 mL/min ***Nephrotoxicity during treatment:*** Consider switching to an alternative antifungal agent or a lipid-based amphotericin formulation Renal replacement therapy: Poorly dialyzed; no supplemental dose or dosage adjustment necessary, including patients on intermittent hemodialysis or CRRT. **Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to amphotericin or any component of the formulation

Adverse Drug Reactions	**Systemic: >10%** **Cardiovascular**: Hypotension **Central nervous system:** Chills, headache, malaise, pain **Endocrine & metabolic:** Hypokalemia, hypomagnesemia **Gastrointestinal**: Anorexia, diarrhea, epigastric pain, heartburn, nausea, vomiting **Hematologic & oncologic:** Anemia (normochromic-normocytic) **Local:** Pain at injection site (with or without phlebitis or thrombophlebitis [incidence may increase with peripheral infusion of admixtures]) **Renal:** Renal function abnormality (including azotemia, renal tubular acidosis, nephrocalcinosis [>0.1 mg/ml]), renal insufficiency **Respiratory:** Tachypnea **Miscellaneous:** Fever ***1% to 10%:*** **Cardiovascular**: Flushing, hypertension **Central nervous system**: Arachnoiditis, delirium, neuralgia (lumbar; especially with intrathecal therapy), paresthesia (especially with intrathecal therapy) **Genitourinary**: Urinary retention **Hematologic & oncologic**: Leukocytosis
Monitoring Parameters	BUN and serum creatinine levels should be determined every other day when therapy is increased and at least weekly thereafter. Renal function (monitor frequently during therapy), electrolytes (especially potassium and magnesium), LFTs, temperature, PT/PTT, CBC; fluid input and output; signs of hypokalemia (muscle weakness, cramping, drowsiness, ECG changes, etc); signs/symptoms of infusion-related reaction (fever, shaking chills, hypotension, anorexia, nausea, vomiting, headache, tachypnea)
Drug Interactions	***Risk X: Avoid combination*** Bromperidol Foscarnet Methoxyflurane Saccharomyces boulardii ***Risk D: Consider therapy modification:*** Amifostine, Arsenic Trioxide, Colistimethate, Obinutuzumab, Sodium Stibogluconate
Pregnancy and Lactation	Pregnancy Risk Factor: B It is not known if amphotericin is excreted into breast milk. Due to its poor oral absorption, systemic exposure to the nursing infant is expected to be decreased; however, because of the potential for toxicity, breast-feeding is not recommended.
Administration	**Administration: IV** May be infused over 2 to 6 hours; an inline filter (≥1 micron mean pore diameter) may be used for administration. To minimize infusion-related immediate reactions, premedicate with the following 30 to 60 minutes prior to drug administration: acetaminophen, diphenhydramine, and/or hydrocortisone. Preinfusion administration of 1 L of NS appears to reduce the risk of nephrotoxicity during treatment **Preparation for Administration:** IV: Add 10 mL of SWFI (without a bacteriostatic agent) to each vial of amphotericin B. Further dilute with 250 to 500 mL D_5W; final concentration should not exceed 0.1 mg/mL (peripheral infusion) or 0.25 mg/mL (central infusion). Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Anaphylaxis: Has been reported with amphotericin B-containing drugs; facilities for cardiopulmonary resuscitation should be available during administration due to the possibility of anaphylactic reaction. If severe respiratory distress occurs, the infusion should be immediately discontinued; during the initial dosing, the drug should be administered under close clinical observation.

	• Infusion reactions: Acute reactions (eg, fever, rigors, hypotension, anorexia, nausea, vomiting, headache, tachypnea) may occur 1 to 3 hours after starting an intravenous infusion. These reactions are usually more common with the first few doses and generally diminish with subsequent doses. Avoid rapid infusion to prevent hypotension, hypokalemia, arrhythmias, and shock. • Leukoencephalopathy: Has been reported following administration of amphotericin B. Total body irradiation has been reported to be a possible predisposition. • Nephrotoxicity: May cause nephrotoxicity; risk factors include underlying renal disease, concomitant nephrotoxic medications and daily and/or cumulative dosing of amphotericin. Avoid use with other nephrotoxic drugs; drug-induced renal toxicity usually improves with interrupting therapy, decreasing dosage, or increasing dosing interval. However permanent impairment may occur, especially in patients receiving a large cumulative dose (eg, >5 g) and in those also receiving other nephrotoxic drugs. Hydration and sodium repletion prior to administration may reduce the risk of developing nephrotoxicity. Frequent monitoring of renal function is recommended. ***Disease-related concerns:*** • Heart failure: In a scientific statement from the American Heart Association, amphotericin has been determined to be an agent that may cause direct myocardial toxicity (magnitude: moderate/major). • Renal impairment: Use with caution in patients with renal impairment. ***Special populations:*** • Patients with neutropenia: Pulmonary reactions may occur in patients with neutropenia receiving leukocyte transfusions; separation of the infusions as much as possible is advised. ***Other warnings/precautions:*** • Therapy interruption: If therapy is stopped for >7 days, restart at the lowest dose recommended and increase gradually.
Storage	• Store intact vials under refrigeration. Protect from light. • Reconstituted vials are stable, protected from light, for 24 hours at room temperature and 1 week when refrigerated. • Parenteral admixtures in D_5W should be used promptly after preparation and protected from light during administration. Refer to manufacturer PIL if there are specific considerations.

2. Anidulafungin

Generic Name	Anidulafungin
Dosage form/strengths	Vial 100mg
Route of administration	*IV*
Pharmacologic category	Antifungal Agent, Parenteral; Echinocandin ATC: J02AX06
Indications	**Candidemia, intra-abdominal or peritoneal candidiasis**: Treatment of candidemia and other forms of Candida infections (intra-abdominal abscess and peritonitis) in adults and pediatric patients ≥1 month of age. **Candidiasis, esophageal refractory disease:** Treatment of esophageal candidiasis in adults. Limitations of use: Dosage for the treatment of disseminated CNS or eye Candida infections has not been established. High relapse rates have occurred in patients treated for esophageal candidiasis.
Dosage Regimen	**Dosing: Adult** **Candidemia, intra-abdominal or peritoneal candidiasis:** **IV:** Initial dose: 200 mg on day 1; subsequent dosing: 100 mg once daily; treatment should continue until 14 days after last positive culture. **Candidiasis, esophageal (alternative agent):** **IV:** 200 mg daily; may transition to oral fluconazole therapy once oral intake tolerable. Transition to an oral antifungal once patient tolerates oral intake if susceptibility allows; total antifungal duration is 14 to 28 days
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary, including dialysis patients. **Dosing: Hepatic Impairment: Adult** No dosage adjustment necessary.
Contra-indications	Hypersensitivity to anidulafungin, other echinocandins, or any component of the formulation; known or suspected hereditary fructose intolerance.
Adverse Drug Reactions	**>10%:** Cardiovascular: Hypotension (15%), hypertension (12%), peripheral edema (11%) Central nervous system: Insomnia (15%) Endocrine & metabolic: Hypokalemia (≤25%), hypomagnesemia (12%) Gastrointestinal: Nausea (7% to 24%), diarrhea (9% to 18%), vomiting (7% to 18%) Genitourinary: Urinary tract infection (15%) Hepatic: Increased serum alkaline phosphatase (12%) Infection: Bacteremia (18%) Respiratory: Dyspnea (12%) Miscellaneous: Fever (9% to 18%) **2% to 10%:** Cardiovascular: Deep vein thrombosis (10%), chest pain (5%) Central nervous system: Confusion (8%), headache (8%), depression (6%) Dermatologic: Decubitus ulcer (5%) Endocrine & metabolic: Hypoglycemia (7%), dehydration (6%), hyperglycemia (6%), hyperkalemia (6%) Gastrointestinal: Constipation (8%), dyspepsia (7%), abdominal pain (6%), oral candidiasis (5%) Hematologic & oncologic: Anemia (8% to 9%), leukocytosis (5% to 8%), thrombocythemia (6%) Hepatic: Increased serum transaminases (≤5%)

	Infection: Sepsis (7%) Neuromuscular & skeletal: Back pain (5%) Renal: Increased serum creatinine (5%) Respiratory: Pleural effusion (10%), cough (7%), pneumonia (6%), respiratory distress (6%)
Monitoring Parameters	LFTs; anaphylaxis or infusion reactions (eg, bronchospasm, dyspnea, flushing, hypotension, pruritus, rash, urticaria).
Drug Interactions	Saccharomyces boulardii: Antifungal Agents (Systemic, Oral) may diminish the therapeutic effect of Saccharomyces boulardii. *Risk X: Avoid combination*
Pregnancy and Lactation	US FDA pregnancy category: Not assigned. Risk summary: Based on results from animal studies, this drug may cause fetal harm when used during pregnancy; no data available on use of this drug in pregnant women to inform a drug-related risk. It is not known if anidulafungin is present in breast milk. Use is not recommended unless the benefit outweighs the risk.
Administration	**Administration: IV** For IV use only; infusion rate should not exceed 1.1 mg/minute (1.4 mL/minute or 84 mL/hour). Do not concurrently infuse with other medications or electrolytes. **Preparation for Administration:** Parenteral: IV: Reconstitute vials using SWFI; reconstitute the 100 mg vial with 30 mL; concentration after reconstitution is 3.33 mg/mL. Further dilute in D5W or NS to a final concentration of 0.77 mg/mL.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Anaphylactic reactions: Immediate treatment for hypersensitivity reactions should be available. Discontinue treatment immediately if reactions occur. • Hepatic effects: Elevated LFTs, hepatitis, and hepatic failure have been reported; monitor for progressive hepatic impairment if increased transaminase enzymes noted. • Infusion reactions: Infusion reactions (eg, bronchospasm, dyspnea, flushing, hypotension, pruritus, rash, urticaria) may occur; do not exceed recommended rate of infusion. ***Special populations:*** • Obesity: Data suggest that clearance increases as a function of body weight. Based on data from another echinocandin, higher doses may be necessary in obese patients. ***Dosage form specific issues:*** • Fructose: Some dosage forms may contain fructose; may precipitate a metabolic crisis (eg, life-threatening hepatic failure, hypoglycemia, hypophosphatemia, lactic acidosis) in patients with hereditary fructose intolerance. Obtain history of hereditary fructose intolerance prior to therapy. • Polysorbate 80 (Tweens): Some dosage forms may contain Tweens. Hypersensitivity reactions, usually a delayed reaction, have been reported. Thrombocytopenia, ascites, pulmonary deterioration, and renal and hepatic failure have been reported in premature neonates after receiving parenteral products containing polysorbate 80.
Storage	• Store intact vials at 2°C to 8°C; excursions at 25°C are permitted for 96 hours and the vial may be returned to storage at 2°C to 8°C. Do not freeze. • The reconstituted solution can be stored for up to 24 hours at temperatures up to 25°C prior to dilution. • The infusion solution may be stored for up to 48 hours at temperatures up to 25°C prior to administration; do not freeze. • Refer to manufacturer PIL if there are specific considerations.

3. Caspofungin

Generic Name	Caspofungin
Dosage form/strengths	Vial 50mg, 70mg
Route of administration	*IV*
Pharmacological category	Antifungal Agent, Parenteral; Echinocandin ATC: J02AX04
Indications	**Aspergillosis, invasive:** Treatment of invasive aspergillosis in patients ≥3 months of age who are refractory to or intolerant of other therapies (eg, amphotericin B, lipid formulations of amphotericin B, itraconazole). Limitations of use: Has not been studied as initial therapy for invasive aspergillosis. **Candidemia and other *Candida* infections:** Treatment of candidemia and the following *Candida* infections in patients ≥3 months of age: Intra-abdominal abscesses, peritonitis, and pleural space infections. Limitations of use: Has not been studied in endocarditis, osteomyelitis, and meningitis due to *Candida*. **Candidiasis, esophageal:** Treatment of esophageal candidiasis in patients ≥3 months of age. Limitations of use: Not approved for the treatment of oropharyngeal candidiasis (OPC). **Neutropenic fever, empiric antifungal therapy:** Empiric therapy for presumed fungal infections in febrile, neutropenic patients ≥3 months of age.
Dosage Regimen	**Dosing: Adult** **Note:** Duration of caspofungin treatment should be determined by patient status and clinical response. **Aspergillosis, invasive (salvage therapy):** IV: Initial dose: 70 mg on day 1; subsequent dosing: 50 mg once daily. Duration of therapy should be a minimum of 6 to 12 weeks and depends on site of infection, extent of disease, and level/duration of immunosuppression. **Candidemia and other *Candida* infections:** IV: Initial dose: 70 mg on day 1; subsequent dosing: 50 mg once daily; generally, continue for at least 14 days after the last positive culture or longer if neutropenia warrants. Higher doses (150 mg once daily infused over ~2 hours) compared to the standard adult dosing regimen (50 mg once daily) have not demonstrated additional benefit or toxicity in patients with invasive candidiasis. **Note:** IDSA Candidiasis guidelines recommend transition to fluconazole (usually after 5 to 7 days in non-neutropenic patients) in clinically stable patients with fluconazole-susceptible isolates and negative repeat cultures. **Candidiasis, esophageal (alternative agent):** IV: 50 mg once daily; some experts favor a loading dose of 70 mg on day 1. May transition to oral fluconazole therapy once oral intake tolerable. In patients with fluconazole-refractory disease, continue caspofungin for 14 to 21 days. **Note:** Among patients with HIV, a higher relapse rate has been reported with echinocandins than with fluconazole **Fungal infections, empiric therapy (neutropenic patients):** IV: Initial dose: 70 mg on day 1; subsequent dosing: 50 mg once daily; continue until resolution of neutropenia; if fungal infection confirmed, continue for a minimum of 14 days (continue for at least 7 days after resolution of both neutropenia and clinical symptoms); if clinical response inadequate, may increase up to 70 mg once daily if tolerated
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary.

	Dosing: Hepatic Impairment: Adult Mild impairment (Child-Pugh class A): No dosage adjustment necessary. Severe and Moderate impairment (Child-Pugh class B, C): 70 mg on day 1 (where recommended), followed by 35 mg once daily; however, pharmacokinetic data suggest that this dose reduction may result in suboptimal drug exposure
Contra-indications	Hypersensitivity to caspofungin or any component of the formulation Documentation of allergenic cross-reactivity for echinocandin antifungals is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty
Adverse Drug Reactions	**>10%:** Cardiovascular: Hypotension, peripheral edema, tachycardia Central nervous system: Chills, headache Dermatologic: Skin rash Gastrointestinal: Diarrhea, vomiting, nausea Hematologic & oncologic: Decreased hemoglobin, decreased hematocrit, decreased white blood cell count, anemia Hepatic: Increased serum alkaline phosphatase, increased serum ALT, increased serum AST, increased serum bilirubin Local: Localized phlebitis Renal: Increased serum creatinine Respiratory: Respiratory failure, cough, pneumonia Miscellaneous: Infusion related reaction, fever, septic shock **1% to 10%:** Cardiovascular: Hypertension, atrial fibrillation, bradycardia, cardiac arrhythmia, edema, flushing, myocardial infarction Central nervous system: Anxiety, confusion, depression, dizziness, drowsiness, fatigue, insomnia, seizure Dermatologic: Erythema, pruritus, skin lesion, urticaria, decubitus ulcer Endocrine & metabolic: Hypomagnesemia, hyperglycemia, hypokalemia, hypercalcemia, hypervolemia Gastrointestinal: Abdominal pain, mucosal inflammation, abdominal distention, anorexia, constipation, decreased appetite, dyspepsia, upper abdominal pain Genitourinary: Urinary tract infection, nephrotoxicity Hematologic & oncologic: Blood coagulation disorder, febrile neutropenia, neutropenia, petechia, thrombocytopenia Hepatic: Decreased serum albumin, hepatic failure, hepatomegaly, hepatotoxicity, hyperbilirubinemia, jaundice Infection: Sepsis, bacteremia Local: Catheter infection, infusion site reaction (pain/pruritus/swelling) Neuromuscular & skeletal: Arthralgia, back pain, limb pain, tremor, weakness Renal: Hematuria, increased blood urea nitrogen, renal failure Respiratory: Dyspnea, pleural effusion, respiratory distress, rales, epistaxis, hypoxia, tachypnea
Monitoring Parameters	Liver function; anaphylaxis, skin rash, or histamine-related reactions (eg, facial swelling, bronchospasm, sensation of warmth)
Drug Interactions	***Risk X: Avoid combination*** Saccharomyces ***Risk D: Consider therapy modification*** Rifampin Cyclosporine

Pregnancy	**Pregnancy Category C** No information is available on the use of caspofungin during breastfeeding. Because caspofungin has poor oral bioavailability, it is unlikely to reach the milk and be absorbed by the infant.
Administration	**Parenteral: IV**: Administer by slow IV infusion over 1 hour (manufacturer); higher doses (eg, 150 mg) have been infused over ~2 hours. Do not administer by IV bolus **Preparation for Administration:** Bring intact vial to room temperature. Reconstitute vials using 10.8 mL NS for injection, SWFI, or bacteriostatic water for injection, resulting in a concentration of 5 mg/mL for the 50 mg vial, and 7 mg/mL for the 70 mg vial (vials contain overfill). Mix gently to dissolve until clear solution is formed; do not use if cloudy or contains particles. Solution should be further diluted with 0.9%, sodium chloride or LR (do not exceed final concentration of 0.5 mg/mL). Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • **Hepatic effects**: Increased transaminases and rare cases of clinically significant hepatic dysfunction (including failure and hepatitis) have been reported in pediatric and adult patients. Monitor liver function tests during therapy; if tests become abnormal or worsen, consider discontinuation. • **Hypersensitivity**: Anaphylaxis, other hypersensitivity reactions, histamine-related reactions have been reported. ***Disease-related concerns:*** • Hepatic impairment: Use with caution in patients with hepatic impairment. Dosage reduction may be necessary in adults with moderate impairment (Child-Pugh class B); safety and efficacy have not been established in children with any degree of hepatic impairment and adults with severe impairment (Child-Pugh class C).
Storage	• Store intact vials at 2°C to 8°C. • Reconstituted solution may be stored at ≤25°C for up to 1 hour prior to dilution. • Solutions diluted in NS, or LR for infusion should be used within 24 hours when stored at ≤25°C or within 48 hours when stored at 2°C to 8°C. • Refer to manufacturer PIL if there are specific considerations.

4. Flubendazole

Generic Name	Flubendazole
Dosage form/strengths	Tablets 100mg Oral suspension: 100mg/5ml
Route of administration	Oral
Pharmacologic category	Anthelmintics ATC: P02CA05
Indications	For treatment of enterobiasis For ascariasis, hookworm infections, and trichuriasis
Dosage Regimen	**in adults and children:** For the treatment of enterobiasis 100 mg is given as a single oral dose, repeated after 2 to 3 weeks. For ascariasis, hookworm infections, and trichuriasis 100 mg is given twice daily for 3 days.
Dosage adjustment	No information
Contra-indications	Pregnancy.
Adverse Drug Reactions	GI disturbances: nausea, abdominal pain and rumbling, soft/loose stools, and dyspepsia fatigue and breathlessness
Monitoring Parameters	Lactation. Monitor blood counts and liver function tests regularly during treatment.
Drug Interactions	Methotrexate The excretion of Methotrexate can be decreased when combined with Flubendazole.
Pregnancy and Lactation	Pregnancy category C No clear data about lactation safety
Administration	Oral Administration with food. Refer to manufacturer PIL if there are specific considerations.
Warnings/Precautions	If side effects are severe, flubendazole may have to be withdrawn.
Storage	store at temperature not exceeding 30°C Refer to manufacturer PIL if there are specific considerations.

5. Fluconazole

Generic Name	Fluconazole
Dosage form/strengths	Capsule 50mg, 150mg, 200mg Oral Syrup (or powder for oral suspension) 25mg/5ml, 50mg/5ml, 200mg/5ml Vial (2mg/ml) 50mg, 100mg, 200mg
Route of administration	*IV, Oral*
Pharmacologic category	Antifungal Agent, Azole Derivative ATC : J02AC01
Indications	Treatment of candidiasis (esophageal, oropharyngeal, peritoneal, urinary tract, vaginal); Systemic candida infections (eg, candidemia, disseminated candidiasis, pneumonia); Cryptococcal meningitis; antifungal prophylaxis in allogeneic hematopoietic cell transplant recipients
Dosage Regimen	**Dosing: Adult** **Conventional dose:** IV, Oral: 400 to 800 mg (6 to 12 mg/kg) once daily **Candidiasis, treatment** • *Urinary tract infection*: Oral: 200 to 400 mg (3 to 6 mg/kg) once daily • *Vaginal/Vulvovaginal*: Oral: 150 mg as a single dose or every 72 hours according to complications • *Oropharyngeal (moderate to severe)*: IV, Oral: Loading dose of 200 mg on day 1, then 100 to 200 mg once daily • *Oropharyngeal, chronic suppression for recurrent infection:* **Note:** Reserve for immunocompromised patients (eg, with HIV and low CD4 count). **Oral:** 100 mg once daily. May discontinue once immune reconstitution occurs • *Candidemia (neutropenic and non-neutropenic patients)*: Initial therapy (alternative agent): **Note:** For use in non-neutropenic patients that are not critically ill and not at high risk of fluconazole-resistant isolate. For use in neutropenic patients that are not critically ill and have had no prior azole exposure. **IV, Oral:** Loading dose of 800 mg (or 12 mg/kg) on day 1, then 400 mg (or 6 mg/kg) once daily; if fluconazole-susceptible *Candida glabrata* isolated, transition to 800 mg (or 12 mg/kg) once daily • *Esophageal, treatment:* **IV, Oral:** 400 mg (or 6 mg/kg) on day 1, then 200 to 400 mg (or 3 to 6 mg/kg) once daily for 14 to 21 days • *Intra-abdominal infection, acute, including peritonitis and/or abscess (alternative agent)*: **IV, Oral:** 800 mg (or 12 mg/kg) on day 1, then 400 mg (or 6 mg/kg) once daily. Total antifungal duration is ≥14 days based on source control and clinical response • *Osteoarticular (osteomyelitis or septic arthritis) (fluconazole-susceptible isolates)*: Initial or step-down therapy: **IV, Oral:** 400 mg (or 6 mg/kg) once daily. Duration for osteomyelitis is 6 to 12 months and for septic arthritis is 6 weeks. • *Peritonitis, associated with peritoneal dialysis*: **Note:** Use for empiric treatment if no prior azole exposure or for directed therapy against fluconazole-susceptible isolates: **IV, Oral:** 200 mg on day 1, then 100 to 200 mg once daily for 2 to 4 weeks ***Tinea:*** Oral: 150 to 300 mg once weekly

	Cryptococcal meningitis: Note: Treatment involves induction, consolidation, and maintenance phases of therapy. Induction (alternative regimens): **Oral:** 800 mg once daily in combination with amphotericin B for 2 weeks Consolidation: **Oral:** 400 to 800 mg once daily for 8 weeks (800 mg once daily preferred for patients who receive a 2-week induction course) Maintenance (suppression): **Oral:** 200 to 400 mg once daily for 6 to 12 months **Dosing: Pediatric** **General dosing, susceptible infection:** Infants, Children, and Adolescents: IV, Oral: Initial: 6 to 12 mg/kg/dose, followed by 3 to 12 mg/kg/dose once daily; duration and dosage depends on severity of infection; Limiting dose to 600 mg/dose.
Dosage adjustment	**Dosing: Renal Impairment:** No adjustment for vaginal candidiasis single-dose therapy. For multiple dosing: administer 100% of the loading/initial dose, then adjust daily doses as follows: IV, Oral: CrCl >50 mL/minute: No dosage adjustment necessary. CrCl ≤50 mL/minute: Reduce maintenance dose by 50%. CrCl less than 10 mL/minute/1.73 m^2: for pediatrics, administer usual loading dose, then reduce maintenance dose by 50% and administer every 48 hours. **Hemodialysis, intermittent (thrice weekly):** IV, Oral: only administer maintenance doses 3 times/week (on dialysis days) after the hemodialysis session; while in pediatrics approximately 50% after a 3-hour session. **Peritoneal dialysis:** IV, Oral: Initial: reduce maintenance doses by 50%. Administer 50% of recommended dose every 48 hours in pediatrics **Dosing: Hepatic Impairment:** There are no dosage adjustments needed; use with caution **Dosing: Obesity: Adult** **body weight dosing:** a loading dose of 12 mg/kg, followed by a maintenance dose of 6 mg/kg
Contra-indications	Hypersensitivity to fluconazole or any component of the formulation coadministration of terfenadine in adult patients receiving multiple doses of 400 mg or higher or with CYP3A4 substrates which may lead to QTc prolongation (eg, astemizole, cisapride, erythromycin, pimozide, or quinidine)
Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** Cardiovascular effects Dermatologic reactions Hepatotoxicity **>10%:** Central nervous system: Headache **1% to 10%:** Central nervous system: Dizziness Dermatologic: Skin rash Gastrointestinal: Nausea, abdominal pain, vomiting, diarrhea, dysgeusia, dyspepsia Frequency not defined: Hepatic: Fulminant hepatitis, hepatitis, increased serum alkaline phosphatase, increased serum aspartate aminotransferase, increased serum transaminases, jaundice
Monitoring Parameters	Periodic liver function tests (AST, ALT, alkaline phosphatase) and renal function tests, potassium

Drug Interactions	• **Risk X: Avoid combination** Aprepitant Astemizole Asunaprevir Bosentan Bosutinib Budesonide (Topical) Cisapride Domperidone Erythromycin Fedratinib Fexinidazole Flibanserin Fosaprepitant Ivabradine Lemborexant Lomitapide Lumateperone Mizolastine Ospemifene Pimozide Quinidine Saccharomyces Boulardii Simeprevir Siponimod Ulipristal Voriconazole • **Risk D: Consider therapy modification** Acalabrutinib Alfentanil Alitretinoin (Systemic) Alprazolam Amiodarone Avanafil Avapritinib Avatrombopag Brigatinib Bromocriptine Budesonide (Systemic) Cilostazol Citalopram Clopidogrel Cobimetinib Colchicine Deflazacort Dronedarone Eliglustat Encorafenib Eplerenone Erdafitinib Fentanyl Fexinidazole Fluvastatin Guanfacine Ibrutinib Ivacaftor Ivosidenib Lorlatinib Lurasidone Lurbinectedin Methadone Midazolam Mobocertinib Naloxegol Olaparib Parecoxib Pemigatinib Pexidartinib QT-Prolonging Class IA Antiarrhythmics QT-Prolonging Class III Antiarrhythmics QT-Prolonging Kinase Inhibitors QT-Prolonging Miscellaneous Agents Ranolazine Rifampin Rimegepant Ruxolitinib (Systemic) Selpercatinib Selumetinib Sirolimus Sonidegib Suvorexant Tacrolimus (Systemic) Tazemetostat Terfenadine Tezacaftor And Ivacaftor Tipranavir Tofacitinib Tolvaptan Triazolam Ubrogepant Vardenafil Venetoclax Vitamin K Antagonists (Eg, Warfarin) Voclosporin Voxelotor Zanubrutinib
Pregnancy	**pregnancy category D** WHO recommendations state that fluconazole is considered compatible with breastfeeding when used in usual recommended doses.
Administration	**Administration: IV** Do not use if cloudy or precipitated. Infuse over ~1 to 2 hours; do not exceed 200 mg/hour **Administration: Oral** May be administered without regard to meals. Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hazardous agent (NIOSH 2016 [group 3]). • Arrhythmias: Cases of QTc prolongation and torsade de pointes associated with fluconazole use have been reported (usually high dose or in combination with agents known to prolong the QT interval); use caution in patients with concomitant medications or conditions which are arrhythmogenic. • CNS effects: May occasionally cause dizziness or seizures; use caution driving or operating machinery. • Hepatotoxicity: Serious (and sometimes fatal) hepatic toxicity (eg, hepatitis, cholestasis, fulminant hepatic failure) has been observed. Monitor patients who develop abnormal liver function tests for the development of more severe hepatic injury; discontinue fluconazole if signs and symptoms consistent with liver disease develop. • Hypersensitivity reactions: Anaphylaxis has been reported rarely; use with caution in patients with hypersensitivity to other azoles. • Skin reactions: Rare exfoliative skin disorders have been observed; fatal outcomes have been reported in patients with serious concomitant diseases. ***Disease-related concerns:*** • Hepatic impairment: Use with caution in patients with preexisting hepatic impairment; monitor liver function closely and discontinue if symptoms consistent with liver disease develop. • Renal impairment: Use with caution in patients with renal impairment; dosage adjustment may be necessary. ***Dosage form specific issues:*** • Sucrose: Oral suspension contains sucrose; avoid use in patients with fructose intolerance,

	glucose-galactose malabsorption, or sucrase-isomaltase insufficiency.
Storage	• Tablet, Powder for oral suspension: Store at <30°C. • Following reconstitution, store at 5°C to 30°C. Discard unused portion after 2 weeks. Don't freeze. • Injection: Store injection in glass at 5°C to 30°C. • Store injection in plastic flexible containers with overwrap at 20°C to 25°C. Do not freeze. Do not unwrap unit until ready for use. • Refer to manufacturer PIL if there are specific considerations.

6. Griseofulvin

Generic Name	Griseofulvin
Dosage form/strengths	**Oral Suspension** 125mg/5ml **Tablets** 125mg **Topical Suspension** 2.5gm/100ml
Route of administration	Oral, Topical
Pharmacologic category	Antifungal Agent ATC (oral): D01BA01 ATC (Systemic): D01AA08
Indications	**Dermatophyte infections:** Treatment of the following dermatophyte infections of the skin, hair, and nails not adequately treated by topical therapy: inea corporis, tinea pedis, tinea cruris, tinea barbae, tinea capitis, tinea unguium (onychomycosis) Limitations of use: Use for the prophylaxis of fungal infections has not been established; not effective for the treatment of tinea versicolor.
Dosage Regimen	**Dosing: Adult** **Dermatophyte infections:** Oral: ***Microsize:*** 500 mg/day in single or divided doses; for more widespread lesions initial doses of 750 to 1,000 mg/day in single or divided doses may be needed; may decrease gradually to 500 mg/day or less if patient responds to higher dose. ***Ultramicrosize:*** 375 mg daily in single or divided doses; doses up to 750 mg/day in divided doses have been used for infections more difficult to eradicate such as tinea unguium and tinea pedis *Duration of therapy depends on the site of infection* Dosage and duration of treatment should be individualized according to the requirements and response of the patient **Dosing: Pediatric** **General dosing; susceptible infection**: Children >2 years and Adolescents: Microsize: Oral: 20 to 25 mg/kg/day in single or 2 divided doses; maximum daily dose: 1,000 mg/day Ultramicrosize: Oral: 10 to 15 mg/kg/day once daily; maximum daily dose: 750 mg/day
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed **Dosing: Hepatic Impairment:** Use is contraindicated in hepatic failure.
Contra-indications	Hypersensitivity to griseofulvin or any component of the formulation; hepatic failure; porphyria; pregnancy
Adverse Drug Reactions	**Frequency not defined** Central nervous system: Confusion, dizziness, fatigue, headache, insomnia Dermatologic: Dermatological reaction (erythema multiforme-like drug reaction), skin photosensitivity, skin rash (most common), urticaria (most common) Gastrointestinal: Diarrhea, epigastric distress, gastrointestinal hemorrhage, nausea, oral candidiasis, vomiting

	Genitourinary: Nephrosis Hematologic & oncologic: Granulocytopenia Hepatic: Hepatotoxicity
Monitoring Parameters	Periodic renal, hepatic, and hematopoietic function tests especially with long-term use
Drug Interactions	***Risk X: Avoid combination*** Progestins (Contraceptive), Ulipristal ***Risk D: Consider therapy modification*** Estrogen Derivatives (Contraceptive) ***Risk C: Monitor therapy*** Alcohol, Barbiturates (Except: Methohexital; Thiopental), Carbocisteine, Cyclosporine, Verteporfin, Vitamin K Antagonists (eg, Warfarin)
Pregnancy and Lactation	**Pregnancy Risk Factor X** It is not known if griseofulvin is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, breastfeeding is not recommended.
Administration	**Administration:** Oral: • Oral suspension, tablets: Administer with a fatty meal (eg, whole milk, ice cream, peanut butter) to increase absorption; shake suspension well before use. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hematologic effects: Leukopenia has been reported (rare); discontinue therapy if granulocytopenia occurs. • Hepatic effects: May cause jaundice and elevated liver function tests or bilirubin (may be serious or even fatal); monitor hepatic function and discontinue therapy if necessary. • Penicillin allergy: Hypersensitivity cross reaction between penicillins and griseofulvin is possible, however, known penicillin-sensitive patients have been treated successfully without complications. • Photosensitivity: Avoid exposure to intense sunlight to prevent photosensitivity reactions. • Skin reactions: Severe skin reactions (eg, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme) have been reported (may be serious or even fatal); discontinue use if severe skin reactions occur. ***Disease-related concerns:*** • Lupus erythematosus: Development of lupus erythematosus, lupus-like syndromes or exacerbation of existing lupus erythematosus has been reported. ***Other warnings/precautions:*** • Appropriate use: Use for the prophylaxis of fungal infections has not been established; not effective for the treatment of tinea versicolor
Storage	Store at 20°C to 25°C. Protect from light. Refer to manufacturer PIL if there are specific considerations.

7. Itraconazole

Generic Name	Itraconazole
Dosage form/ strengths	Capsules 100mg, Syrup 10mg/ml
Route of administration	Oral
Pharmacologic category	Antifungal Agent, Azole Derivative ATC: J02AC02
Indications	**Aspergillosis (100 mg capsules):** Treatment of pulmonary and extrapulmonary aspergillosis in immunocompromised and nonimmunocompromised patients who are intolerant of or refractory to amphotericin B therapy. **Blastomycosis (100 mg capsules):** Treatment of pulmonary and extrapulmonary blastomycosis in immunocompromised and nonimmunocompromised patients. **Candidiasis, esophageal and oropharyngeal (oral solution):** Treatment of oropharyngeal and esophageal candidiasis. **Histoplasmosis (100 mg capsules):** Treatment of histoplasmosis, including chronic cavitary pulmonary disease and disseminated, nonmeningeal histoplasmosis in immunocompromised and nonimmunocompromised patients. **Onychomycosis:** Capsules (100 mg): Treatment of onychomycosis of the toenail, with or without fingernail involvement, and onychomycosis of the fingernail caused by dermatophytes (tinea unguium) in nonimmunocompromised patients.
Dosage Regimen	**Note: Formulations:** Due to differences in bioavailability, itraconazole formulations are not interchangeable. Generally, the oral solution is preferred because of improved absorption. **Therapeutic drug monitoring:** For most indications, adjust dose based on trough serum concentration to ensure efficacy and avoid toxicity. Timing and frequency of concentration monitoring is individualized. **Safety:** Use with caution in patients with heart failure with reduced ejection fraction; discontinue itraconazole if signs or symptoms of heart failure occur **Adults** **General Adult Dosage** **Aspergillosis: Oral:** Solution or capsule (100 mg): 200 mg twice daily **Duration:** Minimum of 6 to 12 weeks, depending on degree/duration of immunosuppression, disease site, and response to therapy **Blastomycosis:** **Note:** For initial treatment of mild to moderate disease or step-down therapy after amphotericin B for more severe infection **Oral:** Solution or capsule (100 mg): Loading dose: 200 mg 3 times daily for 3 days. Maintenance dose: Mild to moderate disease in immunocompetent patients: 200 mg once to twice daily. Moderately severe to severe disease and immunocompromised patients: 200 mg twice daily. CNS infection (alternative agent): 200 mg 2 to 3 times daily **Candidiasis:** **Note:** Generally reserved for fluconazole-refractory disease or as an alternative initial agent. Capsule formulation is not recommended.

	Oral: Solution: 200 mg once daily **Histoplasmosis:** *Treatment, initial therapy for mild to moderate disease or step-down therapy after amphotericin B for more severe infection:* **Oral:** Solution or capsule (100 mg): Loading dose: 200 mg 3 times daily for 3 days. Maintenance dose: Mild to moderate disease in immunocompetent patients: 200 mg once to twice daily. Moderately severe to severe or disseminated disease and immunocompromised patients: 200 mg twice daily. CNS infection: 200 mg 2 to 3 times daily. **Onychomycosis:** **Note:** Other agents are preferred for dermatophyte onychomycosis. **Oral:** Capsule or tablet: *Continuous dosing:* 200 mg once daily for 6 weeks or 12 weeks. *Pulsed dosing:* 200 mg twice daily for 1 week; repeat every 4 weeks for 2 months or 3 months **Dosing: Pediatric** **General dosing, susceptible infection:** Limited data available: Infants, Children, and Adolescents: Oral: 5 mg/kg/dose every 12 hours for treatment; usual maximum daily dose: 200 mg/day; some infections may require up to 400 mg/day
Dosage adjustment	**Dosing: Renal Impairment:** Use with caution in patients with renal impairment; dosage adjustment may be needed. Limited data available. **Dosing: Hepatic Impairment:** Use caution and monitor closely for signs/symptoms of toxicity.
Contra-indications	**Hypersensitivity to itraconazole** or any component of the formulation; **treatment of onychomycosis** (or other non-life-threatening indications) in patients with evidence of ventricular dysfunction, such as congestive heart failure (CHF) or a history of CHF; treatment of onychomycosis in women who are pregnant or contemplating pregnancy
Adverse Drug Reactions	**>10%:** Gastrointestinal: Diarrhea, nausea **1% to 10%:** Cardiovascular: Edema, chest pain, hypertension, Central nervous system: Headache, dizziness, anxiety, depression, fatigue, pain, malaise, abnormal dreams Dermatologic: Skin rash, pruritus, diaphoresis Endocrine & metabolic: Hypertriglyceridemia, hypokalemia Gastrointestinal: Vomiting, abdominal pain, dyspepsia, flatulence, gastrointestinal disease, gingivitis, aphthous stomatitis, constipation, gastritis, gastroenteritis, increased appetite Respiratory: Rhinitis, upper respiratory tract infection, sinusitis Miscellaneous: Fever
Monitoring Parameters	Obtain liver function tests in patients with preexisting disease and in all patients on prolonged therapy (>1 month). Obtain renal function tests and serum concentrations (when clinically indicated). Assess other medicines patient may be taking; alternate therapy or dosage adjustments may be needed. Assess for signs and symptoms of heart or liver toxicity
Drug Interactions	***Risk X: Avoid combination*** Acalabrutinib Alfuzosin Aliskiren Alprazolam Aprepitant Astemizole Asunaprevir Avanafil Avapritinib Barnidipine Bilastine Blonanserin Bosutinib Budesonide (Topical) Cisapride Clobetasone Cobimetinib Conivaptan CYP3A4 Inducers Dabrafenib Dapoxetine Dihydroergotamine Disopyramide Dofetilide Domperidone Dronedarone Efavirenz Elagolix,

	Estradiol, And Norethindrone Eletriptan Eplerenone Ergoloid Mesylates Ergonovine Ergotamine Estazolam Everolimus Felodipine Flibanserin Fluticasone Fosaprepitant Fusidic Acid (Systemic) Halofantrine Ibrutinib Irinotecan Products Savuconazonium Sulfate Ivabradine Lefamulin Lemborexant Lercanidipine Lomitapide Lovastatin Lumateperone Lurbinectedin Macitentan Methadone Methylergonovine Midazolam Mizolastine Naloxegol Netupitant Nimodipine Nisoldipine Pazopanib Piperaquine Quinidine Radotinib Ranolazine Rimegepant Rivaroxaban Rupatadine Salmeterol Silodosin Simeprevir Simvastatin Sonidegib Suvorexant Tamsulosin Tazemetostat Telithromycin Temsirolimus Terfenadine Ticagrelor Tolvaptan Topotecan Trabectedin Triazolam Ubrogepant Udenafil Ulipristal Vincristine Vinflunine Vorapaxar ***Risk D: Consider therapy modification*** Abemaciclib Ado-Trastuzumab Emtansine Afatinib Alfentanil Alitretinoin (Systemic) Almotriptan Amiodarone Antacids Apixaban Aripiprazole Aripiprazole Lauroxil Atogepant Atorvastatin Avacopan Axitinib Bedaquiline Berotralstat Betrixaban Brexpiprazole Brigatinib Bromocriptine Budesonide (Oral Inhalation) (Systemic) Buspirone Cabazitaxel Cabozantinib Cardiac Glycosides Cariprazine Ceritinib Cilostazol Cobicistat Colchicine Copanlisib Crizotinib Cyclosporine Dabrafenib Daclatasvir Darifenacin Darunavir Dasatinib Deflazacort Delamanid Didanosine Docetaxel Duvelisib Edoxaban Elagolix Elbasvir And Grazoprevir Elexacaftor, Tezacaftor, And Ivacaftor Eliglustat Encorafenib Entrectinib Erdafitinib Erlotinib Eszopiclone Fedratinib Fentanyl Fesoterodine Fexinidazole Fluticasone (Oral Inhalation) Fosamprenavir Gilteritinib Glasdegib Guanfacine Halofantrine Histamine H2 Receptor Antagonists Ibrexafungerp Idelalisib Iloperidone Indinavir Ppis And Pcabs Istradefylline Ivacaftor Ixabepilone Lapatinib Larotrectinib Lopinavir Lorlatinib Manidipine Maraviroc Midostaurin Mifepristone Mirodenafil Nifedipine Nilotinib Olaparib Osilodrostat Palbociclib Panobinostat Pemigatinib Pexidartinib Pimavanserin Ponatinib Pralsetinib Quetiapine Relugolix Ribociclib Riociguat Ritonavir Rivaroxaban Ruxolitinib Saquinavir Saxagliptin Selpercatinib Selumetinib Sildenafil Sirolimus Solifenacin Sufentanil Sunitinib Tacrolimus (Systemic) Tadalafil Talazoparib Temsirolimus Tezacaftor And Ivacaftor Thiotepa Tipranavir Tofacitinib Tolterodine Toremifene Trazodone Triamcinolone (Systemic) Valbenazine Vardenafil Vemurafenib Venetoclax Vilazodone Vincristine Voxelotor Zanubrutinib Zopiclone
Pregnancy and Lactation	**Pregnancy Category C** Itraconazole is present in breast milk. No information is available on the clinical use of itraconazole during breastfeeding. Until more data become available, an alternate drug may be preferred, especially while nursing a newborn or preterm infant**.**
Administration	• Oral bioavailability varies depending on whether the drug is administered as capsules or the oral solution; these preparations should *not* be used interchangeably. Do not administer with antacids. • Only the oral solution (not capsules) is indicated for treatment of oropharyngeal or esophageal candidiasis. • The capsules absorption is best if taken with food; therefore, it is best to administer itraconazole after meals at the same time each day. Capsules should be swallowed whole. • The oral solution should be administered *without* food to ensure maximal absorption of the drug • Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks that require mental alertness (eg, operating machinery, driving) • Hearing loss: Transient or permanent hearing loss has been reported. Quinidine (a contraindicated drug) was used concurrently in several of these cases. Hearing loss usually

	resolves after discontinuation, but may persist in some patients. • Heart failure: [US Boxed Warning]: Itraconazole can cause or exacerbate heart failure (HF). Negative inotropic effects have been observed following intravenous administration. Use with caution in patients with risk factors for HF (COPD, renal failure, edematous disorders, ischemic or valvular disease). If signs or symptoms of HF occur or worsen during administration of itraconazole, discontinue use or reassess the risk-benefit of continuing treatment. • Hepatotoxicity: Rare cases of serious hepatotoxicity (including liver failure and death) have been reported (including some cases occurring within the first week of therapy • Hypersensitivity: Hypersensitivity reactions have been reported; discontinue use and institute appropriate supportive care if a hypersensitivity reaction occurs. Use with caution in patients with a history of hypersensitivity to other azoles. • Neuropathy: Cases of peripheral neuropathy have occurred in patients on long-term itraconazole. Monitor for and discontinue if signs or symptoms of neuropathy occur during treatment. ***Disease-related concerns:*** • Cystic fibrosis: Large differences in itraconazole pharmacokinetic parameters have been observed in cystic fibrosis patients receiving the oral solution; if a patient with cystic fibrosis does not respond to therapy, alternate therapies should be considered. • Hepatic impairment: Use with caution in patients with hepatic impairment; monitor liver function closely. Not recommended for use in patients with active liver disease, elevated liver enzymes, or prior hepatotoxic reactions to other drugs unless the expected benefit exceeds the risk of hepatotoxicity. • Renal impairment: Use with caution in patients with renal impairment; limited information is available; dosage adjustment may be needed. ***Concurrent drug therapy issues:*** • High potential for interactions: Life-threatening cardiac dysrhythmias and/or sudden death have occurred in patients taking CYP 3A inhibitors such as cisapride, pimozide, methadone or quinidine. [US Boxed Warning]: Coadministration with itraconazole can cause elevated plasma concentrations of certain drugs and can lead to QT prolongation and ventricular tachyarrhythmias, including torsades de pointes. Coadministration with methadone, disopyramide, dofetilide, dronedarone, quinidine, isavuconazole, ergot alkaloids, irinotecan, lurasidone, oral midazolam, pimozide, triazolam, felodipine, nisoldipine, ivabradine, ranolazine, eplerenone, cisapride, naloxegol, lomitapide, lovastatin, simvastatin, avanafil, ticagrelor and, in subjects with varying degrees of renal or hepatic impairment, colchicine, fesoterodine, and solifenacin is contraindicated. Coadministration with eliglustat is contraindicated in poor or intermediate metabolizers of CYP2D6 and in patients taking strong or moderate CYP2D6 inhibitors. ***Other warnings/precautions:*** • Appropriate use: Itraconazole should NOT be used for voriconazole-refractory aspergillosis because the same antifungal and/or resistance mechanism(s) may be shared by both agents.
Storage	• Capsule: Store at room temperature of 15°C to 25°C. Protect from light and moisture. • Oral solution: Store at ≤25°C; do not freeze. • Refer to manufacturer PIL if there are specific considerations.

8. Ketoconazole

Generic Name	Ketoconazole
Dosage form/strengths	Oral tablets 200 mg Topical Cream/ointment: 2 gm/100g
Route of administration	Oral
Pharmacologic category	Antifungal Agent, Imidazole Derivative ATC (topical): D01AC08 ATC (systemic): J02AB02
Indications	**Fungal infections (systemic):** Treatment of susceptible systemic fungal infections, including blastomycosis, histoplasmosis, paracoccidioidomycosis, coccidioidomycosis, and chromomycosis in patients who have failed or who are intolerant to other antifungal therapies
Dosage Regimen	**Dosing: Adult** **Fungal infections (systemic): Oral:** 200 mg once daily; may increase to 400 mg once daily if response is insufficient. Continue until active fungal infection is resolved; some infections may require a treatment duration of up to 6 months. **Dosing: Pediatric** **Fungal infections (systemic):** Children ≥2 years and Adolescents: Oral: 3.3 to 6.6 mg/kg/day once daily; maximum daily dose: 400 mg/day; duration of therapy variable based on pathogen, patient, and disease-specific factors.
Dosage adjustment	**Dosing: Renal Impairment:** Mild to severe impairment: No dosage adjustment. Hemodialysis: Minimally dialyzable: No dosage adjustment necessary **Dosing: Hepatic Impairment:** Use is contraindicated in acute or chronic liver disease. **Hepatotoxicity during treatment:** If ALT >ULN or 30% above baseline (or if patient is symptomatic), interrupt therapy and obtain full hepatic function panel. Upon normalization of liver function, may consider resuming therapy if benefit outweighs risk (hepatotoxicity has been reported on rechallenge).
Contra-indications	Hypersensitivity to ketoconazole or any component of the formulation; acute or chronic liver disease; coadministration with alprazolam, cisapride, colchicine, disopyramide, dofetilide, dronedarone, eplerenone, ergot alkaloids (eg, dihydroergotamine, ergometrine, ergotamine, methylergometrine), felodipine, HMG-CoA reductase inhibitors (eg, lovastatin, simvastatin), irinotecan, lurasidone, methadone, oral midazolam, nisoldipine, pimozide, quinidine, ranolazine, tolvaptan, triazolam
Adverse Drug Reactions	**Frequency not defined.** Cardiovascular: Orthostatic hypotension, peripheral edema Central nervous system: Fatigue, insomnia, malaise, nervousness, paresthesia Dermatologic: Pruritus (2%), alopecia, dermatitis, erythema, erythema multiforme, skin rash, urticaria, xeroderma Endocrine & metabolic: Hot flash, hyperlipidemia, menstrual disease Gastrointestinal: Nausea (3%), vomiting (3%), abdominal pain (1%), anorexia, constipation, dysgeusia, dyspepsia, flatulence, increased appetite, tongue discoloration, upper abdominal pain, xerostomia Hematologic & oncologic: Decreased platelet count Hepatic: Jaundice

	Hypersensitivity: Anaphylactoid reaction Neuromuscular & skeletal: Myalgia, weakness Respiratory: Epistaxis Miscellaneous: Alcohol intolerance
Monitoring Parameters	Hepatic function tests (baseline and frequently during therapy), including weekly ALT for the duration of treatment; Canadian labeling recommends monitoring hepatic function at baseline, at weeks 2 and 4, and monthly thereafter; calcium and phosphorous (periodically with long-term use); adrenal function as clinically necessary
Drug Interactions	***Risk X: Avoid combination*** Abametapir Abemaciclib Acalabrutinib Alfuzosin Alprazolam Aprepitant Astemizole Asunaprevir Avanafil Avapritinib Barnidipine Bilastine Blonanserin Bosutinib Budesonide (Topical) Cisapride Cobimetinib Conivaptan Dapoxetine Disopyramide Dofetilide Doxorubicin Dronedarone Elbasvir And Grazoprevir Elagolix, Estradiol, And Norethindrone Eletriptan Eplerenone Ergot Derivatives Estazolam Everolimus Felodipine Fexinidazole Flibanserin Fluticasone (Nasal) Fosaprepitant Fusidic Acid (Systemic) Ibrutinib Infigratinib Irinotecan Products Isavuconazonium Sulfate Ivabradine Ivosidenib Lemborexant Lercanidipine Lomitapide Lonafarnib Lovastatin Lumateperone Lurasidone Lurbinectedin Macitentan Mefloquine Methadone Midazolam Mizolastine Mobocertinib Naloxegol Neratinib Nevirapine Nimodipine Nisoldipine Pazopanib Pimozide Quinidine Radotinib Ranolazine Regorafenib Rimegepant Rivaroxaban Rupatadine Ruxolitinib (Topical) Saccharomyces Boulardii Salmeterol Silodosin Simeprevir Simvastatin Sirolimus Sonidegib Suvorexant Tamsulosin Tazemetostat Telithromycin Tepotinib Terfenadine Ticagrelor Tolvaptan Trabectedin Triazolam Ubrogepant Udenafil Vincristine (Liposomal) Vinflunine Voclosporin Vorapaxar ***Risk D: Consider therapy modification*** Ado-Trastuzumab Emtansine Afatinib Alcohol (Ethyl) Alfentanil Alitretinoin (Systemic) Almotriptan Amiodarone Antacids Antihepaciviral Combination Products Apixaban Aripiprazole Aripiprazole Lauroxil Atogepant Avacopan Axitinib Bedaquiline Berotralstat Betrixaban Brexpiprazole Brigatinib Bromocriptine Budesonide (Oral Inhalation) Budesonide (Systemic) Buspirone Cabazitaxel Cabozantinib Carbocisteine Cariprazine Ceritinib Cilostazol Cobicistat Colchicine Copanlisib Crizotinib Cyclosporine CYP3A4 Inducers Dabigatran Etexilate Dabrafenib Daclatasvir Darifenacin Darunavir Dasatinib Deflazacort Delamanid Didanosine Docetaxel Duvelisib Edoxaban Efavirenz Elagolix Elexacaftor, Tezacaftor, And Ivacaftor Eliglustat Encorafenib Entrectinib Erdafitinib Erlotinib Eszopiclone Fedratinib Fentanyl Fesoterodine Fluticasone (Oral Inhalation) Fosamprenavir Gilteritinib Glasdegib Guanfacine Halofantrine Histamine H2 Receptor Antagonists Hyoscyamine Ibrexafungerp Idelalisib Iloperidone Indinavir Inhibitors Of The Proton Pump (Ppis And Pcabs) Istradefylline Ivacaftor Ixabepilone Lapatinib Larotrectinib Levomilnacipran Lopinavir Lorlatinib Lumacaftor And Ivacaftor Manidipine Maraviroc Midostaurin Mifepristone Mirodenafil Nifedipine Nilotinib Olaparib Osilodrostat Palbociclib Panobinostat Pemigatinib Pexidartinib Piflufolastat F18 Pimavanserin Ponatinib Pralsetinib Quetiapine Relugolix Relugolix, Estradiol, And Norethindrone Ribociclib Rifabutin Riociguat Ritonavir Ruxolitinib (Systemic) Saquinavir Saxagliptin Selpercatinib Selumetinib Sildenafil Sirolimus Solifenacin Sufentanil Sunitinib Tacrolimus Tadalafil Temsirolimus Tezacaftor And Ivacaftor Tipranavir Tofacitinib Tolterodine Toremifene Trazodone Triamcinolone Valbenazine Vardenafil Vemurafenib Venetoclax Vilazodone Vincristine Voxelotor Zanubrutinib Zopiclone
Pregnancy and Lactation	Due to the teratogenicity reported in animal reproduction studies and its antiandrogenic effects, ketoconazole is not recommended for the treatment of systemic fungal infections in pregnant women. Systemically: Breastfeeding is not recommended.

	Tpically: Use is generally considered acceptable; caution is recommended. a decision should be made to discontinue breastfeeding or discontinue the drug, taking into account the importance of the drug to the mother.
Administration	Administer oral tablets 2 hours prior to antacids to prevent decreased absorption due to the high pH of gastric contents. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Adrenal suppression: High doses of ketoconazole may depress adrenocortical function; returns to baseline upon discontinuation of therapy. Recommended maximum dosing should not be exceeded. Monitor adrenal function as clinically necessary, particularly in patients with adrenal insufficiency and in patients under prolonged stress (eg, intensive care, major surgery). • Bone fragility: In animal studies, increased long bone fragility with cases of fracture has been observed with high-dose ketoconazole. Careful dose selection may be advisable for patients susceptible to bone fragility (eg, postmenopausal women, elderly). • Hypersensitivity reactions: Cases of hypersensitivity reactions (including rare cases of anaphylaxis) have been reported; some reactions occurred after the initial dose. • Myopathy: Coadministration with HMG-CoA reductase inhibitors (eg, lovastatin, simvastatin) may increase the risk of myopathy. Concomitant use is contraindicated. • Sedation: Coadministration with midazolam, triazolam, and alprazolam may result in elevated plasma concentrations of the benzodiazepines, leading to prolonged hypnotic and sedative effects. Concomitant use is contraindicated. ***Disease-related concerns:*** • ***Achlorhydria:*** Absorption is reduced in patients with achlorhydria; administer with acidic liquids (eg, soda pop). Avoid concomitant use of drugs that decrease gastric acidity (eg, proton pump inhibitors, antacids, H_2-blockers). • ***CNS infections:*** Ketoconazole has poor penetration into cerebral-spinal fluid and should not be used to treat fungal meningitis. • ***Hepatic impairment: [US Boxed Warning]:*** Ketoconazole has been associated with hepatotoxicity, including fatal cases and cases requiring liver transplantation; some patients had no apparent risk factors for hepatic disease. Patients should be advised of the hepatotoxicity risks and monitored closely. Toxicity was observed after a median duration of therapy of ~4 weeks, but has also been noted after as little as 3 days; may occur when patients receive high doses for short durations or low doses for long durations. Cases have been reported in patients treated with ketoconazole for onychomycosis, cutaneous dermatophyte infections, or Candida infections. Use with caution in patients with preexisting hepatic impairment, those on prolonged therapy and/or taking other hepatotoxic drugs concurrently. Hepatic dysfunction is typically (but not always) reversible upon discontinuation. Obtain liver function tests at baseline and frequently throughout therapy; serum ALT should be monitored weekly throughout therapy. Discontinue therapy for elevated hepatic enzymes that persist or worsen or if accompanied by signs/symptoms (eg, jaundice, nausea/vomiting, dark urine) of hepatic injury. • ***Prostate cancer:*** In European clinical trials of men with metastatic prostate cancer, fatalities were reported in a small number of study participants within 14 days of initiating high-dose ketoconazole (1,200 mg daily); a causal effect has not been established. Concurrent drug therapy issues: • ***QT prolongation: [US Boxed Warning]:*** Concomitant use with cisapride, disopyramide, dofetilide, dronedarone, methadone, pimozide, quinidine, and ranolazine is contraindicated due to the possible occurrence of life-threatening ventricular arrhythmias such as torsade de pointes. ***Other warnings/precautions:***

	• ***Appropriate use: [US Boxed Warning]:*** Ketoconazole tablets are not indicated for the treatment of onychomycosis, cutaneous dermatophyte infections, or Candida infections. Use only when other effective antifungal therapy is unavailable or not tolerated and the benefits of ketoconazole treatment are considered to outweigh the risks. Ketoconazole oral tablets are only approved to treat systemic fungal infections.
Storage	Store at 20°C to 25°C Refer to manufacturer PIL if there are specific considerations.

9. Micafungin

Generic Name	Micafungin
Dosage form/strengths	Powder for Solution for I.V Infusion: 50mg
Route of administration	I.V infusion
Pharmacologic category	Antifungal Agent, Parenteral; Echinocandin ATC: J02AX05
Indications	-Treatment of candidemia, acute disseminated candidiasis, and Candida peritonitis and abscesses in adults and pediatric patients ≥4 months of age or in pediatric patients ≤4 months of age without meningoencephalitis and/or ocular dissemination -Treatment of esophageal candidiasis in adults and pediatric patients ≥4 months of age. -Prophylaxis against invasive fungal infections (hematopoietic cell transplant recipients): Prophylaxis of Candida infections in adults and pediatric patients ≥4 months of age undergoing hematopoietic cell transplantation
Dosage Regimen	**-Adult:** **1-Candidiasis:** **-Candidemia (neutropenic and nonneutropenic patients), including disseminated candidiasis:** IV: 100 mg once daily for ≥14 days. Discontinued after first negative blood culture and continues until signs/symptoms of candidemia and neutropenia, if present, have resolved **2-Esophageal, refractory disease (alternative agent):** **-Intra-abdominal infection (eg, peritonitis, abdominal abscess):** IV: 100 mg once daily for ≥14 days and continues until source control and clinical resolution. **3-Prophylaxis against invasive fungal infections:** **-Hematologic malignancy or hematopoietic cell transplant (alternative agent):** IV: 50 to 100 mg once daily. Duration is at least until resolution of neutropenia and varies based on degree and duration of immunosuppression **-Pediatric:** **1-Aspergillosis, treatment, invasive (salvage therapy):** Infants, Children, and Adolescents: -≤40 kg: IV: 2 to 3 mg/kg/dose once daily; higher doses of 4 to 6 mg/kg/dose once daily have also been described ->40 kg: IV: 100 mg/dose once daily; may increase to 150 mg/dose if clinically indicated; maximum daily dose: 150 mg/day **2-Candidiasis, esophageal (alternative agent in patients who cannot tolerate oral therapy):** **-Non-HIV-exposed/-infected:** -Infants ≥4 months, Children, and Adolescents: -≤30 kg: IV: 3 mg/kg/dose once daily. ->30 kg: IV: 2.5 mg/kg/dose once daily; maximum dose: 150 mg/dose. **-HIV-exposed/-infected:** -Children 2 to 8 years and ≤40 kg: IV: 3 to 4 mg/kg/dose once daily. -Children ≥9 years: -≤40 kg: IV: 2 to 3 mg/kg/dose once daily. ->40 kg: IV: 100 mg/dose once daily. -Adolescents: IV: 150 mg/dose once daily.

	3-Candidiasis, systemic (including candidemia and invasive candidiasis): -Infants <4 months: IV: 10 mg/kg/dose once daily -Infants ≥4 months, Children, and Adolescents: IV: Initial: 2 mg/kg/dose once daily; usual maximum dose: 100 mg/dose **4-Empiric antifungal therapy (neutropenic fever):** -Infants ≥4 months, Children, and Adolescents: IV: 2 to 3 mg/kg/dose once daily; maximum dose: 200 mg/dose **5-Fungal infection, prophylaxis in hematopoietic stem cell transplant (HSCT) recipients:** -Infants <4 months: Limited data available: IV: 2 mg/kg/dose once daily -Infants ≥4 months, Children, and Adolescents: IV: 1 mg/kg/dose once daily; maximum dose: 50 mg/dose
Dosage adjustment	**-Renal Impairment:** -No dosage adjustment necessary for any degree of kidney dysfunction **-Hepatic impairment:** -No dosage adjustment necessary.
Contra-indications	-Hypersensitivity to micafungin, other echinocandins, or any component of the formulation
Adverse Drug Reactions	If used in Candidiasis treatment: **>10%:** -Cardiovascular: Phlebitis (19%) -Gastrointestinal: Diarrhea (7% to 11%), vomiting (7% to 18%) -Hematologic & oncologic: Anemia (infants, children, and adolescents: 18%) -Hepatic: Abnormal hepatic function tests (4%; infants, children, and adolescents: <15%), hyperbilirubinemia (infants, children, and adolescents: <15%) -Renal: Renal failure syndrome (infants, children, and adolescents: <15%) -Miscellaneous: Fever (9% to 13%) **1 – 10%:** -Cardiovascular: Atrial fibrillation (adults: 3%), tachycardia (infants, children, & adolescents: 4%) -Dermatologic: Skin rash (2% to 5%) -Endocrine & metabolic: Abnormal aspartate transaminase (3%), hyperkalemia (adults: 5%), hypoglycemia (adults: 6%) -Gastrointestinal: Abdominal distention (infants, children, and adolescents: 2%), abdominal pain (infants, children, and adolescents: 4%), nausea (7% to 10%) -Hematologic & oncologic: Neutropenia (infants, children, and adolescents: 5%), thrombocytopenia (infants, children, and adolescents: 9%) -Hepatic: Increased serum alkaline phosphatase (3% to 6%) -Nervous system: Headache (adults: 9%) **Candidiasis prophylaxis in hematopoietic stem cell transplantation:** **>10%:** Cardiovascular: Tachycardia (16% to 26%) Dermatologic: Pruritus (infants, children, and adolescents: 33%), skin rash (25% to 30%), urticaria (<5%; infants, children, and adolescents: 19%) Gastrointestinal: Abdominal distention (infants, children, and adolescents: 19%), abdominal pain (26% to 35%), diarrhea (77%; infants, children, and adolescents: 51%), nausea (70% to 71%), vomiting (65% to 66%) Genitourinary: Decreased urine output (infants, children, and adolescents: 23%), hematuria (infants, children, and adolescents: 23%) Hematologic & oncologic: Anemia (infants, children, and adolescents: 51%), febrile neutropenia (infants, children, and adolescents: 16%), neutropenia (75% to 77%), thrombocytopenia (72% to 75%)

	Hepatic: Abnormal hepatic function tests (infants, children, and adolescents: <15%), hyperbilirubinemia (infants, children, and adolescents: <15%), increased serum alanine aminotransferase (16%) Nervous system: Anxiety (22% to 23%), headache (adults: 44%), insomnia (adults: 37%) Renal: Renal failure syndrome (infants, children, and adolescents: <15%) Miscellaneous: Fever (infants, children, and adolescents: 61%), infusion-related reaction (infants, children, and adolescents: 16%)
Monitoring Parameters	-Periodic liver function tests -Serum creatinine, BUN -CBC -Infusion reactions including rash, pruritus, facial swelling, and vasodilatation
Drug Interactions	***Risk X: Avoid combination*** Saccharomyces boulardii
Pregnancy and Lactation	Pregnancy Category C **Caution is recommended during lactation**. No information is available on the use of micafungin during breastfeeding. Because micafungin is >99% bound to plasma proteins and has poor oral bioavailability, it is unlikely to reach the milk and be absorbed by the infant.
Administration	-Aseptically add 5 mL of NS (preservative free) or D5W to each 50 or 100 mg vial. To minimize foaming, gently swirl to dissolve; do not shake. Further dilute 50 to 150 mg in 100 mL NS or D5W. Protect infusion solution from light (it is not necessary to protect the drip chamber or tubing from light). -Administer as I.V Infusion over 1 hour; may reduce infusion rate for infusion reaction (eg, rash, pruritus, facial swelling, vasodilatation). Flush line with NS prior to administration. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	-Use with caution in patients that develop worsening renal function during treatment and monitor closely. -Data suggest that micafungin clearance increases as a function of weight; higher doses may be necessary in patients with obesity
Storage	-Store at 25°C; excursions permitted to 15°C to 30°C. -Reconstituted and diluted solutions in D5W or NS are stable for 24 hours at room temperature. Protect infusion solution from light (it is not necessary to protect the drip chamber or tubing from light). Refer to manufacturer PIL if there are specific considerations.

10. Nystatin

Generic Name	Nystatin
Dosage form/ strengths	Oral drops (suspension): 100000IU/ml Cream 10MIU Vaginal suppository 100000IU
Route of administration	Oral Topical
Pharmacologic action	Antifungal Agent, Oral Nonabsorbed/Partially Absorbed ATC (oral): A07AA02 ATC (Topical): D01AA01 ATC (Vaginal): G01AA01
Indications	Oral: Treatment of susceptible cutaneous, mucocutaneous, and oral cavity fungal infections normally caused by the *Candida* species Topical: Fungal infections (cutaneous and mucocutaneous): Treatment of cutaneous and mucocutaneous fungal infections caused by *Candida albicans* and other susceptible *Candida* species.
Dosage Regimen	**Dosing: Adult** **Intestinal infections:** Oral tablets: 500,000-1,000,000 units every 8 hours **Oral candidiasis, mild disease (alternative agent):** Suspension (swish and swallow): 400,000-600,000 units 4 times/day; swish in the mouth and retain for as long as possible (several minutes) before swallowing **Cream, ointment**: Apply to the affected areas twice daily or as indicated until healing is complete **Dosing: Pediatric** **Oral candidiasis:** Oral suspension: Children and Adolescents: Oral: 400,000 to 600,000 units 4 times daily; administer half of dose to each side of mouth; swish and retain in the mouth for as long as possible before swallowing. **Peritonitis (Peritoneal dialysis), prophylaxis for high risk situations (eg, during antibiotic therapy or PEG placement):** Oral Suspension: Infants, Children, and Adolescents: 10,000 units/kg once daily **Topical: Mucocutaneous candidal infections:** Infants, Children, and Adolescents: Manufacturer's labeling: Cream/ointment: Topical: Apply to affected area twice daily
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to nystatin or any component of the formulation
Adverse Drug Reactions	**Oral: 1% to 10%:** Gastrointestinal: Diarrhea, nausea, stomach pain, vomiting **Topical**: Frequency not defined: Dermatologic: Contact dermatitis, Stevens-Johnson syndrome
Monitoring Parameters	Determine that cause of infection is fungal. Avoid skin contact when applying.

Drug Interactions	**Oral**: Saccharomyces boulardii: Antifungal Agents (Systemic, Oral) may diminish the therapeutic effect of Saccharomyces boulardii. *Risk X: Avoid combination* **Topical**: Progesterone: Antifungal Agents (Vaginal) may diminish the therapeutic effect of Progesterone. Risk X: Avoid combination
Pregnancy and Lactation	**Pregnancy Risk Factor C** Excretion into breast milk is not known; however, absorption following oral use is poor.
Administration	**Oral**: Suspension: Shake well before using. Should be swished about the mouth and retained in the mouth for as long as possible (several minutes) before swallowing. **Topical**: For topical external use only; not for systemic, oral, intravaginal, or ophthalmic use. Apply liberally to clean/dry skin. For fungal infection of the feet, the powder should be dusted in all footwear Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity: May occur; immediately discontinue if signs of a hypersensitivity reaction occur. • Irritation: Discontinue if irritation occurs.
Storage	• Suspension: Store at controlled room temperature of 15°C to 25°C • Cream: Store at room temperature. • Refer to manufacturer PIL if there are specific considerations.

11. Voriconazole

Generic Name	Voriconazole
Dosage form/strengths	Tablets 50mg, 200mg Vial 200mg Oral suspension 40mg
Route of administration	Oral, IV
Pharmacologic category	Antifungal Agent, Azole Derivative; ATC: J02AC03
Indications	**Treatment of fungal infections in patients ≥2 years of age**: Treatment of invasive aspergillosis; treatment of esophageal candidiasis; treatment of candidemia (in non-neutropenic patients); treatment of disseminated Candida infections of the skin and abdomen, kidney, bladder wall, and wounds; treatment of serious fungal infections caused by Scedosporium apiospermum and Fusarium spp. (including Fusarium solani) in patients intolerant of, or refractory to, other therapy
Dosage Regimen	**Dosing: Adult** **Aspergillosis, invasive, including disseminated and extrapulmonary infection; treatment:** IV: Initial: 6 mg/kg every 12 hours for 2 doses Maintenance dose: 4 mg/kg every 12 hours Oral: 200 to 300 mg twice daily **or** weight-based dosing (3 to 4 mg/kg twice daily) **Candidiasis, treatment:** *Candidemia (neutropenic and non-neutropenic patients), including disseminated candidiasis (alternative agent):* Initial therapy: **IV:** 400 mg twice daily for 2 doses, then 200 to 300 mg IV or orally twice daily **or** weight-based dosing (6 mg/kg IV twice daily for 2 doses, then 3 to 4 mg/kg IV or orally twice daily) Step-down therapy (for clinically stable patients who have responded to initial therapy with negative repeat cultures) **Oral:** 200 mg twice daily; for susceptible isolates of *Candida glabrata*, use 200 to 300 mg twice daily **or** weight-based dosing (3 to 4 mg/kg twice daily) Duration: Treat for ≥14 days **after** first negative blood culture and resolution of signs/symptoms; continue until resolution of neutropenia, **Fusariosis (alternative agent):** *Invasive:* **IV**: 6 mg/kg twice daily for 2 doses, then 4 mg/kg twice daily **Oral**, following improvement with initial IV therapy: 200 mg twice daily. Duration: Often prolonged and depends on site of infection, severity, immune status, and response to therapy **Scedosporiosis:** **IV:** 6 mg/kg twice daily for 2 doses, then 4 mg/kg twice daily. **Oral:** 400 mg twice daily for 2 doses, then 200 to 300 mg twice daily. Duration: Often prolonged and varies based on clinical response and patient immune status **Dosing: Pediatric** **Note:** In pediatric patients <12 years, bioequivalence between the oral tablet and suspension has not been determined; due to possible shortened gastric transit time in infants and children, absorption of tablets may be different than adults; dosing recommendations for infants and children are based on studies with the oral suspension. Data suggests higher doses (mg/kg) than adults are required in patients <15 years and weighing <50 kg.

	General dosing, susceptible infection: Note: Dosage adjustment may be required if patient does not have adequate response, cannot tolerate dose, or adequate trough concentrations are not achieved; monitor trough concentrations closely. **Children 2 to <12 years**: **Note:** Monitor serum concentrations to maintain trough concentrations of 2 to 6 mcg/mL. Loading dose: IV: 9 mg/kg/dose every 12 hours for 2 doses on day 1. Maintenance: IV: 8 mg/kg/dose every 12 hours. Oral: Oral suspension: 9 mg/kg/dose every 12 hours; maximum dose: 350 mg/dose; **Note:** In most patients, oral therapy is not recommended as initial therapy for treatment; it is recommended to convert from parenteral to oral therapy only after significant clinical improvement has been observed. **Children ≥12 years and Adolescents ≤14 years**: **Note:** In this age group, body weight is more important than age in predicting pharmacokinetics. IV: <50 kg: Loading dose: 9 mg/kg/dose every 12 hours for 2 doses; followed by maintenance dose of 4 to 8 mg/kg/dose every 12 hours. ≥50 kg: Loading dose: 6 mg/kg/dose every 12 hours for 2 doses; followed by maintenance dose of 3 to 4 mg/kg/dose every 12 hours. Oral: <50 kg: 9 mg/kg/dose every 12 hours; maximum dose: 350 mg/dose. ≥50 kg: 200 mg every 12 hours. **Adolescents ≥15 years:** IV: Loading dose: 6 mg/kg/dose every 12 hours for 2 doses; followed by a maintenance dose of 3 to 4 mg/kg/dose every 12 hours. Oral: <40 kg: 100 mg every 12 hours. ≥40 kg: 200 mg every 12 hours.
Dosage adjustment	**Dosing: Renal Impairment: Adult** **Oral:** Mild to severe impairment: No dosage adjustment necessary **IV:** CrCl ≥50 mL/minute: There are no dosage adjustments needed. CrCl <50 mL/minute: There are no specific dosage adjustments necessary while it is recommended to use oral voriconazole in these patients unless an assessment of the benefit: risk justifies the use of IV voriconazole; if IV therapy is used, closely monitor serum creatinine and change to oral voriconazole when possible. IV therapy has been used in select patients with CrCl <50 mL/minute using varying doses (median duration of treatment 7 to 10 days). **Dosing: Hepatic Impairment: Adult & Pediatrics** Mild to moderate impairment (Child-Pugh class A or B): Following standard loading dose, reduce maintenance dosage by 50% Severe impairment (Child-Pugh class C): There are no dosage adjustments provided (has not been studied). Should only be used if benefit outweighs risk; monitor closely for toxicity **Dosing: Obesity: Adult** Use ideal body weight (IBW) for most obese patients in weight-based dosing calculations; consider using an adjusted body weight (adjusted body weight=0.4 [total body weight – IBW] + IBW) in obese patients with life-threatening invasive fungal infections. Confirm selection of an appropriate dose with therapeutic drug monitoring **Dosing: Renal impairment: Pediatric** **Oral**: Children ≥2 years and Adolescents:

	Mild to severe impairment: There are no pediatric dosage adjustments necessary. Dialysis: Poorly dialyzed; no supplemental dose or dosage adjustment necessary. Continuous renal replacement therapy (CRRT): Drug clearance is highly dependent on the method of renal replacement, filter type, and flow rate. Appropriate dosing requires close monitoring of pharmacologic response, signs of adverse reactions due to drug accumulation, as well as drug concentrations in relation to target trough (if appropriate). **Parenteral: IV: Children ≥2 years and Adolescents:** CrCl ≥50 mL/minute: There are no dosage adjustments provided needed. CrCl <50 mL/minute: There are no pediatric-specific dosage adjustments provided; has not been studied. Due to accumulation of the intravenous vehicle (cyclodextrin), It is recommended the use of oral voriconazole unless an assessment of risk benefit justifies the use of IV voriconazole; if IV therapy is used, closely monitor serum creatinine and change to oral voriconazole when possible.
Contra-indications	Hypersensitivity to voriconazole or any component of the formulation; coadministration with astemizole, barbiturates (long acting), carbamazepine, cisapride, efavirenz (≥400 mg daily), ergot derivatives (ergotamine and dihydroergotamine), pimozide, quinidine, rifampin, rifabutin, ritonavir (≥800 mg daily; also avoid low dose [eg, 200 mg daily] dosing if possible), sirolimus, St John's wort, terfenadine
Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** Acute kidney injury Cardiovascular effects Dermatologic reactions Hepatotoxicity Ocular and neurological effects Skeletal effects **>10%:** Cardiovascular: Hypertension (children, adolescents: 11%; adults: <2%) Dermatologic: Skin rash (children, adolescents: 13%; adults: 2% to 4%) (See Table 1) Endocrine & metabolic: Hyperkalemia (≤17%), hypokalemia (children, adolescents: 11%; adults: <1%) Gastrointestinal: Abdominal pain (children, adolescents: 12%; adults: <2%), diarrhea (children, adolescents: 11%; adults: <2%), nausea (children, adolescents: 13%; adults: 1% to 4%), vomiting (children, adolescents: 20%; adults: 1% to 3%) Hepatic: Increased serum alanine aminotransferase (children, adolescents, adults: 2% to 23%), increased serum alkaline phosphatase (children, adolescents, adults: 4% to 23% (See Table 2)), increased serum aspartate aminotransferase (children, adolescents, adults: 2% to 20%) Ophthalmic: Visual disturbance (children, adolescents: 26%, adults: 14% to 16%; likely serum concentration dependent Renal: Increased serum creatinine (children, adolescents: <5%; adults: ≤21%) Respiratory: Epistaxis (children, adolescents: 16%; adults: <2%) Miscellaneous: Fever (children, adolescents: 25%; adults: 2%)
Monitoring Parameters	• Hepatic function at initiation, weekly during the first month and monthly during course of treatment; renal function; serum electrolytes (particularly calcium, magnesium and potassium) prior to initiation and during therapy; visual function (visual acuity, visual field and color perception) if treatment course continues >28 days; phototoxic reactions (especially in pediatric patients); pancreatic function (in patients at risk for acute pancreatitis); total body skin examination yearly (more frequently if lesions noted). • Monitoring of serum trough concentrations is recommended in the following infections: invasive aspergillosis treatment (and prolonged prophylaxis) and endophthalmitis. For other

	infections, consider obtaining voriconazole trough level to assure therapeutics serum concentrations in patients failing therapy or in those exhibiting signs of toxicity. • For invasive aspergillosis, the Infectious Diseases Society of America recommends monitoring trough serum concentrations after steady state has been reached (4 to 7 days after therapy initiation); the need for continued or repeat monitoring is a patient specific decision influenced by many factors (eg, infection severity, cost, assay availability). **Reference Range** Trough recommendations in adult patients: Invasive aspergillosis (non-CNS infection) Efficacy: >1 to 1.5 mcg/mL Minimize toxicity: <5 to 6 mcg/mL CNS aspergillosis (meningitis, ventriculitis): Goal: Trough levels between 2 and 5 mcg/mL Endophthalmitis: Goal: Trough levels between 2 and 5 mcg/mL Other infections Efficacy: >1.0 mcg/mL Minimize toxicity: <4.0 mcg/mL Therapeutic range in adult patients: 1 to 5 mcg/mL
Drug Interactions	***Risk X: Avoid combination*** Amiodarone, Aprepitant, Atazanavir, Barbiturates, Carbamazepine, Cisapride, Conivaptan, Darunavir, Domperidone, Dronedarone, Eplerenone, Ergotamine, Fluconazole, Fluticasone (Nasal), Fosaprepitant, Ivabradine, Lovastatin, Nimodipine, Rifampin, Ritonavir, Simeprevir, Simvastatin, Sirolimus, Tamsulosin, Terfenadine, Ticagrelor, Triazolam ***Risk D: Consider therapy modification*** Alprazolam, Aripiprazole, Atorvastatin, Bromocriptine, Budesonide (Systemic), Buspirone, Calcium Channel Blockers, Cilostazol, Citalopram, Colchicine, Cyclosporine (Systemic), Doxorubicin (Conventional), Efavirenz, Everolimus, Fluticasone (Oral Inhalation), Guanfacine, Tacrolimus(Systemic), Vincristine
Pregnancy and Lactation	**pregnancy category** D Breastfeeding must be stopped on initiation of therapy. It is not known if voriconazole is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, It is recommended a decision be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of treatment to the mother.
Administration	**Preparation for Administration as IV:** Reconstitute 200 mg vial with 19 mL of SWFI resulting in a concentration of 10 mg/mL; use of automated syringe during reconstitution is not recommended. Further dilute reconstituted solution with NS, LR, D_5WLR, $D_5W^1/_2NS$, D_5W, D_5W with KCl 20 mEq/L, $^1/_2NS$, or D5WNS to a final concentration of 0.5 to 5 mg/mL. Do not dilute with 4.2% sodium bicarbonate infusion **Administration: IV** Infuse over 1 to 3 hours (rate not to exceed 3 mg/kg/hour). Do not administer as an IV bolus injection. Do not infuse **concomitantly** into same line or cannula with other drug infusions. Do not infuse **concomitantly** even in separate lines or cannulas with concentrated electrolyte solutions or blood products. May be infused simultaneously with nonconcentrated electrolytes or TPN through a separate IV line. If TPN is infused through a multiple lumen catheter, use a different port than used for voriconazole. **Administration: Oral**

	Administer 1 hour before or 1 hour after a meal. Shake oral suspension for approximately 10 seconds before each use. Enteral tube feedings may decrease oral absorption; may hold tube feedings for 1 hour before and 1 hour after a voriconazole dose Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hazardous agent (NIOSH 2016 [group 3]). • Arrhythmias/QT prolongation: QT interval prolongation has been associated with voriconazole use; rare cases of arrhythmia (including torsade de pointes), cardiac arrest, and sudden death have been reported, usually in seriously ill patients with comorbidities and/or risk factors (eg, prior cardiotoxic chemotherapy, cardiomyopathy [especially with concomitant heart failure], electrolyte imbalance, or concomitant QTc-prolonging drugs). Also use with caution in patients with potentially proarrhythmic conditions (eg, congenital or acquired QT syndrome, sinus bradycardia, or preexisting symptomatic arrhythmias); correct electrolyte abnormalities (eg, hypokalemia, hypomagnesemia, hypocalcemia) prior to initiating and during therapy. • Dermatologic reactions: Rare cases of malignancy (melanoma, squamous cell carcinoma [SCC]) have been reported in patients with prior onset of severe photosensitivity reactions or exposure to standard dose long-term voriconazole therapy (in lung transplant recipients, SCC increased by ~6% per 60 days with a 28% absolute risk increase at 5 years. • Hepatic toxicity: Serious (and rarely fatal) hepatic reactions (eg, hepatitis, cholestasis, fulminant failure) have been observed with voriconazole. • Infusion-related reactions Stop infusion for severe reactions or as clinical presentation indicates. • Ocular effects: Visual changes, including blurred vision, changes in visual acuity, color perception, and photophobia, are commonly associated with treatment. • Renal toxicity: Acute renal failure has been observed; use with caution in patients receiving concomitant nephrotoxic medications. Evaluate renal function (particularly serum creatinine) at baseline and periodically during therapy. • Skeletal effects: Fluorosis and/or periostitis may occur during long-term therapy. If patient develops skeletal pain and radiologic findings of fluorosis or periostitis, discontinue therapy. • Toxicity symptoms: Voriconazole demonstrates nonlinear pharmacokinetics. ***Disease-related concerns:*** • Electrolyte abnormalities: Correct electrolyte abnormalities (eg, hypokalemia, hypomagnesemia, hypocalcemia) prior to initiating and during therapy. • Hepatic impairment: Use with caution; elevated liver function tests and clinical signs of liver damage, such as jaundice, have been associated with voriconazole. Adjustments to maintenance dosing is required in mild to moderate hepatic cirrhosis (Child-Pugh class A and B). In patients with severe hepatic insufficiency use only if the benefit outweighs the potential risk. Evaluate hepatic function (particularly liver function tests and bilirubin) at baseline and periodically during therapy. • Lactose intolerance: Tablets contain lactose and should not be given to patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency, or glucose-galactose malabsorption. • Pancreatitis: Monitor pancreatic function in patients (children and adults) at risk for acute pancreatitis (eg, recent chemotherapy or hematopoietic stem cell transplantation). Pancreatitis has been observed during therapy. • Renal impairment: Avoid the use of IV voriconazole in patients with renal impairment. See "Dosage forms specific issues: Injection: formulation." Evaluate renal function (particularly serum creatinine) at baseline and periodically during therapy. ***Concurrent drug therapy issues:*** • Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

	Special populations: • Pediatric pharmacokinetics: In pediatric patients, voriconazole pharmacokinetics are complex. In patients >14 years of age or 12 to 14 years and weighing >50 kg, data suggest that pharmacokinetics are similar to adults. In patients <12 years of age, the full pharmacokinetic profile for voriconazole is not completely defined and for patients <2 years, the data are sparse. In children 2 to <12 years, current data suggest voriconazole undergoes a high degree of variability in exposure with linear elimination at lower doses and nonlinear elimination at higher doses; therefore, to achieve similar AUC as adults, increased dosage is necessary in children. • Pediatric dermatologic reactions: Frequency of phototoxic reactions is higher in pediatric patients. Stringent photoprotective measures are necessary in children due to the risk of squamous cell carcinoma. In children experiencing photoaging injuries (eg, lentigines or ephelides), avoidance of sun and dermatologic follow-up are warranted even after treatment is discontinued. • Pediatric hepatic reactions: Frequency of hepatotoxic reactions is higher in pediatric patients. Close monitoring of liver function tests is recommended; if tests become markedly elevated from baseline, consider discontinuation.
Storage	**Powder for injection:** Store vials between 15°C to 30°C. Reconstituted solutions are stable for up to 24 hours under refrigeration at 2°C to 8°C. **Powder for oral suspension**: Store at 2°C to 8°C. Reconstituted oral suspension is stable for up to 14 days if stored at 15°C to 30°C Do not refrigerate or freeze. **Tablets**: Store at 15°C to 30°C Refer to manufacturer PIL if there are specific considerations.

12. Posaconazole

Generic Name	Posaconazole
Dosage form/strengths	**Oral Suspension**: 200 mg/5ml **Solution for slow I.V. Infusion**: 300 mg/16.7ml
Route of administration	Oral, IV
Pharmacological category	Antifungal Agent, Azole Derivative ATC: J02AC04
Indications	**Aspergillosis, invasive: injection (patients ≥13 years of age**): Treatment of invasive aspergillosis. **Candidiasis, oropharyngeal: IR oral suspension (patients ≥13 years of age):** Treatment of oropharyngeal candidiasis (including patients refractory to itraconazole and/or fluconazole). Prophylaxis against invasive fungal infections, severely immunocompromised patients: IR oral **suspension (patients ≥13 years of age):** Prophylaxis of invasive Aspergillus and Candida infections in patients who are at high risk of developing these infections due to being severely immunocompromised (eg, hematopoietic stem cell transplant with graft-versus-host disease, hematologic malignancy with prolonged neutropenia due to chemotherapy).
Dosage Regimen	**Dosing: Adult** **Note: Therapeutic drug monitoring:** Adjust dose based on trough serum concentration to ensure efficacy and avoid toxicity. Timing and frequency of concentration monitoring is individualized. **Aspergillosis** *Invasive (including disseminated and extrapulmonary) (alternative agent for patients who are refractory to or intolerant of first-line agents):* **IV:** 300 mg twice daily for 2 doses, then 300 mg once daily. Duration: Minimum of 6 to 12 weeks; total duration depends on degree/duration of immunosuppression, disease site, and response to therapy; immunosuppressed patients may require more prolonged treatment. **Candidiasis: Note:** Generally reserved for fluconazole-refractory disease or as an alternative initial agent for patients with HIV or solid organ transplantation. *Oropharyngeal:* **Oral:** Initial episode (alternative agent): IR suspension: 400 mg twice daily for 1 to 3 days, then 400 mg once daily for a total duration of 7 to 14 days. Fluconazole-refractory disease: IR suspension: 400 mg twice daily **or** 400 mg twice daily for 3 days, then 400 mg once daily. Duration is up to 28 days. **Prophylaxis against invasive fungal infections:** *Hematology malignancy or hematopoietic cell transplant:* **Oral:**IR suspension: 200 mg 3 times daily. **IV:** 300 mg twice daily for 2 doses, then 300 mg once daily. Duration: Varies based on degree and duration of immunosuppression **Dosing: Pediatric** **Aspergillosis, invasive; prophylaxis: Note:** Duration of therapy is based on recovery from neutropenia or immunosuppression. Oral: Immediate-release suspension: Adolescents ≥13 years: Oral: 200 mg 3 times daily. IV: Children ≥2 years and Adolescents <18 years: IV: 6 mg/kg/dose twice daily for 2 doses, followed by 6 mg/kg/dose once daily; maximum dose: 300 mg/dose. Adolescents ≥18 years: IV: 300 mg twice daily for 2 doses, followed by 300 mg once daily.

	Aspergillosis, invasive; treatment (salvage): Note: Duration of therapy is highly dependent on degree/duration of immunosuppression, disease site, and evidence of disease improvement; minimum of 6 to 12 weeks of therapy is recommended. Oral: Adolescents: Immediate-release suspension: Limited data available: Oral: 200 mg 3 times daily or 400 mg twice daily. IV: Adolescents: 300 mg twice daily for 2 doses, followed by 300 mg once daily. **Candidiasis, oropharyngeal; treatment:** *Non-HIV-infected:* Adolescents: Initial episode: Immediate-release suspension: Oral: 100 mg twice daily for 2 doses, followed by 100 mg once daily for 13 days. Refractory infection: Immediate-release suspension: Oral: 400 mg twice daily; duration of therapy is based on underlying disease and clinical response. *HIV-infected:* Adolescents: Initial episode (alternative to fluconazole): Immediate-release suspension: Oral: 400 mg twice daily for 2 doses, followed by 400 mg once daily for 7 to 14 days. Refractory infection: Immediate-release suspension: Oral: 400 mg twice daily for 28 days. **Candidiasis, esophageal (azole-refractory); treatment:** Adolescents (HIV-infected): Oral immediate-release suspension: 400 mg twice daily for 28 days. **Candidiasis, invasive; prophylaxis: Note:** Duration of therapy is based on recovery from neutropenia or immunosuppression. Oral: Immediate-release suspension: Adolescents ≥13 years: Oral: 200 mg 3 times daily. IV: Children ≥2 years and Adolescents <18 years: IV: 6 mg/kg/dose twice daily for 2 doses, followed by 6 mg/kg/dose once daily; maximum dose: 300 mg/dose. Adolescents ≥18 years: IV: 300 mg twice daily for 2 doses, followed by 300 mg once daily.
Dosage adjustment	**Dosing: Renal Impairment:** **IV:** eGFR ≥50 mL/minute/1.73 m2: No dosage adjustment recommended. eGFR <50 mL/minute/1.73 m2: Avoid use unless risk/benefit assessment warrants use; the intravenous vehicle (cyclodextrin) may accumulate. Monitor serum creatinine levels; if increases occur, consider oral therapy. **Oral: Immediate-release suspension:** eGFR ≥20 mL/minute/1.73 m2: No dosage adjustment necessary. eGFR <20 mL/minute/1.73 m2: No dosage adjustment necessary; however, monitor for breakthrough fungal infections due to variability in posaconazole exposure. Hemodialysis: Not removed by dialysis. **Dosing: Hepatic Impairment:** Hepatotoxicity prior to initiating therapy (mild to severe): No dosage adjustment available. Hepatic dysfunction alters the pharmacokinetic parameters of posaconazole. Hepatotoxicity during treatment: Consider discontinuing therapy if signs and symptoms consistent with liver disease that may be attributable to posaconazole develop**.**
Contra-indications	Coadministration with sirolimus, ergot alkaloids (eg, ergotamine, dihydroergotamine), HMG-CoA reductase inhibitors that are primarily metabolized through CYP3A4 (eg, atorvastatin, lovastatin, simvastatin), or CYP3A4 substrates that prolong the QT interval (eg, pimozide, quinidine); hypersensitivity to posaconazole, other azole antifungal agents, or any component of the formulation

Adverse Drug Reactions	**>10%:** Cardiovascular: Hypertension (8% to 20%), hypotension (oral: 14%), lower extremity edema (oral: 15%), peripheral edema (11% to 16%), tachycardia (oral: 12%), thrombophlebitis (IV via peripheral venous catheter: 60%) Dermatologic: Pruritus (11% to 22%), skin rash (3% to 24%) Endocrine & metabolic: Dehydration (oral: 1% to 11%), hyperglycemia (oral: 11%), hypokalemia (14% to 30%), hypomagnesemia (10% to 18%), weight loss (oral: 1% to 14%) Gastrointestinal: Abdominal pain (5% to 27%), anorexia (oral: 2% to 19%), constipation (8% to 21%), decreased appetite (10% to 15%), diarrhea (10% to 42%), nausea (9% to 38%), oral candidiasis (oral: 1% to 12%), stomatitis (11% to 20%), upper abdominal pain (6% to 11%), vomiting (7% to 29%) Hematologic & oncologic: Anemia (2% to 25%), febrile neutropenia (15% to 31%), neutropenia (oral: 4% to 23%; severe neutropenia: 10%), petechia (8% to 11%), thrombocytopenia (7% to 29%) Hepatic: Increased serum alanine aminotransferase (3% to 17%), increased serum alkaline phosphatase (1% to 13%), increased serum aspartate aminotransferase (3% to 17%) Infection: Herpes simplex infection (oral: 3% to 11%) Nervous system: Chills (10% to 16%), dizziness (oral: 11%), fatigue (3% to 17%), headache (8% to 28%), insomnia (oral: 1% to 17%), pain (oral: 1% to 11%), rigors (oral: ≤20%) Neuromuscular & skeletal: Arthralgia (oral: 11%), asthenia (oral: 2% to 13%), musculoskeletal pain (oral: 16%) Respiratory: Cough (3% to 25%), dyspnea (1% to 20%), epistaxis (11% to 17%), pharyngitis (oral: 12%), pneumonia (3% to 13%) Miscellaneous: Fever (6% to 45%), inflammation (mucosal: 14% to 28%) **1% to 10%:** Cardiovascular: Edema (oral: 9%), pulmonary embolism (<5%), torsades de pointes (<5%) Dermatologic: Diaphoresis (oral: 2%) Endocrine & metabolic: Adrenocortical insufficiency (<5%), hypocalcemia (oral: 9%) Gastrointestinal: Dyspepsia (oral: 10%), pancreatitis (<5%) Genitourinary: Vaginal hemorrhage (oral: 10%) Hematologic & oncologic: Hemolytic-uremic syndrome (<5%), thrombotic thrombocytopenic purpura (<5%) Hepatic: Hepatic insufficiency (<5%), hepatitis (<5%), hepatomegaly (<5%), increased liver enzymes (<5%), increased serum bilirubin (3% to 10%), jaundice (<5%) Hypersensitivity: Hypersensitivity reaction (<5%) Nervous system: Paresthesia (<5%) Neuromuscular & skeletal: Back pain (oral: 10%) Renal: Acute kidney injury (<5%)
Monitoring Parameters	• blood pressure • Monitoring of hepatic function Liver function tests should be evaluated at the start of and during the course of posaconazole therapy • serum creatinine • serum electrolytes
Drug Interactions	***Risk X: Avoid Combination*** Acalabrutinib Alcohol (Ethyl) Alfuzosin Alprazolam Aprepitant Astemizole Asunaprevir Atorvastatin Avanafil Avapritinib Barnidipine Blonanserin Bosutinib Budesonide (Topical) Cisapride Cobimetinib Conivaptan Dapoxetine Domperidone Doxorubicin (Conventional) Dronedarone Efavirenz Elagolix, Estradiol, And Norethindrone Eletriptan Eplerenone Ergot Derivatives (Vasoconstrictive CYP3A4 Substrates) Finerenone Flibanserin Fluticasone (Nasal) Fosaprepitant Infigratinib Isavuconazonium Sulfate Ivabradine Lefamulin Lemborexant Lercanidipine Lomitapide Lonafarnib Lovastatin Lumateperone Lurasidone Lurbinectedin Macitentan Mizolastine Naloxegol Neratinib Nimodipine

	Nisoldipine Pimozide Pralsetinib QT-Prolonging CYP3A4 Substrates Quinidine Radotinib Ranolazine Regorafenib Rimegepant Rupatadine Ruxolitinib Salmeterol Silodosin Simeprevir Simvastatin Sirolimus Sonidegib Suvorexant Tamsulosin Tazemetostat Terfenadine Ticagrelor Tolvaptan Trabectedin Triazolam Ubrogepant Udenafil Vincristine (Liposomal) Vinflunine Voclosporin Vorapaxar ***Risk D: Consider Therapy Modification*** Abemaciclib Ado-Trastuzumab Emtansine Alfentanil Alitretinoin (Systemic) Almotriptan Aripiprazole Aripiprazole Lauroxil Atogepant Avacopan Axitinib Brexpiprazole Brigatinib Bromocriptine Budesonide (Oral Inhalation) (Systemic) Buspirone Cabazitaxel Cabozantinib Cariprazine Cilostazol Colchicine Copanlisib Cyclosporine (Systemic) Dabrafenib Daclatasvir Darifenacin Deflazacort Docetaxel Duvelisib Elagolix Elbasvir And Grazoprevir Eliglustat Erdafitinib Erlotinib Eszopiclone Everolimus Fedratinib Felodipine Fentanyl Fesoterodine Fexinidazole Fluticasone (Oral Inhalation) Fosphenytoin-Phenytoin Glasdegib Guanfacine Histamine H2 Receptor Antagonists Ibrexafungerp Ibrutinib Idelalisib Iloperidone Inhibitors Of The Proton Pump (Ppis And Pcabs) Irinotecan Products Istradefylline Ivacaftor Ixabepilone Lapatinib Larotrectinib Lorlatinib Lumacaftor And Ivacaftor Manidipine Maraviroc Midazolam Mifepristone Mirodenafil Nifedipine Olaparib Palbociclib Panobinostat Pazopanib Pemigatinib Pexidartinib Pimavanserin Ponatinib Rifabutin Ruxolitinib (Systemic) Saxagliptin Selpercatinib Selumetinib Sildenafil Solifenacin Sufentanil Sunitinib Tacrolimus (Systemic) Tadalafil Temsirolimus Tezacaftor And Ivacaftor Thiotepa Tofacitinib Tolterodine Trazodone Triamcinolone (Systemic) Valbenazine Vardenafil Vemurafenib Venetoclax Vilazodone Vincristine Voxelotor Zanubrutinib Zopiclone
Pregnancy and Lactation	**Pregnancy Category** C Breastfeeding is not recommended during use of this drug; breastfeeding should be discontinued upon initiation of this drug.
Administration	**Oral (suspension):** •Take this drug with a full meal. If you are not able to eat a full meal, take this drug with a liquid nutrition supplement or an acidic carbonated drink like ginger ale. If you are not able to drink these drinks, talk with your doctor. •Shake well before use. Measure liquid doses carefully **Administration: IV** Infuse over 90 minutes via a central venous line. Do not administer IV push or bolus. Must be infused through an in-line filter (0.22 micron polyethersulfone [PES] or polyvinylidene difluoride [PVDF]). Infusion through a peripheral line should only be used as a one-time infusion over 30 minutes in a patient who will be receiving a central venous line for subsequent doses, or to bridge a period during which a central venous line is to be replaced or is in use for another infusion. May be an irritant. **Preparation for Administration: Pediatric** IV: Equilibrate the refrigerated vial to room temperature. Contents of vial should be withdrawn and admixed with D5W, D5W with KCl 20 mEq, D_5NS, $D5^1/_2NS$, $^1/_2NS$, or NS to achieve a concentration of 1 to 2 mg/mL. The admixed solution may be colorless to yellow. Color variations in this range do not affect potency. Admixture should be used immediately. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hepatic effects: Hepatic dysfunction has occurred, ranging from mild/moderate increases of ALT, AST, alkaline phosphatase, total bilirubin, and/or clinical hepatitis to severe reactions (cholestasis, hepatic failure including death). Elevations in LFTs have been generally reversible after posaconazole has been discontinued; some cases resolved without drug interruption. More severe reactions have been observed in patients with underlying serious medical conditions (eg, hematologic malignancy) and primarily with IR oral suspension total daily doses of 800 mg. Monitor LFTs at baseline and periodically during therapy. If increases occur, monitor for severe

	hepatic injury development. Consider discontinuation of therapy in patients who develop clinical evidence of liver disease that may be secondary to posaconazole. ***Disease-related concerns:*** • Arrhythmias: Use caution in patients with an increased risk of arrhythmia (long QT syndrome, concurrent QTc-prolonging drugs metabolized through CYP3A4, hypokalemia). Development of QTc prolongation, including torsades de pointes, has been reported. • Electrolyte abnormalities: Correct electrolyte abnormalities (eg, hypokalemia, hypomagnesemia, hypocalcemia) prior to initiating and during therapy. • Renal impairment: Do not use injection in patients with eGFR <50 mL/minute/1.73 m^2, unless risk/benefit has been assessed. See "Dosage Forms Specific Issues: Injection Formulation." Evaluate renal function (particularly serum creatinine) at baseline and periodically during therapy. If increases occur, consider oral therapy. Monitor closely for breakthrough fungal infections in patients with severe renal impairment taking delayed-release oral suspension, delayed-release tablets, or IR oral suspension due to variability in posaconazole exposure. ***Dosage form specific issues:*** • Benzyl alcohol and derivatives: Some dosage forms may contain sodium benzoate/benzoic acid; benzoic acid (benzoate) is a metabolite of benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; See manufacturer's labeling. • Injection formulation: Do not give as an IV bolus injection. Avoid/limit use of IV formulation in patients with eGFR <50 mL/minute/1.73 m^2; injection contains excipient cyclodextrin (sulfobutyl ether beta-cyclodextrin [SBECD]), which may accumulate although the clinical significance of this finding is uncertain; consider using oral posaconazole in these patients unless benefit of injection outweighs the risk. If injection is used in patients with eGFR <50 mL/minute, monitor serum creatinine closely; if increases occur, consider changing therapy to oral posaconazole. • Oral formulations: The delayed-release tablet, delayed-release oral suspension, and IR oral suspension are not to be used interchangeably due to dosing differences for each formulation. Monitor patients taking oral formulations who experience severe diarrhea or vomiting for breakthrough fungal infections. • Polysorbate 80: Some dosage forms may contain polysorbate 80 (also known as Tweens). Hypersensitivity reactions, usually a delayed reaction, have been reported following exposure to pharmaceutical products containing polysorbate 80 in certain individuals. • Sorbitol: Some dosage forms may contain sorbitol. ***Special populations:*** • Obesity: Patients weighing >120 kg may have lower plasma drug exposure; monitor closely for breakthrough fungal infections. ***Other warnings/precautions:*** • Appropriate use: For patients prescribed posaconazole IR oral suspension who are unable to eat, take with a high-fat meal, or tolerate nutritional supplements or acidic carbonated beverages (eg, ginger ale) and do not have the option of taking the delayed-release tablet, delayed-release suspension, or injection, consider alternative antifungal therapy or closely monitor for breakthrough fungal infections. Delayed-release suspension is not recommended in adults or pediatric patients >40 kg; recommended dosage cannot be achieved.
Storage	• Suspension: Store at room temperature in a dry place. • Injection: Store intact vials at 2°C to 8°C. Diluted solution for infusion may be stored for ≤24 hours at 2°C to 8°C • Refer to manufacturer PIL if there are specific considerations.

Antimalarial agents

1. Artemether and lumefantrine

Generic Name	Artemether and lumefantrine
Dosage form/strengths	Tablet: 20 mg + 120 mg
Route of administration	*Oral*
Pharmacological category	Antimalarial Agent ATC: P01BF01
Indications	Malaria, treatment: Treatment of acute, uncomplicated malaria infections due to Plasmodium falciparum, including geographical regions where chloroquine resistance has been reported.
Dosage Regimen	**-Adult Dosing:** -Malaria, treatment: 3-day schedule: Oral: Patients ≥35 kg: 4 tablets at hour 0 and hour 8 on the first day, then 4 tablets twice daily on day 2 and day 3 (total of 24 tablets per treatment course). **-Pediatric Dosing:** Infants ≥2 months, Children, and Adolescents: Oral -5 kg to <15 kg: One tablet at hour 0 and at hour 8 on the first day and then one tablet twice daily (in the morning and evening) on days 2 and 3 (total of 6 tablets per treatment course). -15 kg to <25 kg: Two tablets at hour 0 and at hour 8 on the first day and then two tablets twice daily (in the morning and evening) on days 2 and 3 (total of 12 tablets per treatment course). -25 kg to <35 kg: Three tablets at hour 0 and at hour 8 on the first day and then three tablets twice daily (in the morning and evening) on day 2 and 3 (total of 18 tablets per treatment course). -≥35 kg: Four tablets at hour 0 and at hour 8 on the first day and then four tablets twice daily (in the morning and evening) on days 2 and 3 (total of 24 tablets per treatment course).
Dosage adjustment	-**Renal Impairment:** -Mild or moderate impairment: Dosage adjustments are not recommended - Severe impairment: Use with caution (has not been studied). -**Hepatic Impairment:** -Mild or moderate impairment: Dosage adjustments are not recommended -Severe impairment : Use with caution (has not been studied).
Contra-indications	-Hypersensitivity to artemether, lumefantrine, or any component of the formulation -Concurrent use with strong CYP3A4 inducers (eg, rifampin, carbamazepine, phenytoin, St John's wort)
Adverse Drug Reactions	**->10%:** -Cardiovascular: Palpitation (adults: 18%) -Central nervous system: Headache (adults 56%; children 13%), dizziness (adults 39%;

	children 4%), fever (25% to 29%), chills (adults 23%; children 5%), sleep disorder (adults: 22%), fatigue (adults 17%; children 3%) -Gastrointestinal: Anorexia (adults 40%; children 13%), nausea (adults 26%; children 5%), vomiting (17% to 18%), abdominal pain (8% to 17%) -Infection: Plasmodium falciparum (exacerbation: children: 17%) -Neuromuscular & skeletal: Weakness (adults 38%; children 5%), arthralgia (adults 34%; children 3%), myalgia (adults 32%; children 3%) -Respiratory: Cough (adults 6%; children 23%) -Miscellaneous: Fever (25% to 29%) **-3% to 10%:** -Central nervous system: Insomnia (adults: 5%), malaise (adults: 3%), vertigo (adults: 3%) -Dermatologic: Pruritus (adults: 4%), skin rash (3%) -Gastrointestinal: Diarrhea (7% to 8%) -Hematologic & oncologic: Anemia (4% to 9%) -Hepatic: Hepatomegaly (6% to 9%), increased serum AST (≤4%) -Infection: Malaria (≤3%) -Respiratory: Rhinitis (4%), nasopharyngitis (≤3%)
Monitoring Parameters	-Adequate food consumption (to ensure absorption and efficacy) -ECG monitoring if concomitant use of other agents that prolong the QT interval is medically required
Drug Interactions	***Risk X: Avoid combination*** CYP3A4 Inducers (Strong) Fexinidazole Halofantrine St John's Wort ***Risk D: Consider therapy modification*** Antimalarial Agents Dapsone Hormonal Contraceptives Mequitazine Ubrogepant
Pregnancy and Lactation	**Category C** Artemether/lumefantrine may be used to treat chloroquine resistant uncomplicated malaria during the second and third trimesters. Artemether/lumefantrine also may be used as an alternative treatment during the first trimester when preferred agents are not available. In pregnant patients with severe malaria, artemether/lumefantrine is the preferred interim oral therapy when the preferred IV agent is not readily available (discontinue once IV treatment is initiated). Dosing is the same as nonpregnant patients Estimates of its excretion into breastmilk indicate that amounts in milk are very low. The Centers for Disease Control and Prevention consider the drug combination acceptable for use in mothers nursing an infant weighing at least 5 kg.
Administration	-Oral: Administer with a full meal for best absorption. - For patients unable to swallow tablets: Crush tablet and mix with 5-10 mL of water. Administer to patient. Rinse container with water and administer contents to the patient. The crushed mixture should be followed with food/drink if possible. -Repeat dose if vomiting occurs within 2 hours of administration; for persistent vomiting, explore alternative therapy. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Drugs that prolong the QT interval: Avoid use in patients receiving other agents that prolong the QT interval; consider alternative therapy. ECG monitoring is advised if concomitant use of agents that prolong the QT interval is medically required. -Avoid use in patients at risk for QT prolongation, - Not indicated for the treatment of severe or complicated malaria or for the prevention of malaria.

	- In the event of disease reappearance after a quiescent period, patients should be treated with a different antimalarial drug.
Storage	Store at 25°C, excursions permitted to 15°C to 30°C Refer to manufacturer PIL if there are specific considerations.

2. Artesunate

Generic Name	Artesunate		
Dosage form/strengths	-Tablet: 50 mg		
Route of administration	*Oral*		
Pharmacologic category	-Antimalarial Agent -Artemisinin Derivative ATC: P01BE03		
Indications	**Malaria (severe), treatment:** Initial treatment of severe malaria in adult and pediatric patients.		
Dosage Regimen	**-Ault or Pediatric Dosing:** **-Malaria (uncomplicated), treatment:**		

Artesunate - amodiaquine	**Body weight (kg)**	Dose administered orally once daily for 3 days:	
	4.5 to <9	25 mg plus 67.5 mg	
	9 to <18	50 mg plus 135 mg	
	18 to <36	100 mg plus 270 mg	
	≥36	200 mg plus 540 mg	
Artesunate - mefloquine	**Body weight (kg)**	Dose administered orally once daily for 3 days:	
	5 to <9	25 mg plus 55 mg	
	9 to <18	50 mg plus 110 mg	
	18 to <30	100 mg plus 220 mg	
	≥30	200 mg plus 440 mg	
Artesunate - sulfadoxine-pyrimethamine	**Body weight (kg)**	Artesunate (orally once daily for 3 days):	(single dose orally on day 1 of (500 mg sulfadoxine and 25 mg pyrimethamine):
	5 to <10	25 mg	250 mg plus 12.5 mg
	10 to <25	50 mg	500 mg plus 25 mg

	25 to <50	100 mg	1000 mg plus 50 mg
	≥50	200 mg	1500 mg plus 75 mg

if used alone (via the parenteral, rectal, or oral route), artesunate must be administered for five to seven days.

Dosage adjustment

-Adult:
-Renal Impairment:
No dosage adjustment necessary.

-Hepatic Impairment:
No dosage adjustment necessary.

Contra-indications

- Hypersensitivity to artesunate or any component of the formulation.

Adverse Drug Reactions

-1% to 10%:
-Genitourinary: Hemoglobinuria (7%)
-Hepatic: Jaundice (2%)
-Nervous system: Neurological signs and symptoms (1%)
-Renal: Acute renal failure (9%)

Monitoring Parameters

- Signs/symptoms of hypersensitivity
-Hb, reticulocyte count, haptoglobin, lactate dehydrogenase, and total bilirubin once weekly for up to 4 weeks after artesunate initiation

Drug Interactions

- Risk D: Consider therapy modification
Artemether and Lumefantrine, Dapsone

Pregnancy and Lactation

-An increased risk of adverse pregnancy outcomes has not been observed following maternal use of artesunate.
-Severe malaria is especially hazardous during pregnancy, therefore full dose parenteral antimalarial treatment should be administered without delay.
Limited information indicates that a maternal dose of 200 mg orally produced low levels in milk and would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. Withholding breastfeeding for 6 hours after a dose should markedly reduce the dose the infant receives.

Administration

Administration: Oral
Tablets should be swallowed with water. Do not administer with a high fat meal. If patient vomits within 30 minutes of administration, re-administer the dose.

Warnings/ Precautions

- Artesunate has not been evaluated in the treatment of severe malaria due to Plasmodium vivax, Plasmodium malariae or Plasmodium ovale.
Switching to oral treatment regimen
-Acute treatment of severe falciparum malaria with should always be followed by a complete treatment course of an appropriate oral combination antimalarial regimen

Storage

- Store intact vials and diluent at 20°C to 25°C; excursions permitted to 15°C to 30°C. Protect from light.
- Refer to manufacturer PIL if there are specific considerations.

3. Artesunate and amodiaquine

Generic Name	Artesunate and amodiaquine
Dosage form/strengths	Tablets 50mg/200mg
Route of administration	*Oral*
Pharmacologic category	Aminoquinoline (Antimalarial); Antimalarial Agent; Artemisinin Derivative ATC: P01BF03
Indications	**Malaria:** Treatment of uncomplicated malaria due to susceptible strains of *Plasmodium falciparum*.
Dosage Regimen	**Dosing: Adult** **Malaria:** Oral: Artesunate 4 mg/kg (range 2 to 10 mg/kg) and amodiaquine 10 mg/kg (range 7.5 to 15 mg/kg) once daily for 3 days. **Dosing: Pediatric** **Malaria:** Oral: Infants ≥2 months, Children, and Adolescents: Dosing recommendation based on the following weight-based dosing: Artesunate 4 mg/kg (range 2 to 10 mg/kg) and amodiaquine 10 mg/kg (range 7.5 to 15 mg/kg) once daily for 3 days
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments provided; use with caution. **Dosing: Hepatic Impairment:** There are no dosage adjustments provided; use with caution.
Contra-indications	Hypersensitivity to artesunate, amodiaquine, or any component of the formulation; hepatic injury or hematologic abnormality with previous amodiaquine treatment; retinopathy; use for malaria prophylaxis
Adverse Drug Reactions	**1% to 10%:** Central nervous system: Dizziness, drowsiness, headache, insomnia, shivering Gastrointestinal: Abdominal pain, anorexia, nausea, sore throat Hematologic & oncologic: Leukopenia, neutropenia Hepatic: Increased serum transaminases Infection: Common cold, influenza Neuromuscular & skeletal: Asthenia Respiratory: Bronchitis, cough, rhinitis
Monitoring Parameters	Liver function in patients with symptoms of hepatitis; CBC in patients with symptoms of immunosuppression (fever, tonsillitis, mouth ulcers)

Drug Interactions	***Risk X: Avoid combination*** CYP2C8 Inhibitors (Moderate) or (strong) Efavirenz Trimethoprim Zidovudine ***Risk D: Consider therapy modification*** Artemether and Lumefantrine Dapsone (Systemic) Dapsone (Topical) Sulfamethoxazole
Pregnancy and Lactation	Adverse events were observed in some animal reproduction studies using this combination. Agents other than artesunate/amodiaquine are recommended during the first trimester; use later in pregnancy may be considered, although information related to this combination is limited. Also refer to the Artesunate monograph for additional information. Small amounts of artesunate and amodiaquine are present in breast milk. Adverse events in the nursing infant would not be expected. When treatment for malaria is needed, this combination may be used in breastfeeding women.
Administration	**Administration: Oral** Administer at the same time each day with water. Avoid administration with high fat meals. If patient vomits within 30 minutes of administration, repeat full dose. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Cardiovascular effects: Cardiovascular effects have been reported with amino-4-quinolone derivatives. Due to the potential of QT prolongation, use caution • CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks that require mental alertness (eg, operating machinery or driving). • Extrapyramidal symptoms (EPS): May cause extrapyramidal symptoms; can occur after one dose. Symptoms should resolve with discontinuation of therapy; an alternative antimalarial treatment should be initiated. • Hematologic effects: Rare hematologic reactions including anemia, agranulocytosis, and neutropenia have been reported; monitor CBC if signs/symptoms of infection occur. Discontinue treatment if signs/symptoms of severe blood disorder not attributable to underlying disease occur. Use for malaria prophylaxis is contraindicated due to risk of agranulocytosis. ***Disease-related concerns:*** • Hepatic impairment: Use with caution in patients with hepatic impairment; has not been studied. Monitor for signs/symptoms of hepatitis. • Renal impairment: Use with caution in patients with renal impairment; has not been studied. ***Other warnings/precautions:*** • Appropriate use: Artesunate/amodiaquine should not be used to treat complicated malaria or other strains of *Plasmodium* malaria. Artesunate/amodiaquine should not be administered in areas with known resistance to amodiaquine due to an increased risk of treatment failure and development of resistance to artesunate. Use for malaria prophylaxis is contraindicated
Storage	• Store at ≤30°C • Refer to manufacturer PIL if there are specific considerations.

4. Chloroquine

Generic Name	Chloroquine
Dosage form/strengths	Suspension: 80 mg/5 ml Tablet: 250 mg Injection: 200 mg/5ml
Route of administration	*Oral*
Pharmacologic category	Antimalarial Agent, Aminoquinoline (Antimalarial) ATC: P01BA01
Indications	-**Malaria Treatment**: treatment of uncomplicated malaria due to susceptible strains of Plasmodium vivax, Plasmodium malariae, Plasmodium ovale, and Plasmodium falciparum -**Prophylaxis of malaria** (in geographic areas where chloroquine resistance is not present) - **Extraintestinal amebiasis**
Dosage Regimen	-**Adult Dosing:** **Note:** Each 250 mg of chloroquine phosphate is equivalent to 150 mg of chloroquine base. **-Malaria, uncomplicated, treatment:** Oral: 1 g (600 mg base) on day 1, followed by 500 mg (300 mg base) 6-, 24-, and 48 hours after first dose **-Prophylaxis:** Oral: 500 mg (300 mg base) weekly on the same day each week; begin 1 to 2 weeks prior to exposure; continue while in endemic area and for 4 weeks after leaving endemic area. **Extraintestinal amebiasis:** Oral: 1 g (600 mg base) daily for 2 days followed by 500 mg daily (300 mg base) for at least 2 to 3 weeks; may be combined with an intestinal amebicide. **-Pediatric Dosing:** **-Malaria:** **-Treatment, acute attack, uncomplicated:** Infants, Children, and Adolescents: Oral: Initial 16.7 mg/kg chloroquine phosphate (maximum initial dose: 1,000 mg chloroquine phosphate); followed by 8.3 mg/kg chloroquine phosphate (maximum dose: 500 mg chloroquine phosphate/dose) administered at 6, 24, and 48 hours after initial dose for a total of 4 doses **-Chemoprophylaxis:** Infants, Children, and Adolescents: Oral: 8.3 mg/kg chloroquine phosphate once weekly on the same day each week; maximum dose: 500 mg chloroquine phosphate/dose. Begin 1 to 2 weeks prior to exposure; continue while in endemic area and continue for at least 4 weeks after leaving endemic area
Dosage adjustment	**-Adult:** **-Renal Impairment:** -GFR ≥10 mL/minute: No dosage adjustment necessary. -GFR <10 mL/minute: in prolonged use: administer 50% of dose **-Hepatic Impairment:** Chloroquine concentrates in the liver. However, no specific dosage adjustment guidelines are available for patients with hepatic impairmentaution.
Contra-indications	-Hypersensitivity to chloroquine, 4-aminoquinoline compounds, or any component of the formulation -Presence of retinal or visual field changes of any etiology (when used for indications other than acute malaria)

Adverse Drug Reactions	**Frequency not defined:** -Cardiovascular: Atrioventricular block, bundle branch block, cardiac arrhythmia, cardiac failure, cardiomyopathy, ECG changes (including flattened T wave on ECG, inversion T wave on ECG, prolonged QT interval on ECG, widened QRS complex on ECG), hypotension, torsades de pointes, ventricular fibrillation, ventricular tachycardia -Dermatologic: Alopecia, bleaching of hair, blue-gray skin pigmentation (oral mucosa and hard palate, nails, and, erythema multiforme, exacerbation of psoriasis, exfoliative dermatitis, lichen planus, pleomorphic rash, pruritus, skin photosensitivity, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria -Endocrine & metabolic: Exacerbation of porphyria, severe hypoglycemia -Gastrointestinal: Abdominal cramps, anorexia, diarrhea, nausea, vomiting -Hematologic & oncologic: Agranulocytosis (reversible), aplastic anemia, hemolytic anemia (in G6PD-deficient patients), neutropenia, pancytopenia, thrombocytopenia Hepatic: Hepatitis, increased liver enzymes Hypersensitivity: Anaphylaxis, angioedema Immunologic: Drug reaction with eosinophilia and systemic symptoms Nervous system: Agitation, anxiety, confusion, decreased deep tendon reflex, delirium, depression, extrapyramidal reaction (dystonia, dyskinesia, protrusion of the tongue, torticollis), hallucination, headache, insomnia, personality changes, polyneuropathy, psychosis, seizure, sensorimotor neuropathy, sensorineural hearing loss, suicidal tendencies -Neuromuscular & skeletal: Asthenia, myopathy, neuromuscular disease, proximal myopathy -Ophthalmic: Accommodation disturbances, blurred vision, corneal opacity (reversible), macular degeneration (may be irreversible), maculopathy (may be irreversible), night blindness, retinal pigment changes (bull's eye appearance), retinopathy (including irreversible changes in long-term or high-dose therapy), transient scotomata, visual field defect (paracentral scotomas) -Otic: Hearing loss (risk increased in patients with preexisting auditory damage), tinnitus
Monitoring Parameters	- CBC (with differential), liver function, and renal function at baseline and periodically during therapy -Blood glucose (if symptoms of hypoglycemia occur) -Muscle strength -ECG at baseline and as clinically indicated: in patients at elevated risk of QTc prolongation -Ophthalmologic exam at baseline to screen for retinal toxicity, followed by annual screening beginning after 5 years of use (or sooner if major risk factors are present).
Drug Interactions	***Risk X: Avoid combination*** Agalsidase Alfa, Artemether, Cimetidine, Fexinidazole, Lumefantrine, Mefloquine, Pimozide QT-prolonging Strong Aprepitant Cimetidine Ciprofloxacin Clarithromycin Diltiazem Erythromycin Fluconazole Grapefruit juice Itraconazole Ketoconazole Posaconazole Voriconazole Verapamil, Remdesivir ***Risk D: Consider therapy modification*** Agalsidase Beta, Ampicillin, Antacids, Cholera Vaccine, Dapsone, Domperidone, Lanthanum, Rabies Vaccine
Pregnancy and Lactataion	Category C Chloroquine may be used in all trimesters of pregnancy according to guidelines. Dose adjustments could be needed, but data are not sufficient to determine what an appropriate dosing change is when chloroquine is used for the treatment or prophylaxis of malaria during pregnancy. According to WHO Pregnant patients should be closely monitored for

	response to treatment. Very small amounts of chloroquine are excreted in breast milk; when given once weekly, the amount of drug is not sufficient to harm the infant nor is the quantity sufficient to protect the child from malaria. Because no information is available on the daily use of chloroquine during breastfeeding, hydroxychloroquine or another agent may be preferred in this situation, especially while nursing a newborn or preterm infant.
Administration	Oral: Administer with food to decrease GI adverse effects. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Cardiovascular effects: Cases of cardiomyopathy resulting in cardiac failure (sometimes fatal) have been reported during long term therapy at high doses. Monitor for signs and symptoms of cardiomyopathy; discontinue if cardiomyopathy develops. • Extrapyramidal effects: Acute extrapyramidal disorders may occur, usually resolving after discontinuation of therapy and/or symptomatic treatment. • Hematologic effects: Rare hematologic reactions including reversible agranulocytosis, aplastic anemia, neutropenia, pancytopenia, and thrombocytopenia have been reported; monitor CBC during prolonged therapy. Consider discontinuation if severe blood disorders occur that are unrelated to disease. • Hypoglycemia: Severe hypoglycemia, including loss of consciousness, has been reported in patients treated with or without antidiabetic agents. Counsel patients about risk of hypoglycemia and associated signs and symptoms. • Neuromuscular effects: Skeletal muscle myopathy or neuromyopathy, leading to progressive weakness and atrophy of proximal muscle groups have been reported; muscle strength (especially proximal muscles) should be assessed periodically during prolonged therapy; discontinue therapy if weakness occurs. • Retinal toxicity: Retinal toxicity, potentially causing irreversible retinopathy, is predominantly associated with high daily doses and a duration of >5 years of use of chloroquine or hydroxychloroquine in the treatment of rheumatic diseases. ***Disease-related concerns:*** • Auditory damage: Use with caution in patients with preexisting auditory damage; discontinue immediately if hearing defects are noted. • G6PD deficiency: Use chloroquine with caution in patients with these conditions. Blood monitoring for hemolytic anemia in G6PD deficiency patients may be necessary, particularly with concomitant use of other medications associated with hemolysis • Hepatic impairment: Use with caution in patients with hepatic impairment, alcoholism, or concurrent therapy with hepatotoxic agents. • Myasthenia gravis: Use may worsen or precipitate new myasthenia gravis (MG); use only if necessary and monitor for worsening MG. • Porphyria: Use with caution in patients with porphyria; may exacerbate disease symptoms. • Psoriasis: Use with caution in patients with psoriasis; may exacerbate disease symptoms. • Seizure disorder: Use with caution in patients with a history of seizure disorder; may cause seizures. ***Other warnings/precautions:*** • Appropriate use: Chloroquine does not prevent relapses in patients with vivax or ovale malaria (not effective against exoerythrocytic forms); additional treatment with an antimalarial effective against these forms (eg, an 8-aminoquinoline) is required for the treatment of infections with *P. vivax* and *P. ovale*. Do not use for the treatment of complicated malaria (high-grade parasitemia and/or complications [eg, cerebral malaria,

	acute renal failure]). • Chloroquine resistance: Chloroquine is not effective against chloroquine- or hydroxychloroquine-resistant strains of *Plasmodium* species. Chloroquine resistance is widespread in *P. falciparum* and is reported in *P. vivax*. Prior to initiation of chloroquine for prophylaxis, it should be determined if chloroquine is appropriate for use in the region to be visited; do not use for malaria prophylaxis in areas where chloroquine resistance occurs.
Storage	-Store at 25°C, excursions are permitted between 15°C and 30°C. -Protect from light. Refer to manufacturer PIL if there are specific considerations.

5. Hydroxychloroquine

Generic Name	Hydroxychloroquine
Dosage form/strengths	Tablets 200mg
Route of administration	*Oral*
Pharmacologic category	Aminoquinoline (Antimalarial); Antimalarial Agent ATC: P01BA02
Indications	**Lupus erythematosus:** Treatment of chronic discoid erythematosus and systemic lupus erythematosus in adults. **Malaria:** Treatment of uncomplicated malaria caused by susceptible strains of *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium ovale*, and *Plasmodium falciparum*; prophylaxis of malaria in geographic areas where chloroquine resistance is not reported. **Note:** The CDC guidelines also recommend hydroxychloroquine for chloroquine-sensitive *Plasmodium knowlesi* malaria. **Rheumatoid arthritis:** Treatment of acute and chronic rheumatoid arthritis in adults.
Dosage Regimen	**Note:** All doses below expressed as hydroxychloroquine sulfate. Hydroxychloroquine sulfate 200 mg is equivalent to 155 mg hydroxychloroquine base **Adult Dosing:** **Note:** Due to the risk of retinal toxicity, most patients should **not** receive a daily dose >5 mg/kg/day using actual body weight **or** 400 mg, whichever is lower. **Lupus erythematosus:** *Systemic lupus erythematosus:* **Oral:** 200 to 400 mg daily as a single daily dose or in 2 divided doses. *Discoid lupus erythematosus and subacute cutaneous lupus erythematosus:* **Oral:** 200 to 400 mg daily as a single daily dose or in 2 divided doses. **Malaria (alternative agent):** *Prophylaxis:* **Oral:** 400 mg once weekly on the same day each week; begin 1 to 2 weeks before travel to malarious area; continue therapy while in malarious area and for 4 weeks after leaving the area. *Treatment, uncomplicated:* **Oral:** 800 mg once, followed by 400 mg at 6, 24, and 48 hours after initial dose (total dose: 2 g). **Rheumatoid arthritis:** **Oral:** 200 to 400 mg daily as a single daily dose or in 2 divided doses. **Pediatric dosing:** **Malaria:** *Chemoprophylaxis:* Infants, Children, and Adolescents: Oral: 6.5 mg/kg hydroxychloroquine sulfate once weekly on the same day each week; maximum dose: 400 mg/dose hydroxychloroquine sulfate; begin 1 to 2 weeks before travel to malarious area; continue while in malarious area and for 4 weeks after leaving the area. *Treatment, uncomplicated:* Infants, Children, and Adolescents: Oral: Initial: 12.9 mg/kg/dose hydroxychloroquine sulfate (maximum initial dose: 800 mg/dose hydroxychloroquine

	sulfate); followed by 6.5 mg/kg hydroxychloroquine sulfate at 6, 24, and 48 hours after initial dose; maximum dose: 400 mg/dose hydroxychloroquine sulfate. For infection caused by *Plasmodium vivax* or *Plasmodium ovale*, use in combination with appropriate antirelapse treatment (ie, primaquine).
Dosage adjustment	**Dosing: Renal Impairment: Adult** **Mild to severe impairment:** There is no dosage adjustment necessary with short-term use; however, dosage reduction may be needed with prolonged use (eg, systemic lupus erythematosus); use with caution. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments provided in the manufacturer's labeling; use with caution.
Contra-indications	Known hypersensitivity to hydroxychloroquine, 4-aminoquinoline derivatives, or any component of the formulation.
Major Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** • Cardiomyopathy • Hypersensitivity reactions (delayed) • Hypoglycemia • Neuromuscular effects • Neuropsychiatric effects • QT prolongation • Retinal toxicity **1% to 10%:** Ophthalmic: Retinopathy (4%; serum concentration dependent; early changes reversible [may progress despite discontinuation if advanced])
Monitoring Parameters	CBC (with differential) at baseline and periodically; liver function; renal function (in patients at risk for ocular toxicity); blood glucose (if symptoms of hypoglycemia occur); muscle strength (especially proximal) during long-term therapy; in patients at risk of torsades de pointes, monitor ECG at baseline and periodically during therapy to assess for QTc prolongation. Ophthalmologic exam at baseline to screen for retinal toxicity, followed by annual screening beginning after 5 years of use (or sooner if major risk factors are present). Consider annual exams (without deferring 5 years) in patients with significant risk factors.
Common Drug Interactions	***Risk X: Avoid combination*** Lumefantrine Mefloquine Remdesivir ***Risk D: Consider therapy modification*** Dapsone (Systemic) (Topical)
Pregnancy and Lactation	This drug should not be used during pregnancy unless the benefit outweighs the risk to the fetus. US FDA pregnancy category: Not formally assigned to a pregnancy category International experts indicate that hydroxychloroquine is acceptable during breastfeeding
Administration	**Administration: Oral** Administer with food or milk. Do not crush or divide film-coated tablets; the tablets have a bitter taste. In patients unable to swallow tablets, it has been recommended that tablets may be crushed and mixed with a small amount of applesauce, chocolate syrup, or jelly. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Cardiovascular effects: Cardiomyopathy resulting in cardiac failure, sometimes fatal, has been reported (symptoms may present as atrioventricular block, pulmonary hypertension, sick sinus syndrome, or as cardiac complications), and may appear during acute or chronic therapy. Monitor for signs/symptoms of cardiac compromise; discontinue treatment promptly if signs and symptoms of cardiomyopathy occur. May also be associated with QT

	interval prolongation; ventricular arrhythmia and torsades de pointes have been reported (monitor QT-prolonging effects during therapy in at-risk patients or if used in combination with other medications that prolong the QT interval). • Dermatologic effects: Skin reactions to hydroxychloroquine may occur; use with caution in patients on concomitant medications with a propensity to cause dermatitis. • Hematologic effects: Bone marrow suppression (eg, agranulocytosis, anemia, aplastic anemia, leukopenia, thrombocytopenia) have been reported; periodically monitor CBC during prolonged therapy. Discontinue treatment if signs/symptoms of severe blood disorder not attributable to the underlying disease occur. • Hypoglycemia: Severe hypoglycemia, including life-threatening loss of consciousness, has been reported in patients with and without concomitant use of antidiabetic agents. Advise patients of risk of hypoglycemia and associated signs/symptoms; discontinue use in patients who develop severe hypoglycemia. • Neuromuscular effects: Proximal myopathy or neuromyopathy, leading to progressive weakness, proximal muscle atrophy, depressed tendon reflexes, and abnormal nerve conduction may occur, especially with long-term therapy. Curvilinear bodies and muscle fiber atrophy with vacuolar changes have been noted on muscle or nerve biopsy. Muscle strength (especially proximal muscles) and reflexes should be assessed periodically during long term therapy. • Psychiatric effects: Suicidal behavior has been reported rarely. • Retinal toxicity: Retinal toxicity, potentially causing irreversible retinopathy, is predominantly associated with high daily doses and a duration of >5 years of use of chloroquine or hydroxychloroquine in the treatment of rheumatic diseases. If ocular toxicity is suspected, discontinue and monitor closely; retinal changes and visual disturbances may progress after discontinuation. A baseline ocular exam is recommended within the first year of initiating hydroxychloroquine treatment. ***Disease-related concerns:*** • G6PD deficiency: use with caution due to a potential for hemolytic anemia. • Gastrointestinal disorders: Use with caution in patients with gastrointestinal disorders. • Hepatic impairment: Use with caution in patients with hepatic impairment, alcoholism, or concurrent therapy with hepatotoxic agents. • Myasthenia gravis: Use with caution in patients with myasthenia gravis; may exacerbate condition. • Porphyria: Use with extreme caution in patients with porphyria; may exacerbate or precipitate disease. • Psoriasis: Use with extreme caution in patients with psoriasis; may exacerbate or precipitate disease. • Renal impairment: Use with caution in patients with renal impairment; dosage reduction may be needed. ***Special populations:*** • Pediatric: Pediatric patients have an increased sensitivity to aminoquinolines
Storage	Store at 20°C to 25°C; excursions permitted to 15°C- 30°C. Protect from light. Refer to manufacturer PIL if there are specific considerations.

6. Mefloquine

Generic Name	Mefloquine
Dosage form/strengths	Tablet: 250 mg
Route of administration	*Oral*
Pharmacologic category	Antimalarial Agent ATC: P01BC02
Indications	-Malaria prophylaxis: Prophylaxis of Plasmodium falciparum and Plasmodium vivax malaria infections, including prophylaxis of chloroquine-resistant strains of P. falciparum. -Malaria treatment: Treatment of uncomplicated malaria caused by mefloquine-susceptible strains of P. falciparum or by P. vivax.
Dosage Regimen	**-Adult Dosing:** **-Malaria:** Oral (dose expressed as mg of mefloquine hydrochloride): -Uncomplicated malaria, treatment: 750 mg as initial dose, followed 6 to 12 hours later by 500 mg. -**Prophylaxis**: 250 mg weekly starting ≥2 weeks before arrival in endemic area, continuing weekly during travel and for 4 weeks after leaving endemic area **-Pediatric Dosing:** **- Malaria, treatment; chloroquine-resistant (independent of HIV status):** Infants, Children, and Adolescents: Oral: 15 mg/kg once (maximum dose: 750 mg/dose) followed in 6 to 12 hours with 10 mg/kg once (maximum dose: 500 mg/dose); use in combination with other anti-malarial agents **- Malaria; chemoprophylaxis (independent of HIV status):** -Begin ≥2 weeks before arrival in endemic area, administer on the same day each week, and continue weekly during travel and for 4 weeks after leaving endemic area -Infants, Children, and Adolescents: -Weight-based dosing: Oral: 5 mg/kg/dose once weekly; maximum dose: 250 mg/dose
Dosage adjustment	**-Renal Impairment:** No dosage adjustment necessary **-Hepatic impairment:** -No dosage adjustments available. Mefloquine should be used with caution in patients with hepatic disease. The elimination of mefloquine may be prolonged, leading to higher plasma drug concentrations
Contra-indications	-Hypersensitivity to mefloquine, related compounds (eg, quinine and quinidine), or any component of the formulation -Prophylactic use in patients with a history of seizures or psychiatric disorder (including active or recent history of depression, generalized anxiety disorder, psychosis, schizophrenia, or other major psychiatric disorders)
Adverse Drug Reactions	**->10%:** - Central nervous system: Abnormal dreams (14%)insomnia (13%) **-1% to 10%:** -Gastrointestinal: Vomiting (3%)
Monitoring Parameters	On prolonged use, monitor: -Liver function tests

	-Make evaluations for neuropsychiatric effects -Ocular examinations
Drug Interactions	**-Category X: Avoid combination** Abametapir, Aminoquinolines, Artemether, Conivaptan, Halofantrine, Idelalisib, Lumefantrine, Quinidine **-Category D: Consider therapy modification** Anticonvulsants, Clarithromycin Itraconazole Ketoconazole Posaconazole Barbiturates (phenobarbital) Carbamazepine Phenytoin Rifampicin Dabrafenib, Dapsone, Enzalutamide, Mifepristone, Stiripentol
Pregnancy and Lactation	Category B. When other treatment options are not available, mefloquine may be used for the treatment of chloroquine-resistant uncomplicated malaria in pregnancy. Mefloquine concentrations in breast milk are ~3% to 4% of a 250 mg dose. Mefloquine is considered acceptable for use in breastfeeding women. Use caution
Administration	**Oral**: -Administer with food and with at least 240 mL of water. -When used for malaria prophylaxis, dose should be taken once weekly on the same day each week. -If vomiting occurs within 30 minutes after the dose, an additional full dose should be given -If it occurs within 30 to 60 minutes after dose, an additional half-dose should be given. -Tablets may be crushed and suspended in a small amount of water, milk, or another beverage for persons unable to swallow tablets. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Agranulocytosis/aplastic anemia: Agranulocytosis and aplastic anemia have been reported. • Altered cardiac conduction: Mefloquine may cause alterations in the ECG including sinus bradycardia, sinus arrhythmia, first-degree AV block, QT-interval prolongation, and abnormal T waves. Use caution or avoid concomitant use of agents known to cause QT-interval prolongation (eg, halofantrine, quinine, quinidine). • Hypersensitivity reactions: Hypersensitivity reactions have occurred. • Neuropsychiatric effects: **[US Boxed Warning]:** May cause neuropsychiatric adverse effects that can persist after mefloquine has been discontinued. During prophylactic use, if symptoms occur, discontinue therapy and substitute an alternative medication. ***Disease-related concerns:*** • Cardiovascular disease: Use with caution in patients with significant cardiac disease; ECG changes (eg, sinus bradycardia, sinus arrhythmia, first-degree AV block, QT-interval prolongation, abnormal T waves) have been reported. • Hepatic impairment: Use with caution in patients with hepatic impairment; elimination may be prolonged. • Neuropsychiatric disorders: **[US Boxed Warning]:** Do not prescribe for prophylaxis in patients with major psychiatric disorders including patients with active depression, a recent history of depression, generalized anxiety disorder, psychosis, schizophrenia; use is contraindicated in these patients. Use with caution in patients with a previous history of depression. • Ocular effects: Eye disorders (including optic neuropathy and retinal disorders) have been reported during treatment. If visual symptoms develop during treatment, prompt ophthalmologic evaluation is warranted; discontinuation of therapy may be necessary. • *Plasmodium falciparum* infections: Appropriate use: In cases of life-threatening, serious, or overwhelming malaria infections due to *Plasmodium falciparum*, patients should be

	treated with intravenous antimalarial drug. Mefloquine may be given orally to complete the course. • *Plasmodium vivax* infections: Appropriate use: In cases of acute *Plasmodium vivax* infection treated with mefloquine, patients should subsequently be treated with an 8-aminoquinoline derivative (eg, primaquine) to avoid relapse. • Seizure disorder: When using for treatment, use with caution in patients with a history of seizures; may increase risk of seizures. Prophylactic use is contraindicated in patients with seizure disorder. ***Special populations:*** • Pediatric: Early vomiting leading to treatment failure in children has been reported in some studies; consider alternate therapy if a second dose is not tolerated. ***Other warnings/precautions:*** • Appropriate use: Not recommended for the treatment of malaria acquired in Southeast Asia due to drug resistance. • Prolonged use: If mefloquine is to be used for a prolonged period, liver function tests, evaluations for neuropsychiatric effects, and ophthalmic examinations should be performed periodically.
Storage	Store at 20°C to 25°C. 15-30°C is permitted. Refer to manufacturer PIL if there are specific considerations.

7. Pyrimethamine

Generic Name	Pyrimethamine
Dosage form/strengths	Pyrimethamine 25 mg tablets
Route of administration	*Oral*
Pharmacologic category	Antimalarial Agent ATC: P01BD01
Indications	Toxoplasmosis (in combination with a sulfonamide).
Dosage Regimen	**-Adult Dosing:** Toxoplasmosis treatment: Oral: 50 to 75 mg/day for 1 to 3 weeks depending on patient's tolerance and response, then may reduce dose by 50% and continue for 4 to 5 weeks; use with a sulfonamide in combination with leucovorin calcium **-Pediatric Dosing:** **- Toxoplasmosis, acquired infection (including encephalitis); treatment: Non-HIV-exposed/-infected:** Use in combination with leucovorin (to prevent hematologic toxicity) and either sulfadiazine or clindamycin. Infants, Children, and Adolescents: Oral: Initial: 2 mg/kg/day in divided doses twice daily for 2 days followed by 1 mg/kg/day once daily (maximum dose: Chorioretinitis: 25 mg/dose; severe or CNS disease: 50 mg/dose). Continue therapy for 1 to 2 weeks after symptom resolution, for a total therapy of 4 to 6 weeks. **-Toxoplasmosis, congenital infection (independent of HIV status); treatment:** In combination with sulfadiazine and leucovorin: Infants: Oral: Initial: 2 mg/kg/day once daily or in 2 divided doses for 2 days, then 1 mg/kg/day once daily for 2 to 6 months, then 1 mg/kg/dose 3 times weekly (maximum dose: 25 mg/dose; total treatment duration: 12 months
Dosage adjustment	**-Renal Impairment:** No dosage adjustments needed. **-Hepatic Impairment:** Use cautiously in patients with hepatic impairment. Specific dosage recommendations are not available.
Contra-indications	-Hypersensitivity to pyrimethamine or any component of the formulation -Megaloblastic anemia secondary to folate deficiency
Adverse Drug Reactions	**Frequency not defined.** Cardiovascular: Cardiac arrhythmia (large doses) -Dermatologic: Erythema multiforme, skin rash, Stevens-Johnson syndrome, toxic epidermal necrolysis -Gastrointestinal: Anorexia, glossitis (atrophic), vomiting -Hematologic & oncologic: Leukopenia, megaloblastic anemia, pancytopenia, thrombocytopenia -Genitourinary: Hematuria -Hypersensitivity: Anaphylaxis -Respiratory: Eosinophilic pneumonitis

Monitoring Parameters	-CBC, including platelet counts twice weekly with high-dose therapy -Hepatic and renal function
Drug Interactions	***-Risk D: Consider therapy modification*** Artemether and Lumefantrine, Dapsone , Folic Acid
Pregnancy and Lactation	Category C Pyrimethamine should be used with caution in patients with possible folate deficiency, including pregnant women. If administered during pregnancy (ie, for toxoplasmosis), supplementation of folate is strongly recommended. During Breastfeeding, use is considered acceptable according to WHO. Due to the potential for serious adverse reactions in the breastfed infant, It is recommended a decision be made to discontinue breastfeeding or to discontinue the drug, considering the importance of treatment to the mother, as well as use of concomitant medications.
Administration	Oral: Administer with meals to minimize GI distress. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hematologic: Megaloblastic anemia, leukopenia, thrombocytopenia, and pancytopenia have been reported; most commonly with high doses. Monitor CBC and platelets twice weekly in patients receiving high-dose therapy (eg, when used for toxoplasmosis treatment). ***Disease-related concerns:*** • Folate deficiency: Use caution in patients with possible folate deficiency (eg, malabsorption syndrome, alcoholism). • G6PD deficiency: Use with caution in patients with possible G6PD deficiency. • Hepatic impairment: Use with caution in patients with hepatic impairment. • Renal impairment: Use with caution in patients with renal impairment. • Seizure disorders: Use with caution in patients with a history of seizure disorders. ***Other warnings/precautions:*** • Leucovorin: Administer leucovorin to prevent hematologic complications due to pyrimethamine-induced folic acid deficiency state; continue leucovorin during therapy and for 1 week after therapy is discontinued (to account for long half-life of pyrimethamine)
Storage	Store at 15°C to 25°C. Protect from light. Refer to manufacturer PIL if there are specific considerations.

8. Sulfadoxine and Pyrimethamine

Generic Name	Sulfadoxine and Pyrimethamine
Dosage form/strengths	Tablet: Sulfadoxine 500 mg; Pyrimethamine 25 mg
Route of administration	*Oral*
Pharmacologic category	Antimalarial Agent ATC: P01BD51
Indications	Short-term prophylaxis and treatment of uncomplicated Plasmodium falciparum malaria, including areas where chloroquine resistance has been reported.
Dosage Regimen	-**Adult Dosing:** **1- Malaria prophylaxis:** Start 1 to 2 weeks prior to entering a malaria-endemic area, continue throughout the stay and for 4 weeks after returning. - Semi-immune patients: Oral: Sulfadoxine 500 mg/pyrimethamine 25 mg per tablet: 2 or 3 tablets once every 4 weeks. -Nonimmune patients: Oral: Sulfadoxine 500 mg/pyrimethamine 25 mg per tablet: 2 tablets once every 2 weeks or 1 tablet once weekly. **2- Malaria (uncomplicated) treatment:** Oral: Sulfadoxine 1,500 mg/pyrimethamine 75 mg (3 tablets) as a single dose. -**Pediatric Dosing**: 1- **Malaria prophylaxis**: start 1 to 2 weeks prior to entering a malaria-endemic area, continue throughout the stay and for 4 weeks after returning. 5-10 kg: 1/4 (0.25) tablet orally once a week 11-20 kg: 1/2 (0.5) tablet orally once a week 21-30 kg: 3/4 (0.75) tablet orally once a week 31-45 kg: 1 tablet orally once a week >45 kg: 1.5 tablet orally once a week. 2- **Malaria (uncomplicated) treatment**: Oral: Administer the following weight-based sulfadoxine/pyrimethamine dose on day 1. Monotherapy is not recommended. Do not use in infants <2 months of age: 5-10 kg: One-half tablet orally one time 11-20 kg: 1 tablet orally one time 21-30 kg: 1.5 tablet orally one time 31-45 kg: 2 tablets orally one time >45 kg: 3 tablets orally one time
Dosage adjustment	-**Renal impairment:** - Repeated prophylactic use of sulfadoxine; pyrimethamine is contraindicated in patients with renal failure. -**Hepatic Impairment:** Repeated prophylactic use of sulfadoxine; pyrimethamine is contraindicated in patients with hepatic failure.
Contra-indications	Hypersensitivity to sulfadoxine, pyrimethamine, other sulfonamides, or any component of the formulation -Megaloblastic anemia due to folate deficiency -Infants <2 months

	-Prophylactic use in patients with renal failure, hepatic failure, or blood dyscrasias
Adverse Drug Reactions	-Cardiovascular: Allergic myocarditis -Central nervous system: Apathy, ataxia, chills, depression, dizziness, drug fever (with toxic necrosis), fatigue, hallucination, headache, insomnia, peripheral neuropathy, polyneuropathy, seizure -Dermatologic: Alopecia, erythema multiforme, exfoliative dermatitis, pruritus, skin photosensitivity, skin rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria -Gastrointestinal: Abdominal pain, diarrhea, gastrointestinal fullness, gastrointestinal infection, glossitis, nausea, pancreatitis, stomatitis, vomiting -Genitourinary: Anuria, urinary frequency -Hematologic & oncologic: Agranulocytosis, aplastic anemia, eosinophilia, hemolytic anemia, hypoprothrombinemia, leukopenia, megaloblastic anemia, methemoglobinemia, pancytopenia, purpura, thrombocytopenia Hepatic: Hepatic necrosis, hepatitis, increased liver enzymes (may be transient) -Hypersensitivity: Anaphylactoid reaction -Neuromuscular & skeletal: Arthralgia, lupus-like syndrome, myasthenia gravis -Ophthalmic: Conjunctival hyperemia -Otic: Tinnitus -Respiratory: Pulmonary infiltrates -Miscellaneous: Fever
Monitoring Parameters	CBC and urinalysis periodically with prolonged administration of high doses
Drug Interactions	**-Category X**: Aminolevulinic Acid, Artemether, BCG (Intravesical), Cholera Vaccine, Lumefantrine, Methenamine, Procaine, Potassium P-Aminobenzoate -**Category D**: Chloroprocaine, Dapsone, Folic Acid, Methotrexate
Pregnancy and Lactation	Category C Because there is little published experience with sulfadoxine during breastfeeding, an alternate drug may be preferred, especially while nursing a newborn or preterm infant.
Administration	**Oral:** Administer after a meal. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	-Use with caution in patients with: -Hepatic impairment -Renal impairment Severe side effects including fatal Stevens-Johnson syndrome and toxic epidermal necrolysis have occurred in patients taking pyrimethamine-sulfadoxine. Discontinue this medication at the first sign of a skin rash or if a decrease in formed blood elements is noted, or upon the occurrence of active bacterial or fungal infections. Sulfadoxine-pyrimethamine is contraindicated in patients with blood dyscrasias, megaloblastic anemia due to folate deficiency, and in infants less than 2 months of age.. Discontinue if folic acid deficiency develops. Prophylaxis should not be continued for more than 2 years.

Storage	Store below 30°C Refer to manufacturer PIL if there are specific considerations.

Antiretrovirals

a) Nucleoside/Nucleotide reverse transcriptase inhibitors

1. Abacavir (ABC)

Generic Name	Abacavir
Dosage form/strengths	Tablet: 300 mg
Route of administration	*oral*
Pharmacologic category	Nucleoside reverse transcriptase inhibitor(NRTI) ATC: J05AF06
Indications	Used for Treatment of HIV-1 infection for children in the following situations: • First line regimen in combination with lamivudine and dolutegravir • alternative first line regimen in combination with lamivudine and lopinavir/ritonavir • alternative first line regimen in combination with lamivudine and raltegravir • second line regimen in combination with lamivudine and dolutegravir
Dosage Regimen	***Adult*** HIV-1 infection, treatment: Oral: 300 mg twice daily or 600 mg once daily in combination with other antiretroviral agents. ***Infants ≥3 months, Children, and Adolescents: Oral:*** **Twice daily dose regimen** Oral solution: 8 mg/kg/dose twice daily; **maximum dose**: 300 mg/dose. **If body weight ≥14 kg** Tablets (scored 300 mg tablets), oral solution: 14 to <20 kg: 150 mg twice daily. 20 to <25 kg: 150 mg in the morning and 300 mg in the evening. ≥25 kg: 300 mg twice daily. **Once daily dose regimen** In clinically stable patients with undetectable viral load for more than 6 months (24 weeks) on the liquid formulation of abacavir twice daily, the daily dose can be changed from twice daily to once daily with liquid or tablet formulations. Initiation with once-daily dosing is recommended for children who can be treated with tablet formulation ○ **If body weight ≤ 14 kg** Oral solution: 16 mg/kg/dose once daily**; maximum dose**: 600 mg/dose ○ **If body weight ≥14 kg** Tablets (scored 300 mg tablets), oral solution: 14 to <20 kg: 300 mg once daily. 20 to <25 kg: 450 mg once daily. ≥25 kg: 600 mg once daily.
Dosage adjustment	**Dosing: Renal Impairment** There are no dosage adjustments **Dosing: Hepatic Impairment Adults:** • Mild impairment (Child-Pugh class A): 200 mg twice daily (oral solution is recommended).

	• Moderate to severe impairment (Child-Pugh class B or C): Use is contraindicated **Dosing: Hepatic Impairment Pediatrics:** • Mild impairment: Dosing adjustment is required; however, pediatric-specific recommendations are not available Moderate to severe hepatic impairment (Child-Pugh class B or C): Use is contraindicated.
Contra-indications	• Hypersensitivity to abacavir or any component of the formulation • moderate to severe hepatic impairment • patients who are positive for the HLA-B*5701 allele
Major Adverse Drug Reactions	• **Central nervous system**: Headache (adults: ≤13%; infants, children, & adolescents: 1%), fatigue (≤12%), malaise (≤12%) • **Gastrointestinal**: Nausea (7% to 19%) • **Endocrine & metabolic:** Hypertriglyceridemia (2% to 6%) • **Hematologic & oncologic:** Neutropenia (2% to 5%), thrombocytopenia (1%) • **Hepatic:** Increased serum alanine aminotransferase (6%), increased serum aspartate aminotransferase (6%) • Drug-induced hypersensitivity (9%) • **Respiratory:** ENT infection (5%), viral respiratory tract infection (5%), bronchitis (4%), pneumonia (infants, children, & adolescents: 4%) • **Miscellaneous:** Fever (≤9%)
Monitoring Parameters	CBC with differential, CD4 count, HIV RNA plasma levels, serum transaminases, fasting lipid panel; serum creatine kinase, serum amylase (as clinically indicated); *HLA-B*5701* genotype status prior to initiation of therapy and prior to reinitiation of therapy in patients of unknown *HLA-B*5701* status; signs and symptoms of hypersensitivity
Drug Interactions	***Cladribine:*** *Abacavir may diminish the therapeutic effect of Cladribine.* ***Risk X: Avoid combination*** • ***Risk C: Monitor therapy*** Cabozantinib Levomethadone Methadone Orlistat Riociguat
Pregnancy and Lactation	• **Pregnancy** Abacavir is a preferred (NRTI) for pregnant patients living with HIV who are antiretroviral naive, who have had ART therapy in the past but are restarting, or who require a new ART regimen (due to poor tolerance or poor virologic response of current regimen) patients who become pregnant while taking abacavir may continue if viral suppression is effective and the regimen is well tolerated. • **Lactation** Abacavir was detected in the serum of an infant following exposure via breast milk. If a woman is receiving this drug while breastfeeding, her nursing infant should be monitored for these effects : nausea, headache, malaise and fatigue, nausea, vomiting, and dreams/sleep disorders
Administration	Oral: May be administered without regard to food Hazardous agent (NIOSH 2016 [group 2]). Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hypersensitivity reactions**: [US Boxed Warning]: Serious and sometimes fatal hypersensitivity reactions have occurred. Patients who carry the HLA-B*5701 allele are at a higher risk for a hypersensitivity reaction to abacavir • **Immune reconstitution syndrome**: Patients may develop immune reconstitution

	syndrome resulting in the occurrence of an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (eg, Graves disease, polymyositis, Guillain-Barré syndrome) later in therapy; further evaluation and treatment may be required. • **Lactic acidosis/hepatomegaly** • **Coronary heart disease**: Use has been associated with an increased risk of MI in some cohort studies. Consider using with caution in patients with risks for coronary heart disease and minimizing modifiable risk factors (eg, hypertension, hyperlipidemia, diabetes mellitus, smoking) prior to use. • **Hepatic impairment**: Use with caution and adjust dosage in patients with mild hepatic impairment (contraindicated in moderate to severe impairment). May cause mild **hyperglycemia**; more common in pediatric patients.
Storage	Store at 20°C to 25°C , Oral solution may be refrigerated; do not freeze Refer to manufacturer PIL if there are specific considerations.

2. Lamivudine (3TC)

Generic Name	Lamivudine		
Dosage form/strengths	Tablets 100mg, 150mg		
Route of administration	oral		
Pharmacologic category	Antihepadnaviral, Reverse Transcriptase Inhibitor, Nucleoside (Anti-HBV); Antiretroviral, Reverse Transcriptase Inhibitor, Nucleoside (Anti-HIV) ATC: J05AF05		
Indications	**Chronic hepatitis B:** Treatment of chronic hepatitis B associated with evidence of hepatitis B viral replication and active liver inflammation Limitations of use: Use only when an alternative antiviral agent with a higher genetic barrier to resistance is not available or appropriate. Lamivudine-HBV has not been evaluated in patients coinfected with HIV, hepatitis C virus, or hepatitis delta virus; with decompensated liver disease; or in liver transplant recipients. **HIV-1 infection, treatment:** Treatment of HIV-1 in combination with other antiretroviral agents		
Dosage Regimen	**Dosing: Adult** **HIV-1 infection, treatment:** Oral (use in combination with other antiretroviral agents): 150 mg twice daily or 300 mg once daily **Treatment of hepatitis B (Epivir HBV, Heptovir [Canadian product]):** Oral: 100 mg once daily **Treatment of hepatitis B/HIV coinfection (in patients with both infections requiring treatment):** Oral: 150 mg twice daily or 300 mg once daily, in combination with tenofovir and other appropriate antiretrovirals **Dosing: Pediatric:** **HIV-1 infection, treatment** **Twice-daily dosing** **Children ≥3 years and Adolescents:** **Oral tablet:** Weight-band dosing for patients weighing ≥14 kg who are able to swallow tablets (using scored 150 mg tablets): 14 to <20 kg: 75 mg (1/2 tablet) twice daily. 20 to <25 kg: 75 mg (1/2 tablet) in the morning and 150 mg (1 tablet) in the evening. ≥25 kg: 150 mg (1 tablet) twice daily. **Once-daily dosing:** Oral: Note: Not recommended as initial therapy in children. Patients can be transitioned to once daily treatment with the oral solution or tablet after stable on twice-daily treatment for ≥36 weeks with an undetectable viral load and stable CD4 count Oral solution: 10 mg/kg/dose once daily; maximum dose: 300 mg/dose. Oral tablet: Weight-band dosing for patients ≥14 kg who are able to swallow tablets (scored 150 mg tablets) 14to <20 kg: 150 mg (1 tablet) once daily. 20to <25 kg: 225 mg (1 + 1/2 tablet) once daily. ≥25 kg: 300 mg (2 tablets) once daily **Hepatitis B, treatment (non-HIV-exposed/-infected):** **Note:** Use in HBV treatment is discouraged due to rapid resistance development; consider use only if other anti-HBV antiviral regimens with more favorable resistance patterns cannot be used.		

	Adolescents ≥16 years: Oral: 100 mg once daily.
Dosage adjustment	**Renal Impairment: Adult in HIV treatment** CrCl ≥50 mL/minute: No dosage adjustment necessary. CrCl 30 to 49 mL/minute: Administer 150 mg once daily. CrCl 15 to 29 mL/minute: Administer 150 mg first dose, then 100 mg once daily. CrCl 5 to 14 mL/minute: Administer 150 mg first dose, then 50 mg once daily. CrCl <5 mL/minute: Administer 50 mg first dose, then 25 mg once daily. Hemodialysis or Peritoneal dialysis: Administer 50 mg first dose, then 25 mg once daily, dosing after hemodialysis is recommended, Supplemental dosing not needed after Peritoneal dialysis **Treatment of hepatitis B patients:** CrCl ≥50 mL/minute: No dosage adjustment necessary. CrCl 30 to 49 mL/minute: Administer 100 mg first dose, then 50 mg once daily. CrCl 15 to 29 mL/minute: Administer 100 mg first dose, then 25 mg once daily. CrCl 5 to 14 mL/minute: Administer 35 mg first dose, then 15 mg once daily. CrCl <5 mL/minute: Administer 35 mg first dose, then 10 mg once daily. Hemodialysis or Peritoneal dialysis: It is recommended to correct dosage for degree of renal impairment; assuming CrCl <5 mL/minute, administer 35 mg first dose, then 10 mg once daily. **Renal Impairment: Pediatric** Infants, Children, and Adolescents <25 kg: There are no dosage adjustments consider reducing the dose or increasing the dosing interval; use with caution; monitor closely. Children and Adolescents ≥25 kg: the same as in adult **Dosing: Hepatic Impairment:** No dosage adjustment necessary. However, has not been studied in the setting of decompensated liver disease.
Contra-indications	Hypersensitivity to lamivudine or any component of the formulation
Adverse Drug Reactions	**>10%:** Central nervous system: Headache (35%), fatigue (≤27%), malaise (≤27%), paresthesia (≤15%), peripheral neuropathy (≤15%), neuropathy (12%), insomnia (≤11%), sleep disorder (≤11%) Dermatologic: Skin rash (9% to 12%) Gastrointestinal: Nausea (≤33%), diarrhea (adults: 14% to 18%, children: 8%), pancreatitis (≤18%; higher percentage in pediatric patients), sore throat (13%), vomiting (≤13%) Hematologic & oncologic: Neutropenia (7% to 15%) Hepatic: Increased serum alanine aminotransferase (adults: 4% to 27%, children: 1%), hepatomegaly (children: 11%, adults: <1%) Infection: infection (25%; includes ear, nose, and throat) Neuromuscular & skeletal: Musculoskeletal pain (12%) Respiratory: Nasal signs and symptoms (8% to 20%), cough (15% to 18%) Miscellaneous: Fever (children: 25%, adults: ≤10%) **1% to 10%:** Central nervous system: Dizziness (10%), chills (≤10%), depression (9%) Gastrointestinal: Increased serum lipase (adults: 10%, children: 3%), anorexia (≤10%), decreased appetite (≤10%), abdominal pain (9%), abdominal cramps (6%), stomatitis (children: 6%, adults: <1%), dyspepsia (5%) Hematologic & oncologic: Lymphadenopathy (children: 9%), splenomegaly (children 5%, adults <1%), thrombocytopenia (adults: 4%, children: 1%), decreased hemoglobin (2% to 4%) Hepatic: Increased serum aspartate aminotransferase (2% to 4%)

	Neuromuscular & skeletal: Increased creatine phosphokinase (9%), Otic: Ear disease (children: 7%)
Monitoring Parameters	*All patients:* Hepatic function, signs/symptoms of lactic acidosis; signs/symptoms of pancreatitis *HIV patients:* Coinfection with HBV (prior to therapy); HIV viral load and CD4 count; immune reconstitution syndrome *Hepatitis B patients:* Coinfection with HIV (prior to therapy); following discontinuation, monitor hepatic function closely with both clinical and laboratory follow/up for signs/symptoms of HBV relapse/exacerbation (continue for at least several months after stopping treatment)
Drug Interactions	***Risk X: Avoid combination*** Emtricitabine Cladribine ***Risk D: Consider therapy modification*** Sorbitol ***Risk C: Monitor therapy*** Cabozantinib Orlistat Trimethoprim
Pregnancy and Lactation	**pregnancy category C** lamivudine can be used; close fetal monitoring is recommended. Lamivudine has been well studied in HIV-positive nursing mothers and appears to be well tolerated by their breastfed infants.
Administration	May be administered without regard to meals. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Immune reconstitution syndrome: occurrence of an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (eg, Graves disease, polymyositis, Guillain-Barré syndrome) later in therapy; further evaluation and treatment may be required. • Lactic acidosis/hepatomegaly: Lactic acidosis and severe hepatomegaly with steatosis have been reported with nucleoside analogues, including fatal cases; suspend treatment in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity. Use with caution in patients with risk factors for liver disease (risk may be increased with female gender or obesity) (transaminase elevation may/may not accompany hepatomegaly and steatosis). • Pancreatitis: Has been reported, particularly in HIV-infected pediatric patients with a history of nucleoside use. Discontinue treatment if signs of symptoms of pancreatitis occur. ***Disease-related concerns:*** • Chronic hepatitis B: [US Boxed Warning]: Severe acute exacerbations of hepatitis B (some fatal) have been reported in patients with HBV or HIV/HBV coinfection who have discontinued lamivudine; hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months after discontinuation. Initiate antihepatitis B (HBV) medications if clinically appropriate. • Renal impairment: Use with caution in patients with renal impairment; dosage reduction recommended. • Resistance: - HIV: [US Boxed Warning]: HIV-1 resistance may emerge in chronic hepatitis B-infection patients with unrecognized or untreated HIV-1 infection. Counseling and HIV testing should be offered to all patients before beginning treatment with lamivudine for hepatitis B and then periodically during treatment. Lamivudine dosing for hepatitis B is subtherapeutic if used for HIV-1 infection treatment. Lamivudine monotherapy is not appropriate for HIV-1 infection treatment. ***Special populations:***

	• Pediatric: Use with caution in pediatric patients with a history of prior antiretroviral nucleoside exposure or pancreatitis, or other significant risk factors for development of pancreatitis.
Storage	Tablet: Store at 25°C; excursions are permitted between 15°C and 30°C Refer to manufacturer PIL if there are specific considerations.

3. Tenofovir disoproxil fumarate (TDF)

Generic Name	Tenofovir Disoproxil fumarate
Dosage form/strengths	Tablets 245 mg
Route of administration	Oral
Pharmacological category	Reverse Transcriptase Inhibitor; Antihepadnaviral, Nucleotide (Anti-HBV); Antiretroviral, Nucleotide (Anti-HIV) ATC: J05AF07
Indications	**Chronic hepatitis B**: Treatment of chronic hepatitis B virus (HBV) in patients ≥2 years of age weighing ≥10 kg **HIV-1 infection, treatment**: Treatment of HIV-1 infection in patients ≥2 years of age weighing ≥10 kg, in combination with other antiretroviral agents.
Dosage Regimen	**Dosing: Adult** **Hepatitis B infection:** Oral: 300 mg once daily **Note:** Concurrent use with adefovir and/or tenofovir combination products should be avoided. *Treatment duration (AASLD practice guidelines):* Treatment duration for nucleos(t)ide analog-based therapy (eg, tenofovir) is variable and influenced by HBeAg status, duration of HBV suppression, and presence of cirrhosis/decompensation **HIV-1 infection, treatment:** Oral: 300 mg once daily (in combination with other antiretrovirals). **Dosing: Pediatric** **HIV-1 infection, treatment** ***Weight-directed dosing****: Children ≥2 years weighing ≥10 kg and Adolescents: Oral: 8 mg/kg/dose once daily; maximum daily dose: 300 mg/**day*** ***Dosage form specific fixed dosing****:* *Oral tablets:* Children ≥2 years weighing ≥17 kg and Adolescents: Oral: 17 to <22 kg: 150 mg once daily 22 to <28 kg: 200 mg once daily 28 to <35 kg: 250 mg once daily ≥35 kg: 300 mg once daily **HIV-1 nonoccupational postexposure prophylaxis (nPEP)** Children ≥2 years: Oral: Age- and weight-appropriate dosing (see HIV-1 infection, treatment above) for 28 days in combination with other antiretroviral agents. Initiate therapy within 72 hours of exposure. Adolescents: The combination product is recommended **Hepatitis B infection, chronic:** Children ≥2 years weighing ≥10 kg and Adolescents: Oral: 8 mg/kg/dose once daily; maximum daily dose: 300 mg/**day**; see HIV treatment dosing for product-specific dosing. In trials, oral antivirals were continued for 1 to 4 years; Hepatitis B e antigen (HBeAg) seroconversion has been suggested as a therapeutic endpoint followed by an additional 12 months of consolidation
Dosage adjustment	**Dosing: Renal Impairment: Adult** CrCl ≥50 mL/minute: No dosage adjustment necessary. CrCl 30 to 49 mL/minute: 300 mg every 48 hours CrCl 10 to 29 mL/minute: 300 mg every 72 to 96 hours (twice weekly) CrCl <10 mL/minute: has not been studied. avoid use. If no alternative therapy is available,

	then may consider 300 mg every 7 days; use with caution and close monitoring. Hemodialysis: 300 mg following dialysis every 7 days or after a total of ~12 hours of dialysis. **Dosing: Hepatic Impairment: Adult** No dosage adjustment necessary. **Dosing: Renal Impairment: Pediatric** Children ≥2 years and Adolescents: There are no dosage adjustments. Dosage should be decreased in patients with CrCl <50 mL/minute **Dosing: Hepatic Impairment: Pediatric** Children ≥2 years and Adolescents: No dosage adjustment required.
Contra-indications	Hypersensitivity to tenofovir or any component of the formulation
Adverse Drug Reactions	**>10%:** Central nervous system: Insomnia (3% to 18%), headache (5% to 14%), pain (12% to 13%), dizziness (8% to 13%), depression (4% to 11%) Dermatologic: Skin rash (includes maculopapular, pustular, or vesiculobullous rash; pruritus; or urticaria: 5% to 18%), pruritus (16%) Endocrine & metabolic: Hypercholesterolemia (19% to 22%), increased serum triglycerides (1% to 4%) Gastrointestinal: Abdominal pain (4% to 22%), nausea (8% to 20%), diarrhea (9% to 16%), vomiting (2% to 13%) Neuromuscular & skeletal: Decreased bone mineral density (28%; ≥5% at spine or ≥7% at hip), increased creatine phosphokinase (2% to 12%), weakness (6% to 11%) Miscellaneous: Fever (4% to 11%)
Monitoring Parameters	Patients with HIV: CBC with differential, reticulocyte count, creatine kinase, CD4 count, HIV RNA plasma levels, serum phosphorus (baseline and as clinically indicated in patients with chronic kidney disease); serum creatinine, urine glucose, urine protein (baseline and as clinically indicated during therapy); hepatic function tests; bone density (patients with a history of bone fracture or have risk factors for bone loss); testing for HBV is recommended prior to the initiation of antiretroviral therapy; weight (children). Patients with HBV: HIV status (prior to initiation of therapy); serum phosphorus (baseline and as clinically indicated in patients with chronic kidney disease); serum creatinine, urine glucose, urine protein (baseline and as clinically indicated during therapy); bone density (patients with a history of bone fracture or have risk factors for bone loss); LFTs every 3 months during therapy and for several months following discontinuation of tenofovir; signs/symptoms of HBV relapse/exacerbation following discontinuation of therapy.
Drug Interactions	***Risk X: Avoid combination*** Adefovir cladribine ***Risk D: Consider therapy modification*** Atazanavir Diclofenac Didanosine Ledipasvir Nonsteroidal Anti-Inflammatory Agents ***Risk C: Monitor therapy*** Voxilaprevir Velpatasvir Tipranavir Simeprevir Orlistat Lopinavir Ganciclovir-Valganciclovir Darunavir Cidofovir Cabozantinib Aminoglycosides Acyclovir-Valacyclovir
Pregnancy and Lactation	**Pregnancy Category** B Tenofovir disoproxil fumarate is a recommended component of a regimen when acute HIV infection is detected in patients who are breastfeeding. Breastfeeding should be interrupted if acute HIV infection is suspected and not continued if infection is confirmed.
Administration	**Administration: Oral**

	Tablets may be administered without regard to meals. Do not crush oral tablets Consider calcium and vitamin D supplementation. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Decreased bone mineral density • Immune reconstitution syndrome: Patients may develop immune reconstitution syndrome resulting in the occurrence of an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (eg, Graves' disease, polymyositis, Guillain-Barré syndrome) later in therapy; further evaluation and treatment may be required. • Lactic acidosis/hepatomegaly • Osteomalacia and renal dysfunction: May cause osteomalacia with proximal renal tubulopathy. Bone pain, extremity pain, fractures, arthralgias, weakness and muscle pain have been reported. In patients at risk for renal dysfunction, persistent or worsening bone or muscle symptoms should be evaluated for hypophosphatemia and osteomalacia. • Renal toxicity ***Disease-related concerns:*** • Chronic hepatitis B: [US Boxed Warning]: Severe, acute exacerbation of hepatitis B may occur upon discontinuation. Monitor hepatic function several months after discontinuing treatment; reinitiation of antihepatitis B therapy may be required. • Hepatic impairment: Use with caution in patients with hepatic impairment. • Renal impairment: Use with caution in patients with renal impairment (CrCl <50 mL/minute); dosage adjustment required. IDSA guidelines recommend avoiding tenofovir in HIV patients with preexisting kidney disease (CrCl <50 mL/minute and not on hemodialysis or GFR <60 mL/minute/1.73 m^2) when other effective HIV treatment options exist because data suggest risk of chronic kidney disease (CKD) is increased. ***Concurrent drug therapy issues:*** • Concomitant therapy: Do not use in combination with other tenofovir disoproxil fumarate or tenofovir alafenamide products, or with adefovir. ***Other warnings/precautions:*** • Appropriate use: Hepatitis B coinfection: In patients coinfected with HIV and HBV, an appropriate antiretroviral combination should be selected due to HIV resistance potential; these patients should receive tenofovir dosed for HIV therapy.
Storage	Store at 25°C, excursions are permitted between 15°C and 30°C. Dispense only in original container. Refer to manufacturer PIL if there are specific considerations.

4. Zidovudine

Generic Name	Zidovudine
Dosage form/strengths	Capsule 100 mg,250mg Tablet: 300 mg
Route of administration	*Oral*
Pharmacologic category	Antiretroviral, Reverse Transcriptase Inhibitor, Nucleoside (Anti-HIV) ATC: J05AF01
Indications	Treatment of HIV-1 infection in combination with other antiretroviral agents Perinatal HIV-1 transmission, prevention
Dosage Regimen	Adults: **Prevention of perinatal HIV transmission**: Zidovudine should be administered by continuous IV infusion near delivery in women with known or suspected HIV RNA >1,000 copies/mL or unknown HIV RNA status; use may be considered in women with HIV RNA between 50 and 999 copies/mL. If oral zidovudine was part of the antepartum regimen, discontinue during intrapartum IV infusion and Other antiretroviral agents should be continued orally. **IV (preferred route):** During labor and delivery: Loading dose: 2 mg/kg followed by a continuous IV infusion of 1 mg/kg/hour until clamping of the umbilical cord. For scheduled cesarean delivery, begin IV zidovudine 3 hours before surgery. Dosage based on total body weight. **Oral (if IV not possible):** Loading dose: 600 mg, then 400 mg every 3 hours **HIV-1 infection, treatment** Oral: 300 mg twice daily IV: 1 mg/kg/dose administered every 4 hours around-the-clock (6 doses daily) **Pediatrics:** **HIV-1 infection, treatment:** **Infants (postconceptional age [PCA] ≥35 weeks and PNA ≥4 weeks), Children, and Adolescents:** ○ Weight-directed dosing: Oral: <9 kg: 12 mg/kg/dose twice daily. 9 to <30 kg: 9 mg/kg/dose twice daily. ≥30 kg: 300 mg twice daily. ○ BSA-directed dosing: Oral: 240 mg/m2/dose every 12 hours, ○ Range: 180 to 240mg/ m2/ dose every 12 hours (maximum dose: 300 mg/dose). **Dosing adjustment for hematologic toxicity:** interruption of therapy for significant anemia (Hgb <7.5 g/dL or >25% decrease from baseline) and/or significant neutropenia (ANC <750 cells/mm3 or >50% decrease from baseline) until evidence of bone marrow recovery occurs; once bone marrow recovers, dose may be resumed using appropriate adjunctive therapy
Dosage adjustment	**Renal impairment in adults** CrCl ≥15 mL/minute: No dosage adjustment necessary. CrCl <15 mL/minute: Oral: 100 mg 3 or 4 times daily or 300 mg once daily End-stage renal disease on intermittent hemodialysis (administer dose after dialysis on dialysis days): 100 mg 3 times daily or 300 mg once daily **Peritoneal dialysis:** Oral: 100 mg every 6 to 8 hours. **Hepatic impairment in adults:**

	There are no specific dosage adjustments available. However, adjustment may be necessary due to extensive hepatic metabolism. Closely monitor patients for hematologic toxicities.
Contra-indications	Potentially life-threatening hypersensitivity to zidovudine or any component of the formulation Neutrophil count <750/mm3 or hemoglobin <7.5 g/dL
Adverse Drug Reactions	**Central nervous system:** Headache (63%), malaise (53%) **Dermatologic:** Skin rash **Gastrointestinal**: Nausea, anorexia (20%), vomiting **Hematologic & oncologic:** Macrocytosis (infants, children, & adolescents: >50%), anemia (neonates: 22%; infants, children, & adolescents: 4%; adults, grades 3/4: 1%), Lymphadenopathy, neutropenia, splenomegaly, thrombocytopenia **Hepatic:** Hepatomegaly increased ALT, AST **Respiratory**: Cough (infants, children, & adolescents: 15%) Fever (infants, children, & adolescents: 25%) **Cardiovascular:** Cardiac failure (<6%), ECG abnormality, edema Weight loss
Monitoring Parameters	CBC with differential; LFTs; serum creatinine; HIV viral load and CD4 count.
Drug Interactions	***Risk X: Avoid combination*** Amodiaquine BCG (Intravesical) Cladribine Dipyrone Stavudine ***Risk D: Consider therapy modification*** Clarithromycin Deferiprone Doxorubicin (Conventional) Doxorubicin (Liposomal) Ribavirin (Oral Inhalation) Ribavirin (Systemic)
Pregnancy and Lactation	The Health and Human Services (HHS) perinatal HIV guidelines consider zidovudine an alternative NRTI for pregnant females living with HIV who are antiretroviral-naive, who have had ART therapy in the past but are restarting, or who require a new ART regimen (due to poor tolerance or poor virologic response of current regimen). In addition, females who become pregnant while taking zidovudine may continue if viral suppression is effective and the regimen is well tolerated. The pharmacokinetics of zidovudine are not significantly altered in pregnancy and dosing adjustment is not needed. Zidovudine has been well studied during breastfeeding. Milk levels are low and most breastfed infants do not have detectable blood levels. Some breastfed infants have developed anemia during maternal therapy.
Administration	May be administered without regard to meals. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	Hematologic toxicity (neutropenia and severe anemia), Immune reconstitution syndrome, Lactic acidosis/hepatomegaly, lipoatrophy, myopathy
Storage	Store at 15°C to 25°C Protect capsules from moisture. Refer to manufacturer PIL if there are specific considerations.

b) Non-nucleoside reverse transcriptase inhibitors

5. Nevirapine (NVP)

Generic Name	Nevirapine
Dosage form/strengths	Tablet:200 mg
Route of administration	*Oral*
Pharmacologic category	Antiretroviral, Reverse Transcriptase Inhibitor, Non-nucleoside (Anti-HIV) ATC: J05AG01
Indications	Treatment of HIV-1, in combination therapy with other antiretroviral agents, in adults and pediatric patients ≥15 days of age (immediate release) and ≥6 years of age with a BSA of ≥1.17 m^2. Not recommended as a component of initial therapy for the treatment of HIV, unless the benefit outweighs the risk, in adult females with CD4+ cell counts >250 cells/mm3 or adult males with CD4+ cell counts >400 cells/mm3.
Dosage Regimen	**HIV-1 infection, treatment: Oral, Adults**: Initial: *Immediate release:* 200 mg once daily for 14 days Maintenance: *Immediate release:* 200 mg twice daily (in combination with additional antiretroviral agents) if there is no rash or untoward effects during initial dosing period **HIV-1 infection, treatment: Oral, Pediatrics:** ○ Infants and Children <8 years: **With lead-in dosing**: Initial: 200 mg/m^2/dose once daily (maximum dose: 200 mg/dose) for the first 14 days of therapy; increase to 200 mg/m^2/dose twice daily (maximum dose: 200 mg/dose) **Without lead-in dosing:** Infants and Children <2 years: 200 mg/m^2/dose twice daily (maximum dose: 200 mg/dose). ○ Children ≥8 years: **Initial (lead-in dosing):** 120 to 150 mg/m^2/dose once daily (maximum dose: 200 mg/dose) for the first 14 days of therapy; increase to 120 to 150 mg/m^2/dose twice daily (maximum dose: 200 mg/dose) if no rash or other adverse effects occur. ○ Adolescents: **Initial:** 200 mg once daily for the first 14 days; increase to 200 mg every 12 hours if no rash or other adverse effects occur; if patient able to swallow tablets whole, may convert maintenance dose to the extended release formulation (400 mg once daily). If nevirapine therapy is interrupted for ≤14 days (infants/children) or <7 days (adolescents), restart at the full-dose due to mechanisms of nevirapine resistance
Dosage adjustment	**renal impairment** **CrCl <20 mL/minute:** There are no dosage adjustments (has not been studied). **Hemodialysis**: An additional 200 mg *immediate release* dose is recommended following dialysis **hepatic impairment** Permanently discontinue if symptomatic hepatic events occur. Mild impairment (Child-Pugh class A): There are no dosage adjustments; use with caution. Moderate to severe impairment (Child-Pugh class B or C): Use is contraindicated

Contra-indications	Moderate to severe hepatic impairment (Child-Pugh class B or C); use in occupational or nonoccupational postexposure prophylaxis (PEP) regimens hypersensitivity to nevirapine or any component of the formulation
Adverse Drug Reactions	**Endocrine & metabolic:** Increased serum cholesterol (3% to 19%), increased LDL cholesterol **Hematologic & oncologic:** Decreased serum phosphate (≤38%), neutropenia (1% to 13%) **Hepatic:** Increased serum alanine aminotransferase (2% to 14%)
Monitoring Parameters	Monitor CBC and viral load. Intensive monitoring is required during the initial 18 weeks of therapy to detect potentially life-threatening hepatic, dermatologic, and hypersensitivity reactions. Baseline and repeat liver function tests. Assess/evaluate AST/ALT immediately in any patients with a rash
Drug Interactions	***Risk X: Avoid combination*** Atazanavir CarBAMazepine Dolutegravir Elvitegravir Ergonovine Itraconazole Ketoconazole (Systemic) Letermovir Reverse Transcriptase Inhibitors (Non-Nucleoside) Saquinavir Simeprevir St John's Wort Velpatasvir ***Risk D: Consider therapy modification*** Caspofungin Clarithromycin CYP3A4 Inducers (Strong) Daclatasvir Darunavir Fosamprenavir Indinavir Lopinavir Ubrogepant
Pregnancy and Lactation	The Health and Human Services (HHS) perinatal HIV guidelines **do not** recommend nevirapine as an initial non-nucleoside reverse transcriptase inhibitor for use in antiretroviral-naive pregnant patients because of the potential for adverse events, complex dosing, and low barrier to resistance. Use is not recommended (except in special circumstances) Severe, life-threatening, and in some cases fatal hepatotoxicity, particularly in the first 18 weeks, has been reported in patients treated with nevirapine
Administration	May be administered with or without food. May be administered with an antacid. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	Fat redistribution, hepatotoxicity, Severe, life-threatening skin reactions, Immune reconstitution syndrome, Rhabdomyolysis.
Storage	Store at 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.

6. Efavirenz (EFV)

Generic Name	Efavirenz
Dosage form/strengths	Tablets , capsules : 200mg , 600 mg
Route of administration	*Oral*
Pharmacologic category	Antiretroviral, Reverse Transcriptase Inhibitor, Non-nucleoside (Anti-HIV) ATC: J05AG03
Indications	HIV-1 infection: Treatment of HIV-1 infection in combination with other antiretroviral agents in adults and pediatric patients at least 3 months old and weighing at least 3.5 kg. Alternative first-line regimen in adults and adolescents in combination to tenofovir and lamivudine
Dosage Regimen	**Dosing: Adult** **HIV-1 infection, treatment:** **Oral:** 600 mg once daily, in combination with other appropriate agents; 400 mg once daily may be used in combination with tenofovir and lamivudine **Dosing: Pediatric** **HIV-1 infection, treatment:** Use in combination with other antiretroviral agents: Infants <3 months or <3 kg: Not recommended for use. Infants ≥3 months weighing ≥3 kg and Children <3 years: Oral: BSA-directed dosing: Oral: 367 mg/**m²**/dose once daily, maximum dose: 600 mg/dose; recommended by some experts
Dosage adjustment	**Renal impairment:** No dosage adjustment necessary **hepatic impairment** Mild impairment (Child-Pugh class A): No dosage adjustment necessary; use with caution. Moderate-to-severe impairment (Child-Pugh class B or C): Use is not recommended.
Contra-indications	Hypersensitivity (eg, Stevens-Johnson syndrome) to efavirenz or any component of the formulation
Adverse Drug Reactions	Dermatologic: Skin rash (5% to 32%) Endocrine & metabolic: Increased serum cholesterol (20% to 40%), increased HDL cholesterol (25% to 35%), increased serum triglycerides (≥751 mg/dL: 6% to 11%) Gastrointestinal: Diarrhea (3% to 14%) Nervous system: Central nervous system toxicity (53%), dizziness (2% to 28%), depression (3% to 19%), insomnia (7% to 16%), anxiety (2% to 13%), pain (1% to 13%)
Monitoring Parameters	Serum transaminases; cholesterol and triglycerides (prior to therapy and periodically during); signs and symptoms of infection; psychiatric effects
Drug Interactions	**Long list of interactions should be checked before administration, include:** Atazanavir: Efavirenz may decrease the serum concentration of Atazanavir. Management: the adult atazanavir dose should be 400 mg daily, boosted with ritonavir 100 mg daily for treatment-naive patients only; treatment-experienced patients should not use atazanavir with efavirenz. *Risk D: Consider therapy modification* Bromperidol: May enhance the CNS depressant effect of CNS Depressants. *Risk X: Avoid combination* CarBAMazepine: May decrease the serum concentration of Efavirenz. Efavirenz may decrease the serum concentration of CarBAMazepine. *Risk X: Avoid combination* Caspofungin: efavirenz may decrease the serum concentration of Caspofungin.

	Management: Consider using an increased caspofungin dose of 70 mg daily in adults (or 70 mg/m^2, up to a maximum of 70 mg, daily in pediatric patients) *Risk D: Consider therapy modification* Clarithromycin: Efavirenz may enhance the QTc-prolonging effect of Clarithromycin & may decrease the serum concentration of Clarithromycin Management: Consider using an alternative antibiotic in patients taking efavirenz or monitor for decreased therapeutic effect of clarithromycin and for QT interval prolongation. *Risk D: Consider therapy modification* Darunavir: May increase the serum concentration of Efavirenz. Efavirenz may decrease the serum concentration of Darunavir. Management: Monitor for decreased concentrations and effects of darunavir and/or increased concentrations and effects of efavirenz *Risk D: Consider therapy modification* Itraconazole: Efavirenz may decrease the serum concentration of Itraconazole. *Risk X: Avoid combination* Maraviroc: Efavirenz may decrease the serum concentration of Maraviroc. Management: Increase maraviroc adult dose to 600mg twice/day, but only in the absence of a concurrent strong CYP3A4 inhibitor. Not recommended for pediatric patients not also receiving a strong CYP3A4 inhibitor. Do not use in patients with CrCl less than 30 mL/min. *Risk D: Consider therapy modification* Nevirapine: May enhance the adverse/toxic effect of Efavirenz. Efavirenz may enhance the adverse/toxic effect of Nevirapine. Nevirapine may decrease the serum concentration of Efavirenz. *Risk X: Avoid combination* Orphenadrine: CNS Depressants may enhance the CNS depressant effect of Orphenadrine. *Risk X: Avoid combination* Progestins (Contraceptive): Efavirenz may decrease the serum concentration of Progestins (Contraceptive). Management: Use an alternative or additional method of contraception Injected depot medroxyprogesterone acetate does not appear to participate in this interaction. *Risk D: Consider therapy modification* Simeprevir: CYP3A4 Inducers (Moderate) may decrease the serum concentration of Simeprevir. *Risk X: Avoid combination* Voriconazole: Efavirenz may decrease the serum concentration of Voriconazole. Voriconazole may increase the serum concentration of Efavirenz. Management: The voriconazole oral maintenance dose should be increased to 400 mg every 12 hours, and the efavirenz dose should be reduced to 300 mg daily. *Risk D: Consider therapy modification*
Pregnancy and lactation	The Health and Human Services (HHS) perinatal HIV guidelines consider efavirenz an alternative ART for pregnant females living with HIV who are antiretroviral-naive, who have had ART therapy in the past but are restarting, or who require a new ART regimen (due to poor tolerance or poor virologic response of current regimen). Females who become pregnant while taking efavirenz may continue if viral suppression is effective and the regimen is well tolerated. Efavirenz is present in breast milk. Treatment of mothers of HIV-positive mothers with efavirenz does not appear to affect growth and development of their HIV-negative breastfed infants.
Administration	Administer on an empty stomach. Dosing at bedtime is recommended to limit central nervous system effects. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• May cause CNS effects (eg, abnormal dreams, insomnia, impaired concentration, hallucinations, dizziness, drowsiness); symptoms usually begin within 1 to 2 days after

	starting efavirenz, and generally resolve within 2 to 4 weeks of continued therapy; dosing at bedtime may improve tolerability • Fat redistribution: May cause redistribution/accumulation of fat • Hepatotoxicity: Hepatitis, including fulminant hepatitis progressing to hepatic failure (sometimes fatal or requiring transplantation), has been reported, including patients with no preexisting hepatic disease or other identifiable risk factors. • Hypercholesterolemia • Serious psychiatric side effects have been associated with use • QT prolongation • Use with caution in patients with a history of seizure disorder; dementia or hepatic toxicity.
Storage	15°C to 30°C Refer to manufacturer PIL if there are specific considerations.

c) Protease inhibitors

7. Atazanavir (ATV)

Generic Name	Atazanavir
Dosage form/strengths	Capsules: 100 mg, 150 mg, 200 mg.
Route of administration	*Oral*
Pharmacologic category	Antiretroviral, Protease Inhibitor (Anti-HIV) ATC: J05AE08
Indications	Treatment of HIV-1 infections in combination with other antiviral drugs in patients ≥3 months of age weighing ≥5 kg.
Dosage Regimen	**Adults:** 300 mg of atazanavir + 100 mg of ritonavir **or** atazanavir 400 mg once daily in patients unable to tolerate ritonavir in antiretroviral-naïve patients. Note: Atazanavir without ritonavir is not recommended in antiretroviral-experienced patients with prior virologic failure. **Pediatrics: (***Boosted regimen (preferred regimen)* **Oral powder: Infants ≥3 months, Children, and Adolescents: Oral:** 5 to <15 kg: Atazanavir 200 mg once daily plus ritonavir 80 mg once daily. In antiretroviral-naive patients weighing 5 to <10 kg unable to tolerate this dose, may use atazanavir 150 mg once daily plus ritonavir 80 mg once daily with close HIV viral load monitoring. 15 to <25 kg: Atazanavir 250 mg once daily plus ritonavir 80 mg once daily. ≥25 kg (who cannot swallow a capsule): Atazanavir 300 mg oncedaily plus ritonavir 100 mg once daily. **Oral capsule: Children ≥6 years weighing ≥15 kg and Adolescents <18 years: Oral:** 15 kg to <35 kg: Atazanavir 200 mg once daily plus ritonavir 100 mg once daily. ≥35 kg: Atazanavir 300 mg once daily plus ritonavir 100 mg once daily **Adolescents ≥18 years:** Oral: Atazanavir 300 mg once daily plus ritonavir 100mg once daily **Unboosted regimen: Note: Boosted atazanavir dosing regimen is preferred;** guidelines do not recommend unboosted regimens unless patient is ≥13 years and not receiving concurrent tenofovir; closely monitor plasma concentrations to ensure adequate concentrations are achieved. Oral powder should not be used for unboosted regimens. >6 to <13 years: Oral capsule: Oral: Atazanavir 520 mg/m2/dose once daily 13 to <18 years: Oral capsule: Oral: Atazanavir 620 mg/m2/dose once daily Adolescents ≥18 years: Oral capsule: Oral: Atazanavir 400 mg once daily.
Dosage adjustment	**Renal Impairment** **No change in patients with mild to severe impairment.** **End-stage renal disease:** atazanavir is not appreciably removed during hemodialysis Antiretroviral-naive patients: Atazanavir 300 mg plus ritonavir 100 mg once daily Antiretroviral-experienced patients: Not recommended **Hepatic Impairment** **Adult: Atazanavir without ritonavir in antiretroviral-naïvepatients:**

	Mild impairment (Child-Pugh A): 400 mg daily. Moderate impairment (Child-Pugh B): 300 mg daily. Severe impairment (Child-Pugh C): not recommended. *Atammmmmzanavir with ritonavir is not recommended for hepatic patients (has not been studied).* ***Pediatric*** *:*Boosted regimens (with ritonavir): Infants, Children, and Adolescents: Mild to severe impairment: Use is not recommended
Contra-indications	Hypersensitivity to atazanavir or other components of the formulation.
Adverse Drug Reactions	Skin rash – elevated serum cholesterol – elevated amylase – elevated serum bilirubin – jaundice – cough – fever – elevated creatine phosphokinase, cough (more in children), fever .
Monitoring Parameters	Lipid profile – AST – ALT – Billirubin - Virologic response, hypersensitivity reaction,GIT disturbance.
Drug Interactions	***Risk X: Avoid combination*** Abametapir Acalabrutinib Alfuzosin Alprazolam Aprepitant Astemizole Asunaprevir Avanafil Avapritinib Barnidipine Belinostat Blonanserin Bosutinib Budesonide (Topical) Buprenorphine Cisapride Cobimetinib Conivaptan Dapoxetine Domperidone Doxorubicin Dronedarone Elagolix Eletriptan Eplerenone Ergot Derivatives Flibanserin Fluticasone (Nasal) Fosaprepitant Fusidic Acid (Systemic) Glecaprevir And Pibrentasvir Grazoprevir Ibrutinib Indinavir Infigratinib Isavuconazonium Sulfate Ivabradine Lefamulin Lemborexant Lercanidipine Lomitapide Lonafarnib Lovastatin Lumateperone Lurbinectedin Macitentan Midazolam Naloxegol Neratinib Nevirapine Nimodipine Nisoldipine Ombitasvir, Paritaprevir, And Ritonavir Paclitaxel Pazopanib Pimozide Pralsetinib Radotinib Ranolazine Red Yeast Rice Regorafenib Repaglinide Revefenacin Rifampin Rimegepant Rupatadine Sacituzumab Govitecan Salmeterol Saquinavir Silodosin Simeprevir Simvastatin Sonidegib St John's Wort Suvorexant Tamsulosin Tazemetostat Terfenadine Ticagrelor Tipranavir Tolvaptan Topotecan Trabectedin Triazolam Ubrogepant Udenafil Ulipristal Vincristine (Liposomal) Vinflunine Voclosporin Vorapaxar Voriconazole Voxilaprevir
Pregnancy and Lactation	Atazanavir crosses placental barrier in low amounts. Malformative risk with use of this drug in pregnant women is unlikely. The use of atazanavir in pregnancy without a booster is not recommended. Breastfeeding is not recommended during use of this drug; if replacement feeding is not an option, a different drug may be preferred.
Administration	Administer with food. Administer atazanavir 2 hours before or 1 hour after antacids. Administer atazanavir (with ritonavir) simultaneously with, or at least 10hours after, H2-receptor antagonists, 12 hours after proton pump inhibitor Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	Elevated bilirubin - Fat redistribution - Hypersensitivity reactions - Immune reconstitution syndrome - Nephrolithiasis/cholelithiasis Caution in patients with diabetes, Hemophilia A or B, or patients with hepatic or renal diseases
Storage	Store between 15°C and 30°C. Refer to manufacturer PIL if there are specific considerations.

8. Lopinavir and Ritonavir

Generic Name	Lopinavir/Ritonavir
Dosage form/strengths	Solution, oral: Lopinavir 80 mg and ritonavir 20 mg per 1 mL Tablet: Lopinavir 200 mg and ritonavir 50 mg
Route of administration	*Oral*
Pharmacologic category	Antiretroviral, Protease Inhibitor (Anti-HIV)
Indications	Treatment of HIV-1 infection in adults and pediatric patients 14 days and older in combination with other antiretroviral agents. Not recommended as a component of initial therapy for the treatment of HIV.
Dosage Regimen	**HIV-1 infection, treatment (as a component of combination therapy): Oral,** **Adults:** ○ **Patients receiving concomitant antiretroviral therapy without efavirenz, nelfinavir, or nevirapine:** Twice-daily dosing: Lopinavir 400 mg/ritonavir 100 mg twice daily. Once-daily dosing: Therapy-naive or experienced patients with <3 lopinavir Resistance-associated substitutions: Lopinavir 800 mg/ritonavir 200 mg once daily. ○ **Dosage adjustment for combination therapy with efavirenz, nelfinavir, or nevirapine:** Oral: Solution: Lopinavir 520 mg/ritonavir 130 mg (6.5 mL) twice daily. Tablet: Lopinavir 500 mg/ritonavir 125 mg twice daily ○ **Pregnant women**: tablet, oral: Lopinavir 400 mg/ritonavir 100 mg twice, may increasedose of lopinavir 600 mg/ritonavir 150 mg twice daily, or lopinavir 500 mg/ritonavir 125 mg twice daily, during the second and third trimesters of pregnancy avoid use once daily or solution form. **HIV-1 infection, treatment (as a component of combination therapy): Oral** **, Pediatrics:** Use of tablets in patients <15 kg or <0.6 m2 is not recommended; oral solution preferable. Once-daily dosing is not recommended in children <18 years of age. ○ **(Infants (≥42 weeks PMA):** Patients not receiving concomitant efavirenz, nelfinavir, or nevirapine: Lopinavir 16mg/kg/dose or 300mg/ m2/dose, Twice daily. Patients with concomitant efavirenz, nelfinavir, or nevirapine: lopinavir/ritonavir is not recommended in infants who are receiving these agents. ○ **Children and Adolescents:** Patients not receiving concomitant efavirenz, nelfinavir, or nevirapine: <15 kg: Lopinavir 12 mg/kg/dose twice daily. 15 to 40 kg: Lopinavir 10 mg/kg/dose twice daily. >40 kg: Lopinavir 400 mg twice daily. Patients with concomitant efavirenz, nelfinavir, or nevirapine: <15 kg: Lopinavir 13 mg/kg/dose twice daily. ≥15 to 45 kg: Lopinavir 11 mg/kg/dose twice daily. >45 kg: Adult dose **HIV-1 nonoccupational postexposure prophylaxis (nPEP):** Initiate therapy within 72 hours of exposure and continue for 28 days; use in combination with other antiretroviral agents. Oral:

	the same dose of HIV-1infection treatment in pediratric
Dosage adjustment	**renal impairment** No dosage adjustments provided. Hemodialysis: Avoid once-daily dosing **hepatic impairment** • Mild to moderate impairment: There are no dosages adjustments use with caution. • Severe impairment: There are no dosage adjustments (has not been studied); use with caution
Contra-indications	Hypersensitivity (eg, toxic epidermal necrolysis, Stevens-Johnson syndrome,) to lopinavir, ritonavir, or any component of the formulation
Adverse Drug Reactions	**Dermatologic**: Skin rash (children 12%; adults ≤5%) **Endocrine & metabolic**: Hypercholesterolemia (3% to 39%), increased serum triglycerides (3% to 36%), hyrglycemia **Gastrointestinal**: Diarrhea (greater with once-daily dosing), dysgeusia, vomiting **Hepatic**: Increased serum ALT (grade 3/4: 1% to 11%) **Respiratory:** Upper respiratory tract infection (14%) **Cardiovascular**: Vasodilation (≤3%) **Hematologic & oncologic**: Thrombocytopenia (4% children), neutropenia (1% to 5%)
Monitoring Parameters	Prior to therapy, consider genotypic or phenotypic testing for lopinavir resistance-associated substitutions. Triglycerides and cholesterol (prior to initiation then periodically thereafter), LFTs, electrolytes, glucose
Drug Interactions	***Risk X: Avoid combination*** Acalabrutinib Alfuzosin Alprazolam Antihepaciviral Combination Products Aprepitant Astemizole Asunaprevir Avanafil Avapritinib Barnidipine Bilastine Blonanserin Bosutinib Budesonide (Topical) Cabotegravir Cisapride Clobetasone Cobicistat Cobimetinib Conivaptan Dapoxetine Darunavir Disulfiram Domperidone Doxorubicin (Conventional) Dronedarone Elagolix Elagolix, Estradiol, And Norethindrone Eletriptan Eplerenone Everolimus Flecainide Flibanserin Fosamprenavir Fosaprepitant Fusidic Acid (Systemic) Grazoprevir Ibrutinib Infigratinib Isavuconazonium Sulfate Ivabradine Lefamulin Lemborexant Lercanidipine Letermovir Lomitapide Lonafarnib Lovastatin Lumateperone Lurasidone Lurbinectedin Macitentan Meptazinol Methotrimeprazine Metronidazole (Systemic) Midazolam Naloxegol Neratinib Nimodipine Nisoldipine Pazopanib Pazopanib Pimozide Pralsetinib Propafenone Quinidine Quinine Radotinib Ranolazinered Yeast Rice Regorafenib Revefenacin Rifampin Rimegepantrivaroxabanrupatadinesacituzumab Govitecan Salmeterol Silodosin Simeprevir Simvastatin Sonidegib St John's Wortsuvorexant Tamsulosin Tazemetostat Tepotinib Ticagrelor Tipranavir Tolvaptan Topotecan Trabectedin Triazolam Ubrogepant Ulipristal Vardenafi Lvincristine (Liposomal) Vinflunine Voclosporin Vorapaxar Voriconazole Voxilaprevir
Pregnancy and Lactation	Lopinavir has a low level of transfer across the human placenta; fetal exposure is increased with ritonavir. Based on information collected by the Antiretroviral Pregnancy Registry, an increased risk of teratogenic effects has not been observed in humans. Breastfeeding is not recommended during use of this drug.
Administration	**Solution**: Must be administered with food **Tablet**: May be taken with or without food. Swallow whole, do not break, crush, or chew. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Cardiovascular concerns: Possible higher risk of myocardial infarction associated with the cumulative use of lopinavir/ritonavir; consider avoiding lopinavir/ritonavir-based regimens in patients with high cardiac risk.

	• May alter cardiac conduction and prolong the QTc and/or PR interval. • Fat redistribution. • Hepatotoxicity, use with caution in patients with Hepatitis B or C and cirrhosis. • Immune reconstitution syndrome. • Increased cholesterol. • Changes in glucose tolerance, hyperglycemia, exacerbation of diabetes, DKA, • Use with caution in patients with hemophilia A or B • Hepatic impairment: Use with caution; lopinavir concentrations may be increased. • Pancreatitis: Use with caution in patients with increased triglycerides
Storage	Oral solution: Store at 2°C to 8°C, Avoid exposure to excessive heat. If stored at 25°C use within 2 months. Tablet: Store at 15°C to 30°C. Exposure to high humidity outside of the original container >2 weeks is not recommended Refer to manufacturer PIL if there are specific considerations.

9. Darunavir and ritonavir (DRV/r)

Generic Name	Darunavir/ritonavir
Dosage form/strengths	Suspension, Oral: 100 mg/mL (200 mL) Tablet, Oral: 75 mg, 150 mg ,600 mg, 800 mg
Route of administration	*Oral*
Pharmacologic category	Antiretroviral, Protease Inhibitor (Anti-HIV). Binds to the site of HIV-1 protease activity. This results in the formation of immature, noninfectious viral particles. ATC: J05AR26
Indications	• Treatment of HIV-1 infection, coadministered with ritonavir and other antiretroviral agents, in adults and pediatric patients 3 years and older • Alternative second-line regimen in Adults, adolescents, Children and infants in combination with zidovudine and lamivudine HIV-1 infection, nonoccupational postexposure prophylaxisin combination with other antiretroviral agents
Dosage Regimen	***Dosing: Adult*** • ***Treatment naïve or experienced patients with no darunavir resistance-associated substitutions:*** Oral: 800 mg once daily; coadministrated with ritonavir 100 mg • ***Treatment experienced*With ≥1 darunavir resistance-associated substitution or If genotypic testing is not possible:** 600 mg twice daily; coadministrated with ritonavir 100 mg twice daily. • ***Pregnant patients:*** Oral: 600 mg twice daily, coadministered with ritonavir 100 mg twice daily. • **HIV-1 infection, nonoccupational postexposure prophylaxis:** Oral: 800 mg **plus** ritonavir 100 mg once daily (in combination with other antiretroviral agents); initiate therapy within 72 hours of exposure and continue for 28 days ***Dosing: Pediatric*** **Children 3 to 11 years weighing ≥10 kg**: *Treatment-naive patients or treatment-experienced patients without or with darunavir resistance-testing results that demonstrate at least one mutation associated with resistance* Fixed-dosing: Tablets, Oral solution (darunavir: 100 mg/mL): 10 kg to <11 kg: Darunavir 200 mg (2 mL) twice daily **plus** ritonavir 32 mg twice daily. 11 kg to <12 kg: Darunavir 220 mg (2.2 mL) twice daily **plus** ritonavir 32 mg twice daily. 12 kg to <13 kg: Darunavir 240 mg (2.4 mL) twice daily **plus** ritonavir 40 mg twice daily. 13 kg to <14 kg: Darunavir 260 mg (2.6 mL) twice daily **plus** ritonavir 40 mg twice daily. 14 kg to <15 kg: Darunavir 280 mg (2.8 mL) twice daily **plus** ritonavir 48 mg twice daily. 15 kg to <30 kg: Darunavir 375 mg (tablets or 3.8 mL) twice daily **plus** ritonavir 48 mg twice daily. 30 kg to <40 kg: Darunavir 450 mg (tablets or 4.6 mL) twice daily **plus** ritonavir 100 mg twice daily. ≥40 kg: Darunavir 600 mg (tablet or 6 mL) twice daily **plus** ritonavir 100 mg twice daily. **Children ≥12 years and Adolescents weighing 30 to <40 kg:** *Treatment-naive patients or treatment-experienced patients without or with mutations associated with darunavir resistance:*

	Twice-daily regimen: Darunavir 450 mg twice daily **plus** ritonavir 100 mg twice daily. Once-daily regimen: Darunavir 675 mg (combination of tablets) once daily **plus** ritonavir 100 mg once daily; **Children ≥12 years and Adolescents weighing ≥40 kg**: refere to adult dosing
Dosage adjustment	**Dosing: Renal Impairment** No dose adjustment in case of renal impairment **Dosing: Hepatic Impairment** • Mild to moderate impairment (Child-Pugh class A or B): No dosage adjustments necessary • Severe impairment (Child-Pugh class C): Use not recommended.
Contra-indications	• Hypersensitivity to darunavir or any component of the formulation • severe (Child-Pugh class C) hepatic impairment coadministration with amiodarone, apixaban, lidocaine (systemic), rivaroxaban or drugs that are highly dependent on CYP3A for clearance and drugs for which elevated plasma concentrations are associated with serious and/or life-threatening events (narrow therapeutic index).
Adverse Drug Reactions	**Dermatologic:** Skin rash **Endocrine & metabolic:** Increased serum cholesterol, increased LDL cholesterol), increased serum glucose (≤11%) **Gastrointestinal:** Vomiting, nausea, diarrhea (children & adolescents: 11% to 24%; adults: 9% to 14%)
Monitoring Parameters	Viral load, CD4, baseline genotypic and/or phenotypic testing in treatment-experienced patients (if possible); serum glucose; transaminase levels prior to and during therapy (increase monitoring in patients at risk for liver impairment), cholesterol, triglycerides, glucose
Drug Interactions	– **Long list of interactions should be checked before administration, includes:** • **Colchicine:** ritonavir may increase the serum concentration of Colchicine. Management: Colchicine is contraindicated in patients with impaired renal or hepatic function who are also receiving darunavir/ritonavir. In those with normal renal and hepatic function, reduce colchicine dose. *Risk D: Consider therapy modification* • **Domperidone**: darunavir /ritonavir may increase the serum concentration of Domperidone. Management: Drugs listed as exceptions to this monograph are discussed in further detail in separate drug interaction monographs. *Risk X: Avoid combination* • **Dronedarone**: ritonavir may increase the serum concentration of Dronedarone. Management: *Risk X: Avoid combination* • **Efavirenz:** ritonavir may increase the serum concentration of Efavirenz. Efavirenz may decrease the serum concentration of Darunavir. Management: Monitor for decreased concentrations and effects of darunavir and/or increased concentrations and effects of efavirenz *Risk D: Consider therapy modification* • **Eplerenone or ivabradine or lovastatin**: ritonavir may increase the serum concentration of Eplerenone. *Risk X: Avoid combination* • **Estrogen Derivatives (Contraceptive):** Protease Inhibitors may decrease the serum concentration of Estrogen Derivatives (Contraceptive). Management: Use of an alternative, non-hormonal contraceptive is recommended with other protease inhibitors. *Risk D: Consider therapy modification*

	• **Fluticasone (Nasal):** ritonavir may increase the serum concentration of Fluticasone (Nasal). *Risk X: Avoid combination* • **Rifampin or rifapentine**: May decrease the serum concentration of Darunavir. *Risk X: Avoid combination* • **Sildenafil:** ritonavir may increase the serum concentration of Sildenafil. Management: Erectile dysfunction: sildenafil max = 25 mg/48 hrs with ritonavir, contraindicated if sildenafil being used for pulmonary arterial hypertension. *Risk D: Consider therapy modification* • **Simvastatin, lovastatin**: Protease Inhibitors may increase the serum concentration of Simvastatin. *Risk X: Avoid combination* • **Tacrolimus (Systemic):** ritonavir may increase the serum concentration of Tacrolimus (Systemic). Tacrolimus dose reductions or prolongation of dosing interval will likely be required. *Risk D: Consider therapy modification*
Pregnancy and Lactation	• No increased risk of overall birth defects has been observed following first trimester exposure according to data collected by the antiretroviral pregnancy registry. The Health and Human Services (HHS) perinatal HIV guidelines consider darunavir (when combined with low-dose ritonavir boosting) a preferred protease inhibitor for pregnant females living with HIV. Breastfeeding is not recommended during use of this drug; if replacement feeding is not an option, a different drug may be preferred.
Administration	Administer with food. Shake suspension prior to each dose; use provided oral dosing syringe to measure dose. **Missed doses** In patients taking darunavir once daily, if a dose is missed by >12 hours, the next dose should be taken at the regularly scheduled time. If a dose is missed by <12 hours, the dose should be taken immediately and then the next dose should be taken at the regularly scheduled time. In patients taking darunavir twice daily, if a dose is missed by >6 hours, the next dose should be taken at the regularly scheduled time. If a dose is missed by <6 hours, the dose should be taken immediately and then the next dose should be taken at the regularly scheduled time. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Fat redistribution, Hepatotoxicity, Hypersensitivity reactions, Sulfonamide allergy Immune reconstitution syndrome, Diabetes, Hemophilia A or B • Pediatric: Do not administer darunavir with ritonavir in pediatric patients younger than 3 years (toxicity and mortality observed in animal studies).
Storage	Store between 15°C and 30°C. Do not refrigerate or freeze oral suspension. Refer to manufacturer PIL if there are specific considerations.

d) Integrase Inhibitors

10. Dolutegravir (DTG)

Generic Name	Dolutegravir
Dosage form/strengths	Film Coated Tablets: 50 mg
Route of administration	*Oral*
Pharmacologic category	Antiretroviral, Integrase Inhibitor (Anti-HIV) ATC: J05AX12
Indications	Treatment of HIV-1 infection in combination with other antiretroviral agents for treatment naïve or experienced adult or pediatric patients
Dosage Regimen	**Adults:** • **INSTI naive:** 50 mg daily. • **INSTI-naive when coadministered with carbamazepine, efavirenz, or rifampin:** 50 mg twice daily • **INSTI experienced with suspected resistance:** 50 mg twice daily. • **Virologically suppressed patients switching to dolutegravir plus rilpivirine:** 50 mg daily. **Pediatrics:** • *Treatment-naive or treatment-experienced and integrase strand transfer inhibitor (INSTI)-naive:* o Infants and Children weighing 3 to <14 kg: Oral: Soluble tablets for oral suspension: 3 to <6 kg: 5 mg once daily. 6 to <10 kg: 15 mg once daily. 10 to <14 kg: 20 mg once daily. o Infants, Children, and Adolescents weighing ≥14 kg: Oral: Soluble tablets for oral suspension: Preferred in patients <20 kg: 14 to <20 kg: 25 mg once daily. ≥20 kg: 30 mg once daily. Tablets: 14 to <20 kg: 40 mg once daily. ≥20 kg: 50 mg once daily. • *INSTI-experienced with any INSTI-associated resistance mutation or clinically suspected INSTI resistance*: Children and Adolescents weighing ≥40 kg: Oral: Tablets: 50 mg twice daily.
Dosage adjustment	**Dosing: Renal Impairment** ***Treatment-naive or treatment-experienced INSTI-naive:*** **Mild, moderate, or severe impairment:** No dosage adjustment necessary. **INSTI experienced with suspected resistance and creatinie clearance less than 30 ml/min:** it should be used with caution taking into consideration that decreasing dolutegravir doses may lead to loss of therapeutic effect and the development of resistance. **End-stage renal disease:** No dosage adjustments available **Dosing: Hepatic Impairment** **Severe impairment *(*Child-Pugh C):** not recommended Hepatoxicity during therapy (in pediatrics) : If asymptomatic hepatitis, consider

	discontinuation of therapy for ALT or AST >5 times ULN; if symptomatic hepatitis, discontinue therapy
Contra-indications	Hypersensitivity to dolutegravir or any other component in the formulation.
Major Adverse Drug Reactions	Gastrointestinal: Increased serum lipase , Hyperglycemia, Elevated ALT,AST
Monitoring Parameters	ALT – Blood Glucose – Viral load - CD4 count – Monitor signs of hypersensitivity
Drug Interactions	***Risk X: Avoid combination*** Dofetilide Fosphenytoin-Phenytoin Nevirapine Oxcarbazepine Phenobarbital Primidone St John's Wort ***Risk D: Consider therapy modification*** Aluminum Hydroxide Calcium Salts Carbamazepine Dalfampridine Efavirenz Etravirine Fosamprenavir Iron Preparations Magnesium Salts Metformin Multivitamins/Minerals (With ADEK, Folate, Iron) Rifampin Selenium Sucralfate Tipranavir Zinc Salts
Pregnancy and Lactation	A small but significant increase in neural tube defects (NTDs) was observed following maternal use of dolutegravir in a study conducted in Botswana. The risk of NTDs was increased in women who became pregnant while taking dolutegravir, but not in women who started dolutegravir during pregnancy. Dolutegravir has been used safely in HIV-positive mothers during breastfeeding.
Administration	Administer without regard to meals. Administer 2 hours before or 6 hours after cation-containing antacids or laxatives, sucralfate, oral supplements containing iron or calcium. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	Hepatotoxicity, Hypersensitivity reactions, Immune reconstitution syndrome
Storage	Store at 15°C to 30°C, protect from moisture. Refer to manufacturer PIL if there are specific considerations.

11. Raltegravir

Generic Name	Raltegravir
Dosage form/strengths	Tablet, Oral:100 mg ,400mg, 600 mg Sachets, chewable tablets : 25 mg
Route of administration	*Oral*
Pharmacologic category	Antiretroviral, Integrase Inhibitor (Anti-HIV) ATC: J05AX08
Indications	Treatment of HIV-1 infection in combination with other antiretroviral agents HIV-1 nonoccupational& occupational postexposure prophylaxis
Dosage Regimen	**HIV-1 infection, treatment: Adults, Oral:** ○ Treatment-naive patients: 400 mg twice daily or 1,200 mg once daily ○ Treatment-experienced patients: 400 mg twice daily. **HIV-1 nonoccupational & occupational postexposure prophylaxis: Adult, Oral:** 400 mg twice daily for 28 days in combination with other antiretroviral agents. Initiate therapy within 72 hours of exposure **Dosage Modifications,** Treatment-naïve or treatment-experienced when co-administered with rifampin 800 mg (two 400-mg tabs) PO BID. **HIV-1 infection, treatment: Pediatrics:** ○ **Oral Chewable tablets**: Children weighing ≥11 kg: Weight-directed dosing: 6 mg/kg/dose twice daily; maximum dose: 300 mg/dose. ○ **Oral solution:** Infants and Children <20 kg Weight-directed dosing: 6 mg/kg/dose twice daily; maximum dose: 100 mg/dose. ○ **Oral Film Coated Tablets:** Children and Adolescents ≥25 kg to 40 kg: 400 mg twice daily. ○ **Oral Film Coated Tablet:** Children and Adolescents ≥40 kg: 1,200 mg once daily.
Dosage adjustment	**renal impairment** **Mild, moderate, and severe impairment:** No dosage adjustment necessary. **End-stage renal disease (ESRD) on intermittent hemodialysis (IHD):** Dose after dialysis on dialysis days. **hepatic impairment** **Mild-to-moderate impairment**: No dosage adjustment necessary. **Severe impairment**: There are no dosage adjustments (has not been studied). **Film-coated tablet (600 mg formulation**): Use is not recommended in mild, moderate and severe (has not been studied).
Contra-indications	Hypersensitivity to raltegravir or any other component of the formulation.
Adverse Drug Reactions	**Hepatic:** Increased serum ALT, hyperbilirubinemia, increased serum alkaline phosphatase (≤2%), hepatitis (<2%) **Central nervous system**: Headache (≤4%), insomnia (≤4%), abnormal dreams (≥2%), suicidal ideation (<2%), **Endocrine & metabolic:** Increased serum glucose (126 to 250 mg/dL: 7% to 10%; 251 to 500 mg/dL: 2% to 3%) **Gastrointestinal:** Increased serum lipase (≤5%), increased serum amylase **Hematologic & oncologic**: Decrease in absolute neutrophil count (1% to 4%), thrombocytopenia (≤3%), decreased hemoglobin (≤1%)

Monitoring Parameters	Viral load, CD4 count, signs of skin rash, signs/symptoms of depression and suicidal ideation.
Drug Interactions	***Risk X: Avoid combination*** Aluminum Hydroxide Fosamprenavir Magnesium Salts ***Risk D: Consider therapy modification*** Calcium Carbonate Polyvalent Cation Containing Products Rifampin
Pregnancy and Lactation	No increased risk of overall birth defects has been observed following first trimester exposure according to data collected by the antiretroviral pregnancy registry. The Health and Human Services (HHS) Perinatal HIV Guidelines consider raltegravir a preferred integrase strand transfer inhibitor (INSTI) for pregnant females living with HIV Once daily dosing is not recommended for use during pregnancy, Breastfeeding is not recommended while taking Raltegravir
Administration	• May be administered without regard to meals. • Oral suspension: pour packet contents into water at a concentration of 10 mg/mLand swirl in a circular motion for 45 seconds; do not shake. Do not turn the mixing cup upside down. Administer within 30 minutes of mixing with water. Discard any remaining suspension in the trash. • Film-coated tablets and chewable tablets or oral suspension are not bioequivalent and are not substitutable on a mg/mg basis • Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	-Immune reconstitution syndrome, Myopathy, Skin and hypersensitivity reactions. At birth, the enzyme responsible for the metabolism of raltegravir (UGT1A1) is low and Raltegravir elimination in neonates may be prolonged. The activity of UGT1A1 increasee Rapidly over the first 4 to 6 weeks of life. -Do not use in combination with darunavir and ritonavir in patients with HIV RNA >100,000 copies/mL and/or CD4 count <200 cells/mm3, or in combination with abacavir and lamivudine in patients with HIV RNA >100,000 copies/mL).
Storage	Store at 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.

Antitubercular Agent

1. Ethambutol

Generic Name	Ethambutol
Dosage form/strengths	Tablets 500mg
Route of administration	Oral
Pharmacological action	Antitubercular Agent ATC: J04AK02
Indications	**Tuberculosis:** Treatment of pulmonary tuberculosis in conjunction with other antituberculosis agents.
Dosage Regimen	Must be used in conjunction with other antimycobacterial agents for treatment of active (clinical) TB, Can be used in daily or intermittent (e.g., 2 or 3 times weekly) multiple-drug TB regimens **Treatment of Active (Clinical) Tuberculosis:** **Oral: Note:** Always administer in combination with other antitubercular drugs. 15 mg/kg once daily in previously untreated adults. In previously treated adults: 25 mg/kg once daily for 60 days, followed by 15 mg/kg once daily. *Dosing:* Doses should be based on lean body weight for patients within a normal weight range for their height (optimal dosing for obese patients has not been established): Once-daily therapy: **Note:** The preferred frequency of administration is once daily; however, 5-days-per-week administration by directly observed therapy (DOT) is an acceptable alternative Adults weighing 40–55 kg: 800 mg once daily, 2 g twice weekly, or 1.2 g 3 times weekly recommended by ATS, CDC, and IDSA. Adults weighing 56–75 kg: 1.2 g once daily, 2.8 g twice weekly, or 2 g 3 times weekly recommended by ATS, CDC, and IDSA. Adults weighing 76-90 kg: 1.6 g once daily, 4 g twice weekly, or 2.4 g 3 times weekly recommended by ATS, CDC, and IDSA **Treatment of Active (Clinical) Tuberculosis in Children** Children <15 years of age or weighing ≤40 kg 15–25 mg/kg once daily If an intermittent regimen is used, 50 mg/kg twice weekly a maximum dose is 1 g per dose; AAP and others recommend a maximum of 2.5 g per dose. **Treatment of Active (Clinical) Tuberculosis in Adolescents** Adolescents ≥15 years of age weighing 40–55 kg: 800 mg daily, 2 g twice weekly, or 1.2 g 3 times weekly. Adolescents ≥15 years of age weighing 56–75 kg: 1.2 g daily, 2.8 g twice weekly, or 2 g 3 times weekly recommended by ATS, CDC, and IDSA. Adolescents ≥15 years of age weighing 76-90 kg: 1.6 g daily, 4 g twice weekly, or 2.4 g 3 times weekly recommended by ATS, CDC, and IDSA. Adolescents: AAP and others recommend 15–25 mg/kg (up to 2.5 g) once daily or 50 mg/kg twice weekly (up to 2.5 g per dose)
Dosage adjustment	**Altered kidney function Adult:** CrCl ≥30 mL/minute: No dosage adjustment necessary. CrCl <30 mL/minute: If usual recommended dose is administered once daily, then do not adjust the

	dose, but only administer 3 times weekly Hemodialysis, intermittent (thrice weekly): Dialyzable: Dose as CrCl <30 mL/minute; administer after hemodialysis on dialysis days. Use with caution and close monitoring, as hemodialysis patients may develop optic adverse effects, even with properly adjusted doses Peritoneal dialysis: Likely dialyzable **Dosing: Renal Impairment: Pediatric** There are no dosage recommendations specific for pediatric patients; ethambutol is primarily renally excreted; monitor serum levels to determine adjustments; experience in adult patients suggests dosing adjustment necessary. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed; use with caution.
Contra-indications	Hypersensitivity to ethambutol or any component of the formulation; optic neuritis (risk vs benefit decision); use in young children, unconscious patients, or any other patient who may be unable to discern and report visual changes
Adverse Drug Reactions	**Cardiovascular:** Myocarditis, pericarditis **Central nervous system:** Confusion, disorientation, dizziness, hallucination, headache, malaise, peripheral neuritis **Dermatologic:** Dermatitis, erythema multiforme, exfoliative dermatitis, pruritus, skin rash **Endocrine & metabolic**: Acute gout attack, hyperuricemia Gastrointestinal: Abdominal pain, anorexia, gastric distress, nausea, vomiting **Hematologic & oncologic**: Eosinophilia, leukopenia, lymphadenopathy, neutropenia, thrombocytopenia **Hepatic:** Abnormal hepatic function tests, hepatitis, hepatotoxicity (possibly related to concurrent therapy) **Hypersensitivity:** Anaphylaxis, anaphylactoid reaction, hypersensitivity reaction (syndrome includes cutaneous reactions, eosinophilia, and organ-specific inflammation) **Neuromuscular & skeletal:** Arthralgia **Ophthalmic:** Color blindness, decreased visual acuity, optic neuritis, scotoma, visual disturbance (usually reversible with discontinuation; irreversible blindness has been described) **Renal:** Nephritis **Respiratory:** Pneumonitis, pulmonary infiltrates (with or without eosinophilia) **Miscellaneous:** Fever
Monitoring Parameters	Baseline and periodic (monthly) visual testing (Snellen test) and color discrimination tests (each eye individually, as well as both eyes tested together) in patients receiving >15 mg/kg/day; baseline and periodic renal, hepatic, and hematopoietic tests
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Aluminum Hydroxide Sodium Picosulfate Typhoid Vaccine ***Risk C: Monitor therapy*** BCG Vaccine Lactobacillus and Estriol
Pregnancy	**Pregnancy factor C** Ethambutol is present in breast milk. Breastfeeding only if benefits to the mother outweigh the possible risk to the infant. Limited information indicates that maternal doses of ethambutol up to 15 mg/kg daily produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. Breastfed infants should be monitored for jaundice
Administration	Administer orally without regard to meals. If GI upset occurs, administer with food. Tablet may be pulverized and mixed with apple juice or apple sauce. Do not mix with other juices or syrups since

	they do not mask ethambutol's bitter taste or are not stable. Administer ethambutol at least 4 hours before aluminum hydroxide. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hepatic toxicity: Has been reported, possibly due to concurrent therapy. Monitor liver function prior to and during treatment. • Optic neuritis: May cause optic neuritis (unilateral or bilateral), resulting in decreased visual acuity or other vision changes. Discontinue promptly in patients with changes in vision, color blindness, or visual defects (effects normally reversible, but reversal may require up to a year). Irreversible blindness has been reported. Monitor visual acuity prior to and during therapy. ***Disease-related concerns:*** • Ocular disease: Evaluation of visual acuity changes may be more difficult in patients with cataracts, optic neuritis, diabetic retinopathy, and inflammatory conditions of the eye; consideration should be given to whether or not visual changes are related to disease progression or effects of therapy • Renal impairment: Use with caution in patients with renal impairment; dosage modification recommended. Monitor renal function prior to and during treatment. ***Special populations:*** • Pediatric: Use only in children whose visual acuity can accurately be determined and monitored (not recommended for use in children <13 years of age unless the benefit outweighs the risk).
Storage	Store at controlled room temperature of 20°C to 25°C Refer to manufacturer PIL if there are specific considerations.

2. Ethambutol, Isoniazid, Rifampicin, and Pyrazinamide

Generic Name	**Ethambutol , Isoniazid, Rifampicin and Pyrazinamide**
Dosage form/strengths	Tablets: Ethambutol 275 mg ; Rifampicin 150mg ; Isoniazid 75 mg ; Pyrazinamide 400 mg
Route of administration	Oral
Pharmacologic action	Antibacterial (antimycobacterial) ATC: J04AM06
Indications	used to treat tuberculosis (TB) in adults and children at least 15 years old.
Dosage Regimen	**Rifampin, Isoniazid, Pyrazinamide, and Ethambutol tablets** The World Health Organization (WHO) recommends the fixed-dose combination of rifampin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg, and ethambutol 275 mg for the daily administration in the initial phase of tuberculosis treatment **Usual Adult Dose** [Tuberculosis] Patients weighing between 30 and 39 kg: Oral, 2 tablets once a day Patients weighing between 40 and 54 kg: Oral, 3 tablets once a day Patients weighing between 55 and 70 kg: Oral, 4 tablets once a day Patients weighing 71 kg or more: Oral, 5 tablets once a day **Usual Pediatric Dose** [Tuberculosis] Infants and children under 30 kg of body weight: Use is not recommended. Children weighing 30 kg or more: See Usual adult dose The duration of treatment with an antituberculosis regimen is at least 6 months, and treatment may be continued for 2 years
Dosage adjustment	**Renal function impairment** Moderate renal impairment (creatinine clearance 30 – 60 ml/min): use with caution Severe renal impairment (creatinine clearance < 30 ml/min): use is contra-indicated **Hepatic function impairment:** use with caution in impaired liver function. contraindicated in patients with a history of drug induced hepatitis and in patients with acute liver diseases
Contra-indications	Hypersensitivity to rifampin, isoniazid, pyrazinamide, ethionamide, niacin (nicotinic acid), rifabutin, rifapentine, or other chemically related medications
Adverse Drug Reactions	Refer to individual drug monographs.
Monitoring Parameters	Hepatic function determinations (ALT [SGPT], AST [SGOT], alkaline phosphatase, and serum bilirubin determinations may be indicated prior to and monthly or more frequently during treatment, Ophthalmologic examinations, Uric acid concentrations, serum
Drug Interactions	Refer to individual drugs
Pregnancy and Lactation	**Pregnancy Category C** breastfeeding should not be discouraged in women taking this drug. breastfed infants should be monitored for the signs/symptoms of toxicity (e.g., arthralgia, fever,

	hepatitis, jaundice, loss of appetite, nausea, rash, thrombocytopenia, vomiting).
Administration	tablets are administered orally. The tablets should be given as a single dose (number of tablets depending on the patient's bodyweight), in a fasting state at least 1 hour before a meal.
Warnings/ Precautions	Alcoholism, active or in remission (increased risk of hepatitis with daily consumption of alcohol Gout, history of (pyrazinamide and ethambutol can increase serum uric acid concentrations and precipitate an acute attack of gout » Hepatic function impairment, severe (rifampin, isoniazid, and pyrazinamide are metabolized in the liver and may also be hepatotoxic » Hypersensitivity to isoniazid, ethambutol, ethionamide, pyrazinamide, niacin (nicotinic acid), or other chemically related medications Hypersensitivity to rifampin, rifabutin, and/or rifapentine » Optic neuritis (ethambutol may cause retrobulbar optic neuritis » Renal function impairment (ethambutol is excreted primarily through the kidneys, patients with a renal function impairment may require a reduction in dosage; there may be an increased risk of isoniazid toxicity in patients who have severe renal failure [creatinine clearance < 10 mL/min or 0.17 mL/sec] Seizure disorders (isoniazid may be neurotoxic and cause seizure)
Storage	Do not store above 25°C. Store in the original package in order to protect from moisture. Refer to manufacturer PIL if there are specific considerations.

3. Isoniazid

Generic Name	Isoniazid
Dosage form/strengths	Tablets: 50mg, 100mg, 200mg, 300mg
Route of administration	Oral
Pharmacological action	Antitubercular Agent ATC: J04AC01
Indications	**Active tuberculosis infections:** Treatment of susceptible active tuberculosis (eg, *Mycobacterium tuberculosis*) infections. **Latent tuberculosis infection:** Treatment of latent tuberculosis infection (LTBI) caused by *Mycobacterium tuberculosis* (also referred to as prophylaxis or preventive therapy).
Dosage Regimen	Used in conjunction with other antimycobacterial agents for treatment of active (clinical) TB. Used alone for treatment of Latent TBI **Adults** **Treatment of Active (Clinical) Tuberculosis** Oral *Dosing:* Once-daily therapy: 5 mg/kg/dose (usual dose: 300 mg) once daily **Note:** The preferred frequency of administration is once daily during the intensive and continuation phases; however, 5 days per week administration by directly observed therapy (DOT) is an acceptable alternative. Three-times-weekly DOT: 15 mg/kg/dose (usual dose: 900 mg) administered 3 times weekly Twice-weekly DOT: 15 mg/kg/dose (usual dose: 900 mg) administered twice weekly Once-weekly DOT: 15 mg/kg/dose (usual dose: 900 mg) administered once weekly ***Regimens:*** Treatment regimens for pulmonary tuberculosis and tuberculous meningitis consist of an initial 2-month phase of a 4-drug regimen, followed by a continuation phase of an additional 4 to 7 months of isoniazid and rifampin for pulmonary tuberculosis and a continuation phase of an additional 7 to 10 months of isoniazid and rifampin for tuberculous meningitis (optimal duration is not defined although continuation phase must continue for a minimum of 7 additional months). Adjunctive corticosteroid therapy (eg, dexamethasone, prednisolone) tapered over 6 to 8 weeks is also recommended for tuberculous meningitis. Isoniazid frequency and dosing differs depending on treatment regimen selected; consult current Drug-sensitive TB guidelines **Latent Tuberculosis Infection (LTBI)** **Oral** ***Isoniazid monotherapy (alternative regimen)*** 5 mg/kg (up to 300 mg) once daily or 15 mg/kg (up to 900 mg) twice weekly recommended by ATS, CDC, IDSA, USPHS, and others. Adults weighing >30 kg: 300 mg once daily The usual duration of isoniazid monotherapy for treatment of LTBI is 9 months. A 6-month regimen may be used in some adults, but a 9-month regimen should be used in immunocompromised or HIV-infected individuals or those with fibrotic lesions on chest radiographs **Pediatric Patients** **Tuberculosis** **Treatment of Active (Clinical) Tuberculosis**

	Oral Children: 10–15 mg/kg (up to 300 mg) once daily or 20–40 mg/kg (up to 900 mg) 2 or 3 times weekly recommended. Children <15 years of age or weighing ≤40 kg: 10–15 mg/kg (up to 300 mg) once daily or 20–30 mg/kg (up to 900 mg) twice weekly recommended by ATS, CDC, IDSA, AAP, and others. Adolescents ≥15 years of age: 5 mg/kg (up to 300 mg) once daily or 15 mg/kg (up to 900 mg) 1–3 times weekly recommended by ATS, CDC, and IDSA **Latent Tuberculosis Infection (LTBI)** **Oral** Infants, children, and adolescents: 10–20 mg/kg (up to 300 mg) once daily or 20–40 mg/kg (up to 900 mg) twice weekly. The usual duration of isoniazid monotherapy for treatment of LTBI in children is 9 months, especially in HIV-infected individuals. A 6-month regimen is not recommended for children. ATS and CDC recommend that completion of therapy for LTBI be based on total number of administered doses rather duration of therapy alone. When the 9-month once-daily isoniazid regimen is used, at least 270 doses should be administered within 12 months.
Dosage adjustment	**Dosing: Renal Impairment:** No dosage adjustment necessary, monitor closely in severe renal impairment. Hemodialysis: No dosage adjustment necessary; administer after hemodialysis on dialysis days **Dosing: Hepatic Impairment:** Use with caution, may accumulate and additional liver damage may occur in patients with preexisting liver disease
Contra-indications	Hypersensitivity to isoniazid or any component of the formulation, including drug-induced hepatitis; acute liver disease; previous history of hepatic injury during isoniazid therapy; previous severe adverse reaction (drug fever, chills, arthritis) to isoniazid
Adverse Drug Reactions	**>10%**: Hepatic: Increased serum transaminases (mild and transient 10% to 20%)
Monitoring Parameters	Baseline and periodic (more frequently in patients with higher risk for hepatitis) liver function tests (ALT and AST); sputum cultures monthly (until 2 consecutive negative cultures reported); monitoring for prodromal signs of hepatitis
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine, Methoxyflurane, Pimozide ***Risk D: Consider therapy modification*** Fosphenytoin, Lemborexant, Lomitapide, Phenytoin, Prothionamide Sodium Picosulfate, Triazolam, Typhoid Vaccine, Ubrogepant, ***Risk C: Monitor therapy,*** Acetaminophen, Alcohol, BCG Vaccine (Immunization), Carbamazepine, Chlorzoxazone, Corticosteroids, Cycloserine, CYP2E1 Inhibitors, Dofetilide, Ethionamide, Flibanserin, Itraconazole, Ketoconazole (Systemic), Lactobacillus and Estriol, Levodopa-Containing Products, Nimodipine, Propacetamol, Rifamycin Derivatives, Safinamide, Theophylline Derivatives
Pregnancy and Lactation	**Pregnancy Category C** Isoniazid is considered compatible with breastfeeding Breastfed infants should be monitored for jaundice; discontinue breastfeeding or consider changing to a different maternal medication if jaundice develops. Pyridoxine supplementation is recommended for the mother and infant
Administration	**Oral Administration**

	Administer orally in the fasting state. Do not administer with food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hepatitis: [US Boxed Warning]: Severe and sometimes fatal hepatitis may occur; usually occurs within the first 3 months of treatment, although may develop even after many months of treatment. ***Disease-related concerns:*** • Hepatic impairment: Use with caution in patients with hepatic impairment; contraindicated in patients with acute liver disease or previous isoniazid-associated hepatic injury. Treatment with isoniazid for latent tuberculosis infection (LTBI) should be deferred in patients with acute hepatic diseases. • Renal impairment: Use with caution in patients with severe renal impairment. ***Other warnings/precautions:*** • Appropriate use: Multidrug regimens should be utilized for the treatment of active tuberculosis to prevent the emergence of drug resistance. • Monitoring: Use should be carefully monitored in the following groups: Daily users of alcohol, active chronic liver disease, severe renal dysfunction, age >35 years, concurrent use of any chronically administered drug, history of previous isoniazid discontinuation, existence of or conditions predisposing to peripheral neuropathy, pregnancy, injection drug use, women in minority groups (particularly postpartum), HIV seropositive patients.
Storage	Tablet: Store at 20°C to 25°C. Protect from moisture and light. Refer to manufacturer PIL if there are specific considerations.

4. Pyrazinamide

Generic Name	Pyrazinamide
Dosage form/strengths	Tablets 500mg
Route of administration	Oral
Pharmacologic category	Antitubercular Agent ATC: J04AK01
Indications	**Tuberculosis:** Treatment of tuberculosis in combination with other antituberculosis agents.
Dosage Regimen	**Dosing: Adult** **Tuberculosis, treatment (drug-susceptible): Oral: Note:** Always administer in combination with other antitubercular drugs. *Dosing:* Doses should be based on **lean** body weight for patients within a normal weight range for their height (optimal dosing for obese patients has not been established): • Once-daily therapy: 40 to 55 kg: 1,000 mg once daily **Note:** The preferred frequency of administration is once daily; however, 5-days per week administration by directly-observed therapy (DOT) is an acceptable alternative. 56 to 75 kg: 1,500 mg once daily. 76 to 90 kg: 2,000 mg once daily. • Three-times-weekly DOT: 40 to 55 kg: 1,500 mg 3 times weekly. 56 to75 kg: 2,500 mg 3 times weekly. 76 to 90 kg: 3,000 mg 3 times weekly. **Tuberculosis, treatment (drug-resistant) (alternative agent):** **Note:** Expert consultation for optimal regimen and duration of treatment is advised. **Oral:** 25 to 40 mg/kg once daily **Dosing: Pediatric** **Note:** Recommendations often change due to epidemiology (resistance) and emerging information; consult CDC and WHO for current recommendations, as appropriate. **Active TB infection, treatment:** • *Once daily or 5-times-weekly (DOT):* Infants, Children, and Adolescents weighing <40 kg: Oral: 35 mg/kg/dose once daily or 5 times weekly DOT; suggested range: 30 to 40 mg/kg/dose Children and Adolescents weighing ≥40 kg: **Note:** Doses should be based on lean body weight for patients within a normal weight range for their height (optimal dosing for obese patients has not been established): Oral: Weight-band dosing for whole tablets: 40 to 55 kg: 1,000 mg (18.2 to 25 mg/kg/dose) once daily or 5-times-weekly (DOT) 56 to 75 kg: 1,500 mg (20 to 28.6 mg/kg/dose) once daily or 5-times-weekly (DOT) 76 to 90 kg: 2,000 mg (22.2 to 26.3 mg/kg/dose) once daily or 5-times-weekly (DOT) • *Three-times-weekly DOT:* Infants, Children, and Adolescents weighing <40 kg: Oral: 50 mg/kg/dose 3 times weekly Children and Adolescents weighing ≥40 kg:

	Oral: Weight-band dosing for whole tablets: 40 to 55 kg: 1,500 mg (27.3 to 37.5 mg/kg/dose) three-times-weekly 56 to 75 kg: 2,500 mg (33.3 to 44.6 mg/kg/dose) three-times-weekly 76 to 90 kg: 3,000 mg (33.3 to 39.5 mg/kg/dose) three-times-weekly
Dosage adjustment	**Dosing: Renal Impairment:** It may be prudent to select doses at the low end of the dosing range. Dosing is based on lean body weight **Dosing: Hepatic Impairment:** Use is contraindicated in cases of severe hepatic impairment.
Contra-indications	Hypersensitivity to pyrazinamide or any component of the formulation; acute gout; severe hepatic damage
Adverse Drug Reactions	**1% to 10%:** Central nervous system: Malaise Gastrointestinal: Anorexia, nausea, vomiting Neuromuscular & skeletal: Arthralgia, myalgia
Monitoring Parameters	Periodic liver function tests, serum uric acid, sputum culture, chest x-ray 2-3 months into treatment and at completion
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Rifampin Sodium Picosulfate Typhoid Vaccine
Pregnancy and Lactation	**Pregnancy Risk Factor C** breastfeeding should not be discouraged in women taking this drug. breastfed infants should be monitored for the signs/symptoms of toxicity (e.g., arthralgia, fever, hepatitis, jaundice, loss of appetite, nausea, rash, thrombocytopenia, vomiting).
Administration	Oral: May take without regard to food Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hepatotoxicity: Dose-related hepatotoxicity ranging from transient ALT/AST elevations to jaundice, hepatitis and/or liver atrophy (rare) has occurred. ***Disease-related concerns:*** • Alcoholism: Due to concerns for preexisting hepatic dysfunction, use with caution in patients with a history of alcoholism. • Diabetes: Use with caution in patients with diabetes mellitus. • Gout: May inhibit uric acid excretion; acute gouty attacks have been reported. Use with caution in patients with chronic gout; contraindicated with acute gout. • Porphyria: Use with caution in patients with porphyria. • Renal impairment: Use with caution in patients with renal failure. ***Concurrent drug therapy issues:*** • Hepatotoxic agents: Use with caution in patients receiving concurrent medications associated with hepatotoxicity (particularly with rifampin). The Infectious Diseases Society of America and Centers for Disease Control and Prevention recommend that the 2-month rifampin-pyrazinamide regimen should not generally be used in patients with LTBI
Storage	Store at controlled room temperature of 15°C to 30°C Refer to manufacturer PIL if there are specific considerations.

5. Rifampicin

Watch Group

Generic Name	Rifampicin
Dosage form/ strengths	Capsule 150mg, 300mg, Oral Suspension 2% (100mg/5ml) Ampoule Lyophilized Powder 250mg
Route of administration	Oral, IV
Pharmacologic category	Antitubercular Agent; Rifamycin ATC: J04AB02
Indications	**Meningococcal prophylaxis:** Treatment of asymptomatic carriers of *Neisseria meningitidis* to eliminate meningococci from the nasopharynx. **Tuberculosis:** Treatment of tuberculosis in combination with other agents.
Dosage Regimen	**Adult Dosing:** **Meningococcal disease, chemoprophylaxis after close contact with a patient with invasive disease:** **Oral:** 600 mg twice daily for 2 days. **Note:** Administer prophylaxis as soon as possible following exposure (ideally <24 hours after identification of index patient). Close contacts include persons with prolonged exposure (≥8 hours) in close proximity (<3 feet) to index patient or direct exposure to oral secretions (eg, household contacts, childcare center contacts). **Tuberculosis, active (drug susceptible):** **Note:** Always administer in combination with other antitubercular drugs **Oral, IV:** ○ *Initial intensive phase*: 10 mg/kg (maximum dose: 600 mg) once daily (or 5 days per week by directly observed therapy [DOT]) as part of a standard 4-drug regimen for 2 months ○ *Continuation phase:* 10 mg/kg (maximum dose: 600 mg) once daily (or 5 days per week by DOT) in combination with isoniazid for at least 4 months or longer for cavitary disease with positive cultures (7 months), bone and joint disease (6 to 9 months), and CNS disease (≥12 months) . ○ *Alternative dosing intervals:* Daily or 5-times-weekly dosing is preferred, particularly during the intensive phase. If neither is feasible, alternatives in order of preference are: daily (or 5-times-weekly) dosing for the intensive phase followed by 3-times-weekly dosing during the continuation phase; 3-times-weekly dosing for the duration of treatment; and daily dosing for 2 weeks followed by twice-weekly dosing. Use DOT for <7 days/week dosing. **Tuberculosis, latent infection:** **Oral:** 10 mg/kg (maximum dose: 600 mg) once daily as a single agent for 4 months or in combination with isoniazid for 3 months **Pediatric Patients** **General Dosage for Infants and Children** **Oral or IV** Children ≥1 month of age: AAP recommends 10–20 mg/kg (up to 600 mg) daily given in 1 or 2 divided doses for mild to moderate infections or 20 mg/kg (up to 600 mg) daily in 2 divided doses for severe infections **Meningococcal disease, chemoprophylaxis after close contact with a patient with invasive disease:** Infants, Children, and Adolescents: Oral: 20 mg/kg/**day** in divided doses every 12 hours for 2 days; maximum dose: 600 mg/dose. **Tuberculosis, active (drug-susceptible); treatment**:

	Note: Always administer in combination with other antitubercular drugs. Doses of 20 to 30 mg/kg/dose have been recommended for infants and young children or for treating disseminated tuberculosis or tuberculous meningitis. *Initial intensive phase:* **Note:** Administer part of a standard 4-drug regimen for 2 months. Infants, Children, and Adolescents <15 years weighing ≤40 kg: Oral, IV: 10 to 20 mg/kg/dose once daily (or 5 days/week by directly observed therapy [DOT]); maximum dose: 600 mg/dose. Children and Adolescents <15 years weighing >40 kg or Adolescents ≥15 years: Oral, IV: 10 mg/kg/dose once daily (or 5 days/week by DOT); maximum dose: 600 mg/dose. *Continuation phase:* **Note:** Administer in combination with isoniazid for ≥4 months; continuation phase duration should be longer for cavitary disease with positive cultures at completion of intensive phase (7 months), bone and joint disease (≥4 to 7 months), and CNS disease (7 to 10 months). Infants, Children, and Adolescents <15 years weighing ≤40 kg: Oral, IV: 10 to 20 mg/kg/dose once daily (or 5 days/week by DOT); maximum dose: 600 mg/dose. Children and Adolescents <15 years weighing >40 kg or Adolescents ≥15 years: Oral, IV: 10 mg/kg/dose once daily (or 5 days/week by DOT); maximum dose: 600 mg/dose.
Dosage adjustment	**Dosing: Renal Impairment:** No dosage adjustment necessary. CrCl <15 mL/minute, Hemodialysis: No dosage adjustment necessary for usual indication-specific doses ≤600 mg/day. For usual indication-specific doses ≥900 mg/day, consider limiting dose to 600 mg/day or monitoring more closely for adverse effects **Dosing: Hepatic Impairment:** **Hepatic impairment prior to treatment initiation:** Rifampin is substantially eliminated by the liver and the clearance of rifampin would be expected to be decreased in patients with liver impairment. use with caution. **Hepatotoxicity during treatment:** New or worsening hepatic damage: Discontinue rifampin.
Contra-indications	Hypersensitivity to rifampin, any rifamycins, or any component of the formulation; concurrent use of atazanavir, darunavir, fosamprenavir, praziquantel, ritonavir/saquinavir, saquinavir, or tipranavir. Jaundice associated with reduced bilirubin excretion; premature and newborn infants; breastfeeding women; hepatic function impairment
Adverse Drug Reactions	**Frequency not defined:** Cardiovascular: Decreased blood pressure, flushing, shock, vasculitis Central nervous system: Ataxia, behavioral changes, confusion, dizziness, drowsiness, fatigue, headache, lack of concentration, myasthenia, numbness, peripheral pain, sore mouth Dermatologic: Erythema multiforme, pemphigoid reaction, pruritus, skin rash, urticaria Endocrine & metabolic: Adrenocortical insufficiency, menstrual disease Gastrointestinal: Abdominal cramps, anorexia, diarrhea, epigastric discomfort, flatulence, glossalgia, heartburn, nausea, staining of tooth, vomiting Genitourinary: Hemoglobinuria, hematuria Hematologic & oncologic: Decreased hemoglobin, disorder of hemostatic components of blood (vitamin K-dependent), disseminated intravascular coagulation, eosinophilia, hemolysis, hemolytic anemia, hemorrhage, leukopenia, thrombocytopenia (especially with high-dose therapy) Hepatic: Abnormal hepatic function tests, hepatic insufficiency, hyperbilirubinemia, jaundice

	Hypersensitivity: Hypersensitivity reaction Neuromuscular & skeletal: Myopathy Ophthalmic: Conjunctivitis, visual disturbance Renal: Acute renal failure, interstitial nephritis, renal insufficiency, renal tubular necrosis Respiratory: Dyspnea, flu-like symptoms, wheezing Miscellaneous: Fever
Monitoring Parameters	Baseline LFTs (AST, ALT, bilirubin), serum creatinine, CBC; periodic (every 2 to 4 weeks during therapy) monitoring of liver function in patients with preexisting hepatic impairment and periodic monitoring of serum creatinine and CBC in patients with baseline abnormalities. Mental status, sputum culture, chest X-ray 2 to 3 months into treatment. Monitor coagulation tests during treatment in patients at risk of vitamin K deficiency.
Drug Interactions	***Risk X: Avoid combination*** Apixaban, Aprepitant, Atazanavir, BCG (Intravesical), Bosutinib, Cholera Vaccine, Dabigatran ***Risk D: Consider therapy modification*** Antifungal Agents (Azole Derivatives, Systemic), Aripiprazole, Atorvastatin, Brivaracetam, Calcium Channel Blockers, Canagliflozin, Caspofungin, Cephalosporins, Clarithromycin, Clozapine, Cyclosporine (Systemic), Dexamethasone (Systemic)
Pregnancy and Lactation	**Pregnancy Category C** Breastfeeding is not a contraindication during therapy for drug-susceptible tuberculosis in patients deemed noninfectious who are treated with first-line agents (ie, rifampin).
Administration	**Administration: IV** Administer IV preparation by slow IV infusion over 30 minutes to 3 hours at a final concentration not to exceed 6 mg/mL. Do **not** administer IM or SubQ. Avoid extravasation. **Administration: Oral** Administer on an empty stomach with a glass of water (ie, 1 hour prior to, or 2 hours after meals or antacids) to increase total absorption (food may delay and reduce the amount of rifampin absorbed). The compounded oral suspension must be shaken well before using. May mix contents of capsule with applesauce or jelly. **Preparation for Administration:** Reconstitute vial with 10 mL SWFI. Prior to injection, dilute in appropriate volume of a compatible solution (ie, D5W, NS) at a final concentration not to exceed 6 mg/mL. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Coagulopathy: May cause vitamin K-dependent coagulation disorders and bleeding. Monitor coagulation tests during treatment in patients at risk of vitamin K deficiency (eg, chronic liver disease, poor nutritional status, prolonged use of antibacterial agents or anticoagulants). Consider discontinuation if abnormal coagulation tests and/or bleeding occurs; consider supplemental vitamin K administration when appropriate. • Dermatologic reactions: Cases of severe cutaneous adverse reactions (SCAR) such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), acute generalized exanthematous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome have been reported. Discontinue treatment immediately and institute appropriate therapy if signs or symptoms of SCAR develop. • Flu-like syndrome: Regimens of >600 mg once or twice weekly in adults have been associated with a high incidence of adverse reactions including a flu-like syndrome. • Hematologic effects: May cause thrombocytopenia, leukopenia, or anemia with regimens >600 mg once or twice weekly in adults. • Hepatotoxicity: Hepatotoxicity of hepatocellular, cholestatic, and mixed patterns has been reported; may include asymptomatic elevations in liver enzymes, isolated

	jaundice/hyperbilirubinemia, symptomatic self-limited hepatitis, or fulminant liver failure and death. Severe reactions, including fatalities, have occurred in patients with preexisting hepatic failure and in patients receiving concomitant hepatotoxic agents. Monitor for signs and symptoms of liver injury, especially if treatment is prolonged or given with other hepatotoxic drugs. Patients with impaired liver function should only be given rifampin when medically indicated and with monitoring of LFTs (AST, ALT, bilirubin) prior to therapy and then every 2 to 4 weeks during therapy. Discontinue use if hepatocellular damage occurs or worsens. • Hypersensitivity: Hypersensitivity reactions have been reported. Signs and symptoms of hypersensitivity reactions may include fever, rash, urticaria, angioedema, hypotension, acute bronchospasm, conjunctivitis, thrombocytopenia, neutropenia, elevated liver transaminases, or flu-like syndrome. Monitor patients for signs/symptoms of hypersensitivity; discontinue therapy if signs/symptoms suggestive of hypersensitivity (eg, fever, lymphadenopathy, eosinophilia, liver abnormalities) occur, even if rash is not evident. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Alcoholism: Use with caution in patients with a history of alcoholism (even if ethanol consumption is discontinued during therapy). • Diabetes mellitus: Use with caution in patients with diabetes mellitus; management of diabetes may be more difficult in patients taking rifampin. • Hepatic impairment: Use with caution and close monitoring in patients with hepatic impairment. • Meningococcal disease: Do not use for treatment of meningococcal disease, only for short-term treatment of asymptomatic carrier states. • Porphyria: Use with caution in patients with porphyria; exacerbations have been reported due to enzyme-inducing properties. ***Concurrent drug therapy issues:*** • Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information. ***Other warnings/precautions:*** • Appropriate administration: Do not administer IV form via IM or SubQ routes; restart infusion at another site if extravasation occurs. • Compliance: Monitor for compliance in patients on intermittent therapy. • Contact lenses: Remove soft contact lenses during therapy since permanent staining may occur. • Discoloration: Teeth (may be permanent), urine, feces, saliva, sweat, and tears may be discolored (yellow, orange, red, or brown)
Storage	**Capsule**: Store at 25°C, avoid excessive heat. **Injection**: Store intact vials at 25°C avoid excessive heat (>40°C). Protect the intact vials from light. Reconstituted vials are stable for 30 hours at room temperature. Stability of parenteral admixture at room temperature (25°C) is 8 hours for D_5W or 6 hours for NS. Refer to manufacturer PIL if there are specific considerations.

6. Rifampicin and Isoniazid

Generic Name	Rifampicin+ Isoniazid
Dosage form/strengths	Capsule/Tablets: 300 Rifampicin + 150 Isoniazid
Route of administration	Oral
Pharmacologic category	Antibiotic, Miscellaneous ATC: J04AM02
Indications	Management of active tuberculosis, see individual agents for additional information
Dosage Regimen	**Dosing: Adult** **Tuberculosis:** Oral: **Note:** Concomitant antituberculosis medications should be administered according to current guideline recommendations *Capsules:* Rifampin 300 mg/isoniazid 150 mg per capsule/tablet: 2 capsules/tablets once daily *Tablets:* **Dosing: Pediatric** **Tuberculosis:** Adolescents ≥15 years: Refer to adult dosing
Dosage adjustment	**Dosing: Renal Impairment: Adult** There are no dosage adjustments needed. Use with caution in severe renal impairment. Also see individual agents. **Dosing: Hepatic Impairment: Adult** *Hepatic impairment prior to treatment initiation:* There are no dosage adjustments needed; use with caution. Use is contraindicated in patients with severe or acute hepatic impairment or in cases of previous isoniazid-associated hepatic injury. *Hepatotoxicity during treatment:* New or worsening hepatic damage: Discontinue treatment.
Contra-indications	Hypersensitivity to rifampin or other rifamycins, isoniazid, or any component of the formulation; severe hepatic damage; acute hepatic disease; acute gout; history of severe adverse reactions to isoniazid (eg, drug-induced hepatitis, drug fever, chills, arthritis); concurrent use of atazanavir, darunavir, fosamprenavir, praziquantel, saquinavir, saquinavir/ritonavir, or tipranavir.
Adverse Drug Reactions	See individual agents.
Monitoring Parameters	Baseline and periodic LFTs (AST, ALT), serum uric acid, serum bilirubin, serum creatinine, CBC, ophthalmic examinations (including ophthalmoscopy); patients at higher risk for hepatitis (eg, existing hepatic impairment, older patients, ethanol consumption, alcoholism) should undergo evaluation of LFTs every 2 to 4 weeks; signs/symptoms of hepatotoxicity; monitor sputum cultures monthly (until 2 consecutive negative cultures reported); monitor chest x-ray 2 to 3 months into treatment and at completion. Monitor coagulation tests during treatment in patients at risk of vitamin K deficiency.
Drug Interactions	***Risk X: Avoid Combination*** Abemaciclib Alpelisib Antihepaciviral Combination Products Apixaban Apremilast Aprepitant Artemether Asunaprevir Atazanavir Atovaquone Avanafil Avapritinib Axitinib BCG (Intravesical) Bedaquiline Betrixaban Bictegravir Bortezomib Bosutinib Brigatinib Cabotegravir Capmatinib Cariprazine Ceritinib Cholera Vaccine Cobicistat Cobimetinib Copanlisib Crizotinib Dabigatran Etexilate Daclatasvir Darolutamide Darunavir Dasabuvir Deflazacort Delamanid Delavirdine

	Dexlansoprazole Dienogest Diltiazem Doravirine Doxorubicin Dronedarone Duvelisib Edoxaban Elagolix, Estradiol, And Norethindrone Elbasvir Elexacaftor, Tezacaftor, And Ivacaftor Eliglustat Elvitegravir Encorafenib Entrectinib Erdafitinib Esomeprazole Etravirine Fedratinib Fimasartan Flibanserin Fosamprenavir Fosaprepitant Fosnetupitant Fostamatinib Fostemsavir Gemigliptin Gilteritinib Glasdegib Glecaprevir And Pibrentasvir Grazoprevir Ibrutinib Idelalisib Indinavir Irinotecan Products Isavuconazonium Sulfate Istradefylline Itraconazole Ivabradine Ivacaftor Ivosidenib Ixazomib Lansoprazole Ledipasvir Lemborexant Letermovir Lonafarnib Lorlatinib Lumacaftor And Ivacaftor Lumateperone Lumefantrine Lurasidone Lurbinectedin Macimorelin Methoxyflurane Midostaurin Mifepristone Mycophenolate Naldemedine Naloxegol Nelfinavir Neratinib Netupitant Nifedipine Nilotinib Nimodipine Nintedanib Nisoldipine Olaparib Omeprazole Ozanimod Palbociclib Panobinostat Pazopanib Pemigatinib Perampanel Pexidartinib Pimavanserin Pimozide Piperaquine Praziquantel Pretomanid Quinineranolazine Regorafenib Revefenacin Rilpivirine Rimegepant Ripretinib Ritonavir Rivaroxaban Roflumilast Romidepsin Sacituzumab Govitecan Saquinavir Selpercatinib Selumetinib Simeprevir Siponimod Sofosbuvir Sonidegib Sorafenib Tasimelteon Tazemetostat Telithromycin Tenofovir Alafenamide Tezacaftor And Ivacaftor Ticagrelor Tipranavir Toremifene Trabectedin Tucatinib Ubrogepant Ulipristal Upadacitinibvalbenazine Vandetanib Velpatasvir Venetoclax Vincristine Vinflunine Voclosporin Vorapaxar Voriconazolevoxilaprevir Zanubrutinib Zolpidem
Pregnancy and Lactation	Isoniazid and rifampin cross the placenta. Refer to individual monographs for additional information. It is considered compatible with breastfeeding. Use caution breastfed infants should be monitored for the signs/symptoms of toxicity (e.g., arthralgia, fever, hepatitis, jaundice, loss of appetite, nausea, rash, thrombocytopenia, vomiting).
Administration	Administer with a full glass of water 1 hour before or 2 hours after a meal. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Coagulopathy: May cause vitamin K-dependent coagulation disorders and bleeding. Monitor coagulation tests during treatment in patients at risk of vitamin K deficiency (eg, chronic liver disease, poor nutritional status, prolonged use of antibacterial agents or anticoagulants). Consider discontinuation if abnormal coagulation tests and/or bleeding occur; consider supplemental vitamin K administration when appropriate. • Flu-like syndrome: Flu-like syndrome (eg, fever, chills, malaise) may occur; higher incidence is associated with regimens of rifampin >600 mg once or twice weekly. • Hematologic effects: May cause thrombocytopenia, leukopenia, or anemia; higher incidence is associated with regimens of rifampin >600 mg once or twice weekly. • Hepatotoxicity: [US Boxed Warning]: Severe and sometimes fatal hepatitis may occur with isoniazid; increased transaminase concentrations usually occur within the first few months of treatment, although may develop at any time. Liver enzymes often return to normal despite continuance of drug; however, progressive hepatic dysfunction may occur. The risk of developing hepatitis is age related; daily ethanol consumption may also increase the risk. Patients must report symptoms of hepatitis, such as fatigue, weakness, malaise, anorexia, nausea, or vomiting, immediately. Discontinue therapy immediately if hepatocellular damage occurs or is suspected; if therapy must be restarted, initiate once symptoms and laboratory abnormalities have resolved and at small and gradually increasing doses. Defer treatment in patients with acute hepatic disease • Hypersensitivity: Hypersensitivity reactions, including severe and potentially fatal reactions have occurred with antituberculosis therapy. Signs and symptoms of hypersensitivity reactions may include fever, rash, urticaria, angioedema, hypotension, acute bronchospasm, conjunctivitis, thrombocytopenia, neutropenia, elevated liver transaminases, or flu-like

	syndrome. discontinue therapy if signs/symptoms suggestive of hypersensitivity (eg, fever, lymphadenopathy, eosinophilia, liver abnormalities) occur, even if rash is not evident. • Peripheral neuropathies: Pyridoxine is recommended in individuals at risk for development of peripheral neuropathies (eg, HIV infection, nutritional deficiency, diabetes, pregnancy). ***Disease-related concerns:*** • Alcoholism: Use with caution in patients with a history of alcoholism (even if ethanol consumption is discontinued during therapy). • Diabetes: Use with caution in patients with diabetes mellitus. • Hepatic impairment: Use with caution; contraindicated in patients with severe hepatic damage or acute hepatic disease. • Porphyria: Use with caution in patients with porphyria; exacerbations have been reported. • Renal impairment: Use with caution in patients with severe renal impairment. ***Other warnings/precautions:*** • Appropriate use: Multidrug regimens should be utilized for the treatment of active tuberculosis to prevent the emergence of drug resistance**.** Monitor for compliance. Not recommended for intermittent therapy; avoid intentional or accidental interruption of therapy (renal hypersensitivity reactions may occur upon resumption of therapy [rare]). • Contact lenses: Remove soft contact lenses during therapy since permanent staining may occur. • Ophthalmic examinations: Periodic ophthalmic examinations are recommended even when visual symptoms do not occur. • Red/orange discoloration: Teeth (may be permanent), urine, feces, saliva, sputum, sweat, tears, and CSF may be discolored (yellow, orange, red, or brown).
Stoarge	Store at 25°C; excursions permitted to 15°C to 30°C. Protect from excessive humidity. Refer to manufacturer PIL if there are specific considerations.

Antiviral

1. Acyclovir

Generic Name	Acyclovir
Dosage form/strengths	Tablet 400mg, 800mg Capsule 200mg Suspension 200mg/5ml, 400mg/5ml, Cream 5% Vial 250mg, 500mg eye ointment 3%
Route of administration	Oral, Topical, IV, ophthalmic
Pharmacologic action	Antiviral ATC (Topical): D06BB03 ATC (systemic): J05AB01 ATC (Ophthalmic): S01AD03
Indications	Oral: Herpes simplex virus (HSV), genital: Treatment of initial episodes and the management of recurrent episodes of genital herpes. Herpes zoster (shingles): Acute treatment of herpes zoster (shingles). Varicella (chickenpox): Treatment of varicella (chickenpox). Injection: Herpes simplex encephalitis: Treatment of herpes simplex encephalitis. Herpes simplex virus (HSV), genital infection (severe): Treatment of severe initial clinical episodes of genital herpes in immunocompetent patients. Herpes simplex virus (HSV), mucocutaneous infection in immunocompromised patients: Treatment of initial and recurrent mucosal and cutaneous herpes simplex (HSV-1 and HSV-2) in immunocompromised patients. Herpes simplex virus (HSV), neonatal: Treatment of neonatal herpes infections. Herpes zoster (shingles) in immunocompromised patients: Treatment of herpes zoster (shingles) in immunocompromised patients. Topical: Herpes virus: Cream: Treatment of recurrent herpes labialis (cold sores) in immunocompetent children ≥12 years of age, adolescents, and adults
Dosage Regimen	**Dosing: Adult: Note:** Use ideal body weight or 40% adjusted body weight for weight-based dosing in obese patients to avoid overdosing and subsequent toxicity (eg, acute renal failure) • **Encephalitis: IV:** 10 mg/kg/dose every 8 hours. for 14 to 21 days • **Meningitis: IV:** 10 mg/kg/dose every 8 hours is 10 to 14 days; • **Herpes simplex virus, mucocutaneous infection:** ○ **Oral:** 400 mg 3 times daily **or** 200 mg 5 times daily for 7 to 10 days ○ Immunocompromised patients: **Oral:** 400 mg 5 times daily for 14 to 21 days • ***Genital:*** ○ **Oral:** 400 mg 3 times daily **or** 200 mg 5 times daily for 7 to 10 days, while extend treatment duration until complete resolution in Immunocompromised patients. ○ **IV** (for severe disease): 5 to 10 mg/kg/dose every 8 hours for 2 to 7 days followed by oral acyclovir (or similar antiviral) to complete ≥10 days of therapy total and until complete resolution

- *recurrent episode*: **Oral:** 400 mg 3 times daily for 5 days **or** 800 mg twice daily for 5 days **or** 800 mg 3 times daily for 2 days
- *Suppressive therapy (eg, for severe and/or frequent recurrences)*:
  - Immunocompetent patients: **Oral:** 400 mg twice daily. **Note:** Reassess periodically (eg, annually)
  - Immunocompromised patients: **Oral:** 400 to 800 mg 2 to 3 times daily. **Note:** Reassess periodically (eg, annually)

- ***Orolabial***:
  - **Oral:** 400 mg 3 times daily for 5 to 10 days, while in immunocompromised patients extend until complete lesion resolution
  - **IV** (for severe disease in immunocompromised patients): 5 mg/kg/dose every 8 hours; switch to oral acyclovir (or similar antiviral) once lesions begin to regress and continue until complete resolution
  - *Suppressive therapy (eg, for severe and/or frequent recurrences)*: **Oral:** 400 mg twice daily. **Note:** Reassess periodically
  - **Topical cream**: Apply 5 times daily for 4 days
- **Herpes zoster (shingles), treatment:**
  - **Oral:** 800 mg 5 times daily for 7 days
  - *Extensive cutaneous lesions or visceral involvement:* **IV:** 10 mg/kg/dose every 8 hours
- **Varicella (chickenpox), treatment:**
  - *Uncomplicated infection:* **Oral:** 800 mg 5 times daily for ≥5 to 7 days and until all lesions have crusted
  - *Severe or complicated infection*: **IV:** 10 mg/kg/dose every 8 hours for 7 to 10 days
- **Herpetic keratitis:** Ophthalmic: Apply a ½-inch ribbon of ointment in the lower conjunctival fold of the affected eye(s) 5 times daily (approximately every 3 hours while awake) until the corneal ulcer heals, then apply a ½-inch ribbon 3 times daily for 7 days.
- **Herpes labialis (cold sores), recurrent**: Topical cream: Apply 5 times daily for 4 days

Dosing: Pediatric:

- **Mucocutaneous, Ocular, and Systemic Herpes Simplex Virus (HSV) Infections**

Treatment of Mucocutaneous HSV Infections

Oral

Immunocompromised children: 1 g daily given in 3–5 divided doses for 7–14 days**.**

IV

Immunocompromised children <12 years of age: 10 mg/kg every 8 hours for 7–14 days.

HIV-infected or immunocompromised adolescents and children ≥12 years of age: 5 mg/kg every 8 hours for 7–14 days. Alternatively, after lesions begin to regress, consider switching to oral acyclovir in a dosage of 400 mg 3 times daily and continue until lesions are completely healed

- **HSV Gingivostomatitis**

Oral

HIV-infected children with mild, symptomatic gingivostomatitis: CDC and others recommend 20 mg/kg (up to 400 mg) 3 times daily for 7–14 days.

Immunocompetent children: 15 mg/kg (up to 200 mg) 5 times daily for 7 days has been used in a few children 1–6 years of age.

IV

HIV-infected children with moderate to severe gingivostomatitis: CDC and others recommend 5–10 mg/kg 3 times daily for 7–14 days. Consider chronic oral suppressive or maintenance therapy (secondary prophylaxis) in those with frequent or severe recurrences of gingivostomatitis

- **Chronic Suppressive or Maintenance Therapy (Secondary Prophylaxis) of HSV Infections**

Oral

HIV-infected infants and children: 80 mg/kg daily (up to 1 g daily) in 3 or 4 divided doses.

HIV-infected adolescents: 200 mg 3 times daily or 400 mg twice daily.

- **Prophylaxis Against Recurrent Ocular HSV Disease**

Oral

Children ≥12 years of age: 400 mg twice daily. AAP recommends 80 mg/kg daily (up to 1 g daily) given in 3 divided doses.

Optimum duration of prophylaxis unclear; has been continued for 12–18 months in clinical studies.

- **Treatment of HSV Encephalitis or Disseminated Disease**

IV

Immunocompromised children: 20 mg/kg every 8 hours in those 3 months to 12 years of age and 10–15 mg/kg every 8 hours in those ≥12 years of age. AAP and others recommend 14–21 days for disseminated or CNS infections.

HIV-infected children: CDC and others recommend 10 mg/kg or 500 mg/m^2 3 times daily for 21 days.

HIV-infected adolescents: CDC and others recommend 10 mg/kg 3 times daily for 14–21 days.

- **Treatment of Neonatal HSV Infections**

IV

Neonates and children ≤3 months of age: 10 mg/kg every 8 hours for 10 days

Neonates and children ≤3 months of age: 20 mg/kg every 8 hours given for 14 days for infections of skin, eyes, or mouth or 21 days for disseminated or CNS infections.

HIV-infected or -exposed neonates: 20 mg/kg 3 times daily given for 14 days for infections of skin, eyes, or mouth or 21 days for disseminated or CNS infections.

- **Prevention of HSV Recurrence in Hematopoietic Stem Cell Transplant (HSCT) Recipients**

Oral

HSV-seropositive children: 0.6–1 g daily given in 3–5 divided doses.

HSV-seropositive adolescents: 200 mg 3 times daily.

Initiate prophylaxis at beginning of conditioning therapy and continue until engraftment or until mucositis resolves (approximately 30 days after allogeneic HSCT). Routine prophylaxis for >30 days after HSCT not recommended.

IV

HSV-seropositive children: 250 mg/m^2 every 8 hours or 125 mg/m^2 every 6 hours.

HSV-seropositive adolescents: 250 mg/m^2 every 12 hours.

Initiate prophylaxis at beginning of conditioning therapy and continue until engraftment or until mucositis resolves (approximately 30 days after allogeneic HSCT). Routine prophylaxis for >30 days after HSCT not recommended.

- **Genital Herpes**

Treatment of First Episodes

Oral

Children: AAP recommends 40–80 mg/kg daily (maximum 1 g daily) given in 3 or 4 divided doses for 5–10 days.

Adolescents: CDC recommends 400 mg 3 times daily or 200 mg 5 times daily for 7–10 days; duration may be extended if healing is incomplete after 10 days.

HIV-infected adolescents: CDC and others recommend 20 mg/kg (up to 400 mg) or 400 mg 3 times daily for 7–14 days.

IV

Adolescents and children ≥12 years of age with severe initial episodes: 5–10 mg/kg every 8 hours. 5–7 days of IV acyclovir or until clinical improvement occurs, followed by an oral antiviral to complete at least 10 days of treatment.

- **Episodic Treatment of Recurrent Episodes**

Oral

Adolescents: CDC recommends 400 mg 3 times daily for 5 days, 800 mg twice daily for 5 days, or

800 mg 3 times daily for 2 days.
HIV-infected adolescents: CDC recommends 400 mg 3 times daily for 5–10 days. Alternatively, acyclovir can be given for 7–14 days.
Initiate episodic therapy at the earliest prodromal sign or symptom of recurrence or within 1 day of the onset of lesions.

- **Chronic Suppression of Recurrent Episodes**

Oral
Adolescents: CDC recommends 400 mg twice daily.
HIV-infected adolescents: CDC recommends 400–800 mg 2 or 3 times daily.
Discontinue periodically (e.g., after 12 months or once yearly) to reassess need for continued therapy.

- **Varicella-Zoster Infections**

Treatment of Varicella (Chickenpox)
Oral
Immunocompetent children ≥2 years of age: 20 mg/kg 4 times daily (maximum 80 mg/kg daily) for 5 days in those weighing ≤40 kg and 800 mg 4 times daily for 5 days in those weighing >40 kg. Alternatively, some clinicians recommend 20 mg/kg (up to 800 mg) 4 times daily for 5 days.
HIV-infected children with mild immunosuppression and mild varicella: CDC and others recommend 20 mg/kg (up to 800 mg) 4 times daily for 7 days or until no new lesions have appeared for 48 hours.
Initiate therapy at the earliest sign or symptom of infection (within 24 hours of onset of rash).
IV
Immunocompromised children: AAP recommends 10 mg/kg 3 times daily for 7–10 days for those <1 year of age and 500 mg/m2 3 times daily for 7–10 days in those ≥1 year of age.
Immunocompromised adolescents and children: Some clinicians recommend 20 mg/kg every 8 hours for 7–10 days in those ≤12 years of age and 10 mg/kg every 8 hours for 7 days in those >12 years of age.
HIV-infected children with moderate or severe immunosuppression and varicella associated with high fever or necrotic lesions: CDC and others recommend 10 mg/kg 3 times daily for 7 days or until no new lesions have appeared for 48 hours. Alternatively, a dosage of 500 mg/m2 every 8 hours has been suggested for those ≥1 year of age.
HIV-infected adolescents: CDC and others recommend 10 mg/kg every 8 hours for 7–10 days. After defervescence and if there is no evidence of visceral involvement, switch to oral acyclovir in a dosage of 800 mg 4 times daily.

- **Treatment of Herpes Zoster (Shingles, Zoster)**

Oral
Immunocompetent children ≥12 years of age: 800 mg every 4 hours 5 times daily (4 g daily) for 5–10 days.
HIV-infected children with mild immunosuppression and mild varicella: CDC and others recommend 20 mg/kg (up to 800 mg) 4 times daily for 7–10 days.
Initiate therapy preferably within 48 hours of onset of rash.
IV
Immunocompetent children: AAP recommends 10 mg/kg 3 times daily for 7–10 days for those <1 year of age and 500 mg/m2 3 times daily for 7–10 days in those ≥1 year of age.
Immunocompromised children: 20 mg/kg every 8 hours for 7–10 days in those <12 years of age and 10 mg/kg every 8 hours for 7 days in those ≥12 years of age.
HIV-infected children with severe immunosuppression and extensive multidermatomal zoster or zoster with trigeminal nerve involvement: CDC and others recommend 10 mg/kg 3 times daily for 7–10 days.
HIV-infected adolescents: CDC and others recommend 10 mg/kg every 8 hours until cutaneous

	and visceral disease resolves **Topical**: **Herpes labialis (cold sores), recurrent:** Topical cream: Apply 5 times daily for 4 days **Prescribing Limits** **Pediatric Patients** **Oral:** Maximum 20 mg/kg 4 times daily (1 g daily) in children ≥2 years of age weighing ≤40 kg**.** **IV:** Maximum 20 mg/kg every 8 hours**.** **Adults:** **Oral:** 800 mg per dose**.** **IV:** Maximum 20 mg/kg every 8 hours
Dosage adjustment	**Renal Impairment:** Oral: CrCl >25 mL/minute/1.73 m^2: No dosage adjustment necessary. CrCl 10 to 25 mL/minute/1.73 m^2: If the usual recommended dose is 800 mg 5 times daily: Administer 800 mg every 8 hours CrCl <10 mL/minute/1.73 m^2: If the dose is 200 mg 5 times daily or 400 mg every 12 hours: Administer 200 mg every 12 hours If the dose is 800 mg 5 times daily: Administer 200 mg every 12 hours Intermittent hemodialysis (IHD): Dialyzable (60% reduction following a 6-hour session): same doses as CrCl <10 mL/minute/1.73 m^2 Continuous ambulatory peritoneal dialysis (CAPD): 600 to 800 mg daily IV: *If the usual recommended dose is 5-10 mg/kg/dose every 8 hours:* CrCl >50 mL/minute/1.73 m^2: No dosage adjustment necessary. CrCl 25 to 50 mL/minute/1.73 m^2: 5-10 mg/kg/dose every 12 hours CrCl 10 to <25 mL/minute/1.73 m^2: 5-10 mg/kg/dose every 24 hours CrCl <10 mL/minute/1.73 m^2: 2.5-5 mg/kg/dose every 24 hours Intermittent hemodialysis (IHD): Dialyzable (60% reduction following a 6-hour session): 2.5 to 5 mg/kg/dose every 24 hours Peritoneal dialysis (PD): 2.5 to 5 mg/kg/dose every 24 hours; **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to acyclovir, valacyclovir, or any component of the formulation
Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** Acute kidney injury Neurotoxicity Thrombotic microangiopathy **>10%:** Hematologic & oncologic: Decreased hemoglobin (neonates: 13%), decrease in absolute neutrophil count (neonates: 3% to 16%) Nervous system: Malaise (oral: 12%) **1% to 10%:** Central nervous system: Headache Dermatologic: Pruritus, skin rash, urticaria

	Gastrointestinal: Nausea, vomiting, diarrhea Hematologic & oncologic: Thrombocytopenia Hepatic: Increased serum bilirubin, increased serum transaminases Local: Inflammation at injection site, injection site phlebitis Renal: Increased blood urea nitrogen, increased serum creatinine
Monitoring Parameters	Urinalysis, BUN, serum creatinine, urine output; liver enzymes, CBC; monitor for neurotoxicity and nephrotoxicity in pediatric patients when using high dose therapy; neutrophil count at least twice weekly in neonates receiving acyclovir 60 mg/kg/day IV. Monitor infusion site.
Drug Interactions	Systemic treatment: ***Risk X: Avoid combination*** Cladribine, Foscarnet, Varicella Virus Vaccine, Zoster Vaccine (Live/Attenuated) ***Risk D: Consider therapy modification*** Tizanidine ***Risk C: Monitor therapy*** Clozapine, Mycophenolate, Tenofovir Products, Theophylline Derivatives, Zidovudine
Pregnancy and Lactation	**Pregnancy Category** B Acyclovir is considered compatible with breastfeeding
Administration	**Administration: Oral** Administer with or without food. **Administration: IV** For IV infusion only. Avoid rapid infusion. Infuse over 1 hour to prevent renal damage. Maintain adequate hydration of patient. Check for phlebitis and rotate infusion sites. Do not administer IM or SubQ. Acyclovir IV is an irritant (depending on concentration); avoid extravasation. If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); remove needle/cannula; elevate extremity. Apply dry warm compresses. Intradermal hyaluronidase may be considered for refractory cases. **Preparation for Administration:** Powder for injection: Reconstitute acyclovir 500 mg powder with SWFI 10 mL (final concentration 50 mg/mL); do not use bacteriostatic water containing benzyl alcohol or parabens. For intravenous infusion, dilute reconstituted powder for injection or solution for injection in D5W or NS to a final concentration ≤7 mg/mL. Concentrations >10 mg/mL increase the risk of phlebitis. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	Systemic treatment: • **CNS effects:** Neurotoxicity (eg, tremor/myoclonus, confusion, agitation, lethargy, hallucination, impaired consciousness) has been reported; risk may be increased with higher doses and in patients with renal failure. Monitor patients for signs/symptoms of neurotoxicity; • **Extravasation**: Acyclovir IV is an irritant. • **Renal effects:** Renal failure (sometimes fatal) has been reported. Dehydration, preexisting renal disease, and nephrotoxic drugs increase risk • **Thrombotic microangiopathy**: Has been reported in immunocompromised patients receiving acyclovir. ***Disease-related concerns:***

	• Varicella: Appropriate use: For maximum benefit, treatment should begin within 24 hours of appearance of rash; oral route not recommended for routine use in otherwise healthy children with varicella but may be effective in patients at increased risk of moderate-to-severe infection (>12 years of age, chronic cutaneous or pulmonary disorders, long-term salicylate therapy, corticosteroid therapy).
Storage	***Solid form:*** store at 15°C to 25°C ***Solution****:* Store solution at 20°C to 25°C ***Reconstituted solutions*** *or solutions diluted* for infusion with NS or D5W, Do not refrigerate, use within 24 hours. ***Cream:*** Store at or below 25°C Refer to manufacturer PIL if there are specific considerations.

2. Adefovir Dipivoxil

Generic Name	Adefovir Dipivoxil
Dosage form/strengths	Tablet 10 mg
Route of administration	Oral
Pharmacologic category	Antihepadnaviral, Reverse Transcriptase Inhibitor, Nucleotide (Anti-HBV) ATC: J05AF08
Indications	Treatment of chronic hepatitis B with evidence of active viral replication (based on persistent elevation of ALT/AST or histologic evidence)
Dosage Regimen	**Dosing: Adult, Geriatric** Hepatitis B (chronic): Oral: 10 mg once daily. Treatment duration for is variable and influenced by HBeAg status, duration of HBV suppression, and presence of cirrhosis/decompensation **Dosing: Pediatric** Children 2 to <7 years: Limited data available, Oral: 0.3 mg/kg/dose once daily; maximum dose: 10 mg Children ≥7 to <12 years: Limited data available; Oral: 0.25 mg/kg/dose once daily; maximum dose: 10 mg Children ≥12 years and Adolescents: Oral: 10 mg once daily; in HIV-exposed/-positive patients not requiring combination antiretroviral therapy or receiving a lamivudine- or emtricitabine-containing HIV-suppressive regimen, adefovir may be considered as HBV alternate therapy. Hepatitis B infection, chronic: Note: Optimal duration of treatment not established, continuation of therapy for at least 12 months after seroconversion has been suggested. Prolonged therapy (up to 4 years) has been reported to be safe and well-tolerated in pediatric patients (2 to 18 years).
Dosage adjustment	**Renal Impairment: Adult** CrCl ≥50 mL/minute: No dosage adjustment necessary CrCl 30-49 mL/minute: 10 mg every 48 hours CrCl 10-29 mL/minute: 10 mg every 72 hours **Hemodialysis:** Dialyzable: 10 mg every 7 days (following dialysis) Not been evaluated in patients with creatinine clearance < 10 mL/minute **Dosing: Altered Kidney Function: Pediatric** Children ≥12 years and Adolescents: no data available; consider dosage reduction. **Dosing: Hepatic Impairment: Adult** No adjustment required.
Contra-indications	Hypersensitivity to adefovir or any component of the formulation
Adverse Drug Reactions	**>10%:** Central nervous system: Headache (24% to 25%) Gastrointestinal: Abdominal pain (15%), diarrhea (≤13%) Genitourinary: Hematuria (grade ≥3: 11%) Hepatic: Hepatitis (exacerbation; ≤25% within 12 weeks of adefovir discontinuation) Neuromuscular & skeletal: Weakness (≤25%)

	1% to 10%: Dermatologic: Pruritus, skin rash Endocrine & metabolic: Hypophosphatemia (<2 mg/dL: 1% and 3% in pre-/post-liver transplant patients, respectively) Gastrointestinal: Flatulence (≤8%), dyspepsia (5% to 9%), nausea, vomiting Neuromuscular & skeletal: Back pain (≤10%) Renal: Increased serum creatinine (≥0.5 mg/dL: 2% to 3% in compensated liver disease; incidence may be higher in patients with decompensated cirrhosis or in liver transplant recipients), renal failure Respiratory: Cough (6% to 8%), rhinitis (≤5%)
Monitoring Parameters	HIV status (prior to initiation of therapy); Renal function (prior to initiation, during therapy and following discontinuation) Hepatic function with both clinical and laboratory follow-up at repeated intervals for several months following discontinuation
Drug Interactions	***Risk X: Avoid combination*** Cladribine, Tenofovir Products ***Risk D: Consider therapy modification*** Fexinidazole ***Risk C: Monitor therapy*** Ataluren Cabozantinib Nitisinone Orlistat Pretomanid Teriflunomide
Pregnancy and Lactation	Category C There are no adequate and well-controlled studies in pregnant women Breastfeeding is not recommended during use of this drug.
Administration	**Oral** without regard to food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • **[US Boxed Warning]: Fatal cases of lactic acidosis and severe hepatomegaly with steatosis have been reported with the use of nucleoside analogues alone or in combination with other antiretroviral;** use with caution in patients with risk factors for liver disease (risk may be increased with female gender, obesity, pregnancy or prolonged exposure) and suspend treatment in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or hepatotoxicity (transaminase elevation may/may not accompany hepatomegaly and steatosis). ***Disease-related concerns:*** • **[US Boxed Warning]: Severe, acute exacerbation of hepatitis B may occur upon discontinuation.** Exacerbations may occur in up to 25% of patients and usually within 12 weeks and may be self-limited or resolve upon resuming treatment; risk may be increased with advanced liver disease or cirrhosis. Monitor liver function several months after stopping treatment; reinitiating of ant hepatitis B therapy may be required. Ethanol should be avoided in hepatitis B infection due to potential hepatic toxicity. • **[US Boxed Warning]: May cause the development of HIV resistance in chronic hepatitis B patients with unrecognized or untreated HIV infection.** Determine HIV status prior to initiating treatment with adefovir. • **[US Boxed Warning]: Use with caution in patients with renal dysfunction or in patients at risk of renal toxicity (including concurrent nephrotoxic agents or NSAIDs).** Chronic administration

	may result in nephrotoxicity. Dosage adjustment is required in adult patients with renal dysfunction or in patients who develop renal dysfunction during therapy; no data available for use in children ≥12 years or adolescents with renal impairment. Calculation of creatinine clearance in all patients is recommended prior to initiating therapy. ***Other warnings/precautions:*** Current clinical hepatitis B practice guidelines do not recommend adefovir for initial use in the management of chronic HBV due to high rate of resistance with long-term use; other antiviral agents with a high barrier to drug resistance are preferred (eg, tenofovir or entecavir). In the setting of lamivudine-resistant HBV, adefovir is also not a preferred strategy to manage antiviral resistance If used, combination therapy with lamivudine should be used to decrease the risk of resistance in patients with lamivudine-resistant HBV. **Additional Pediatric Considerations** Efficacy in pediatric patients <12 years has not been reported; in clinical trials of children 2 to 12 years, positive responses to adefovir therapy were observed (13% to 17% of subjects evaluated); however, findings did not reach statistical significance.
Storage	Store controlled room temperature of 25°C Refer to manufacturer PIL if there are specific considerations.

3. Daclatasvir

Generic Name	Daclatasvir
Dosage form/strengths	Tablets 30mg, 60mg
Route of administration	*Oral*
Pharmacologic action	Antihepaciviral, NS5A Inhibitor ATC: J05AP07
Indications	**Chronic hepatitis C:** Treatment of chronic hepatitis C virus (HCV) genotype 1 or genotype 3 infection in combination with sofosbuvir, with or without ribavirin.
Dosage Regimen	**Dosing: Adult** **Note:** Not indicated as monotherapy. **Chronic hepatitis C (genotype 1):** Oral: – Patients without cirrhosis or with compensated cirrhosis (Child-Pugh class A): 60 mg once daily with concomitant sofosbuvir for 12 weeks. – Patients with decompensated (Child-Pugh class B or C) cirrhosis or post–liver transplant: 60 mg once daily with concomitant sofosbuvir and ribavirin for 12 weeks. **Chronic hepatitis C (genotype 3)**: – Patients without cirrhosis: 60 mg once daily with concomitant sofosbuvir for 12 weeks. – Patients with compensated (Child-Pugh class A) or decompensated cirrhosis (Child-Pugh class B or C) or post–liver transplant: 60 mg once daily with concomitant sofosbuvir and ribavirin for 12 weeks.
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary. **Dosing: Hepatic Impairment: Adult** Child-Pugh class A, B, or C: No dosage adjustment necessary.
Contra-indications	Hypersensitivity to daclatasvir or any component of the formulation; concurrent use with strong inducers of CYP3A4 and P-glycoprotein (P-gp) Concurrent use of strong CYP3A inducers (eg, carbamazepine, phenytoin, rifampin, St John's wort). When used in combination with other agents (eg, ribavirin), the contraindications to those agents also apply (refer to respective labeling information).
Adverse Drug Reactions	**>10%:** Central nervous system: Fatigue (14% to 15%), headache (12% to 14%) Gastrointestinal: Nausea (8% to 15%) Hematologic & Oncologic: Anemia (20%) **1% to 10%:** Central nervous system: Drowsiness, insomnia Dermatologic: Skin rash Gastrointestinal: Diarrhea, increased serum lipase (>3x ULN, transient)
Monitoring Parameters	– Baseline hepatitis C virus (HCV) genotype and subtype, quantitative HCV viral load. Baseline (within 6 months prior to treatment initiation) CBC, INR, hepatic function (albumin, total and direct bilirubin, ALT, AST, alkaline phosphatase), calculated GFR. Before initiating DAA therapy, serum pregnancy test (women of childbearing

	age) and assessment for HIV coinfection. – During treatment, monitor CBC, serum creatinine, calculated GFR, hepatic function panel as clinically indicated. Quantitative HCV viral load testing at ≥12 weeks after completion of therapy. Hepatitis B virus (HBV) surface antigen, HBV core antibody, and HBV surface antibody prior to initiation (AASLD/IDSA 2020). – Prior to treatment initiation in genotype 1a patients with cirrhosis, consider screening for the presence of NS5A polymorphisms at amino acid positions M28, Q30, L31, and Y93 in patients with cirrhosis. – In patients with serologic evidence of HBV infection, monitor for clinical and laboratory signs of hepatitis flare or HBV reactivation during treatment and during post-treatment follow-up. – If used in combination with amiodarone or in patients who discontinued amiodarone just prior to initiating sofosbuvir in combination with daclatasvir, inpatient cardiac monitoring for the first 48 hours of coadministration, then outpatient self-monitoring of heart rate daily through at least the first 2 weeks of treatment. – In patients with diabetes, monitor blood glucose and for signs/symptoms of hypoglycemia; in patients taking warfarin, monitor INR during and post-therapy
Drug Interactions	***Risk X: Avoid combination*** Abametapir Amiodarone Asunaprevir Bilastine Conivaptan CYP3A4 Inducers Doxorubicin Elagolix Elagolix, Estradiol, And Norethindrone Grazoprevir Idelalisib Ozanimod Pazopanib Revefenacin Rimegepant St John's Wort Topotecan Vincristine (Liposomal) Voxilaprevir ***Risk D: Consider Therapy Modification*** Afatinib Alpelisib Berotralstat Betrixaban Cladribine Colchicine CYP3A4 Inducers CYP3A4 Inhibitors Dabrafenib Dexamethasone (Systemic) Digoxin Eluxadoline Lefamulin Mifepristone Nevirapine Relugolix Rifapentine Sirolimus Stiripentol Ubrogepant Venetoclax
Pregnancy and Lactation	FDA pregnancy category: Not assigned. Risk summary: No data available on use of this drug in pregnant women to inform a drug-related risk. Breastfeeding is not recommended during use of this drug.
Administration	Administer with or without food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Bradycardia: When used in combination with sofosbuvir and amiodarone, symptomatic bradycardia has been reported; pacemaker intervention may be required. Risk factors include concomitant beta blocker use, underlying cardiac morbidities, and/or advanced hepatic disease. Bradycardia usually resolves after HCV treatment discontinuation. ***Disease-related concerns:*** • Cardiovascular disease: Patients with underlying cardiac morbidities and also taking concomitant amiodarone are at increased risk for symptomatic bradycardia; use with caution and monitor for bradycardia. • Diabetes: Rapid reduction in hepatitis C viral load during direct-acting antiviral (DAA) therapy for hepatitis C may lead to improvement in glucose metabolism in patients with diabetes, potentially resulting in symptomatic hypoglycemia if

	antidiabetic agents are continued at the same dose. Monitor for changes in glucose tolerance and inform patients of the risk of hypoglycemia during DAA therapy, particularly within the first 3 months. Modification of antidiabetic therapy may be necessary. • Hepatic disease: Patients with advanced hepatic disease and also taking concomitant amiodarone are at increased risk for symptomatic bradycardia; use with caution. Sustained virologic response rates are reduced in HCV genotype 3-infected patients with cirrhosis. Optimal duration of treatment for HCV genotype 3-infected patients with cirrhosis or HCV genotype 1 patients with Child-Pugh class C cirrhosis has not been established. • Hepatitis B virus reactivation: [US Boxed Warning]: Hepatitis B virus (HBV) reactivation has been reported in hepatitis C virus (HCV)/HBV coinfected patients who were receiving or had completed treatment with HCV direct-acting antivirals and were not receiving HBV antiviral therapy; some cases have resulted in fulminant hepatitis, hepatic failure, and death. Test all patients for evidence of current or prior HBV infection prior to initiation of daclatasvir; monitor HCV/HBV co-infected patients for hepatitis flare or HBV reactivation during treatment and post-treatment follow-up. Initiate treatment for HBV infection as clinically indicated. ***Other warnings/precautions:*** • Appropriate use: Do not use as monotherapy; use only in combination with other antihepatitis C virus drugs
Storage	Store at 25°C; excursions permitted between 15°C and 30°C. Refer to manufacturer PIL if there are specific considerations.

4. Entecavir

Generic Name	Entecavir
Dosage form/strengths	**Tablets/capsules** 0.5mg, 1mg **Oral solution** 0.25mg/5ml (0.5mg/10ml)
Route of administration	*Oral*
Pharmacologic action	Antihepadnaviral, Reverse Transcriptase Inhibitor, Nucleoside (Anti-HBV) ATC: J05AF10
Indications	**Chronic hepatitis B:** Treatment of chronic hepatitis B virus (HBV) infection in adults and pediatric patients ≥2 years of age with evidence of active viral replication and either evidence of persistent transaminase elevations or histologically-active disease. **Note:** In adults, indication is based on data in patients with compensated and decompensated liver disease; in children, indication is based on data in patients with compensated, HBeAg-positive liver disease.
Dosage Regimen	**Adults** **Hepatitis B virus infection, treatment: Oral:** **Nucleoside-treatment naive, compensated liver disease:** 0.5 mg once daily. **Decompensated liver disease:** 1 mg once daily. ***Treatment duration (AASLD practice guidelines):*** Treatment duration is variable and influenced by HBeAg status, duration of hepatitis B virus (HBV) suppression, and presence of cirrhosis/decompensation **Dosing: Pediatric** **Note:** Oral tablets and solution may be used interchangeably on a mg: mg basis. **Hepatitis B infection (HBV), chronic:** Oral: **Note:** Optimal duration of treatment not established for nucleoside analogs, a minimum of 12 months and typically longer required; consolidation therapy of at least 6 months after seroconversion and complete viral suppression has been suggested. Children and Adolescents 2 to <16 years with compensated liver diseases: Treatment naive: 10 to 11 kg: 0.15 mg oral solution once daily >11 to 14 kg: 0.2 mg oral solution once daily >14 to 17 kg: 0.25 mg oral solution once daily >17 to 20 kg: 0.3 mg oral solution once daily >20 to 23 kg: 0.35 mg oral solution once daily >23 to 26 kg: 0.4 mg oral solution once daily >26 to 30 kg: 0.45 mg oral solution once daily >30 kg: 0.5 mg oral solution or tablet once daily Lamivudine-experienced: 10 to 11 kg: 0.3 mg oral solution once daily >11 to 14 kg: 0.4 mg oral solution once daily >14 to 17 kg: 0.5 mg oral solution once daily >17 to 20 kg: 0.6 mg oral solution once daily >20 to 23 kg: 0.7 mg oral solution once daily >23 to 26 kg: 0.8 mg oral solution once daily >26 to 30 kg: 0.9 mg oral solution once daily >30 kg: 1 mg oral solution or tablet once daily Adolescents ≥16 years:

	Nucleoside treatment naïve with compensated liver disease: 0.5 mg once daily Lamivudine-refractory or known lamivudine or telbivudine-resistant mutations: 1 mg once daily
Dosage adjustment	**Dosing: Renal Impairment: Adult** Daily-dosage regimen preferred: CrCl ≥50 mL/minute: No dosage adjustment necessary. CrCl 30 to 49 mL/minute: Administer 50% of usual dose daily or administer the normal dose every 48 hours CrCl 10 to 29 mL/minute: Administer 30% of usual dose daily or administer the normal dose every 72 hours CrCl <10 mL/minute (including hemodialysis and CAPD): Administer 10% of usual dose daily or administer the normal dose every 7 days; administer after hemodialysis **Dosing: Hepatic Impairment: Adult** No dosage adjustment necessary. **Dosing: Renal Impairment: Pediatric** Children and Adolescents: Insufficient data to recommend a specific dose adjustment in pediatric patients with renal impairment; a reduction in the dose or an increase in the dosing interval similar to adjustments for adults should be considered. **Dosing: Hepatic Impairment: Pediatric** Children ≥ 2 years and Adolescents: No adjustment necessary.
Contra-indications	Hypersensitivity to entecavir or any component of the formulation
Adverse Drug Reactions	**>10%:** **Hepatic:** Increased serum alanine aminotransferase (>5 x ULN: 11% to 12%; >10 x ULN and >2 x baseline: 2%) **1% to 10%:** Dermatologic: Skin rash Endocrine & metabolic: Glycosuria, hyperglycemia Gastrointestinal: Abdominal pain, diarrhea, dyspepsia, increased serum lipase, nausea, vomiting Genitourinary: Hematuria Hepatic: Increased serum bilirubin Nervous system: Fatigue, headache Renal: Increased serum creatinine
Monitoring Parameters	HIV status (prior to initiation of therapy); periodic monitoring of hepatic function is recommended during treatment and for at least several months after treatment in patients who discontinue anti-hepatitis B therapy. Monitor patients for signs and symptoms of lactic acidosis and hepatotoxicity. Renal function at baseline and at least annually; monitor renal function more frequently in patients at high risk of renal dysfunction.
Drug Interactions	Cladribine: Agents that Undergo Intracellular Phosphorylation may diminish the therapeutic effect of Cladribine. *Risk X: Avoid combination*
Pregnancy and Lactation	**pregnancy category** C Entecavir has not been studied in nursing mothers. An alternate drug may be preferred, especially while nursing a newborn or preterm infant.
Administration	**Administration:**

	Oral: Administer on an empty stomach (2 hours before or after a meal). Oral solution: Do not dilute or mix oral solution with water or other beverages; use calibrated oral dosing syringe. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Lactic acidosis/hepatomegaly: [US Boxed Warning]: Lactic acidosis and severe hepatomegaly with steatosis (including fatal cases) have been reported with nucleoside analogue inhibitors ***Disease-related concerns:*** • Chronic hepatitis B: [US Boxed Warning]: Severe, acute exacerbation of hepatitis B may occur upon discontinuation of antihepatitis B therapy, including entecavir. Monitor liver function for at least several months after stopping treatment; reinitiation of antihepatitis B therapy may be required. • HIV: [US Boxed Warning]: May cause the development of HIV resistance in chronic hepatitis B patients with unrecognized or untreated HIV infection. Determine HIV status prior to initiating treatment with entecavir. **Not recommended for HIV/HBV coinfected patients unless also receiving antiretroviral therapy.** • Hepatic impairment: Dose adjustment not required. Limited data supporting treatment of chronic hepatitis B in patients with decompensated liver disease; observe for increased adverse reactions, including hepatorenal dysfunction. • Renal impairment: Use with caution in patients with renal impairment or patients receiving concomitant therapy which may reduce renal function; dose adjustment recommended for CrCl <50 mL/minute. ***Special populations:*** • Children: There are limited data available on the use of entecavir in lamivudine-experienced pediatric patients; use in these patients only if the potential benefit justifies the potential risk to the child. ***Dosage form specific issues:*** • Polysorbate 80: Some dosage forms may contain polysorbate 80 (also known as Tweens). Hypersensitivity reactions, usually a delayed reaction, have been reported following exposure to pharmaceutical products containing polysorbate 80 in certain individuals. Thrombocytopenia, ascites, pulmonary deterioration, and renal and hepatic failure have been reported in premature neonates after receiving parenteral products containing polysorbate 80. ***Other warnings/precautions:*** • Resistance: Cross-resistance may develop in patients failing previous therapy with lamivudine
Storage	Store at 25°C; excursions permitted to 15°C to 30°C. Protect from light. After opening, oral solution can be used up to expiration date on the bottle. Refer to manufacturer PIL if there are specific considerations.

5. Famciclovir

Generic Name	Famciclovir
Dosage form/strengths	Tablets 125,250,500 mg
Route of administration	Oral
Pharmacologic category	Antiviral ATC: J05AB09
Indications	Treatment of acute herpes zoster (shingles) in immunocompetent patients Treatment and suppression of recurrent episodes of genital herpes in immunocompetent patients Treatment of herpes labialis (cold sores) in immunocompetent patients Treatment of recurrent orolabial/genital (mucocutaneous) herpes simplex in adult patients with HIV
Dosage Regimen	**Dosing: Adult** **Genital herpes simplex virus infection**: ***Immunocompetent patients:*** Recurrence: 125 mg twice daily for 5 days or 500 mg as a single dose, followed by 250 mg twice daily for 2 days. Suppressive therapy: 250 mg twice daily. Note: Duration not established, but efficacy/safety have been demonstrated for 1 year. ***Immunocompromised patients (including patients with HIV):*** *Initial or recurrent episodes:* 500 mg twice daily for 5 to 10 days; extend treatment duration if lesions have not healed completely after 10 days. **Herpes labialis/orolabial (cold sores):** Oral: Note: Initiate therapy as soon as possible after diagnosis and within 72 hours of rash onset. ***Immunocompetent patients:*** Recurrent episodes: 1,500 mg as a single dose; initiate therapy at first sign or symptom such as tingling, burning, or itching (initiated within 1 hour). ***Immunocompromised patients (including patients with HIV):*** Treatment: 500 mg twice daily for 5 to 10 days; extend treatment duration if lesions have not healed completely after 10 days. **Herpes zoster (shingles):** Oral: Note: Initiate therapy as soon as possible after diagnosis and within 1 week of rash onset or any time before full crusting of lesions. ***Immunocompetent patients:*** 500 mg every 8 hours for 7 days. **Dosing: Pediatric** **Herpes simplex virus (HSV) genital infection:** ***Immunocompetent patients:*** **Initial episode:** Children weighing ≥45 kg and Adolescents: Oral: 250 mg 3 times daily for 7 to 10 days. Note: Treatment can be extended if healing is incomplete after 10 days of therapy. **Recurrence: Adolescents: Note:** Initiate treatment within 1 day of lesion onset or during the prodrome that precedes some outbreaks. One-day regimen: Oral: 1,000 mg twice daily for 1 day Two-day regimen: Oral: 500 mg once as a single dose, followed 12 hours later by 250 mg twice daily for a total of 2 days Five-day regimen: Oral: 125 mg twice daily for 5 days

Suppressive therapy: Adolescents: Oral: 250 mg twice daily. **Note:** Duration not established; efficacy/safety have been demonstrated for 1 year.

HIV-exposed/-positive patients:
Initial or recurrent episodes: Adolescents: Oral: 500 mg twice daily for 5 to 10 days. Note: Treatment can be extended if healing is incomplete after 10 days of therapy.

Chronic suppressive therapy: Adolescents: Oral: 500 mg twice daily; suppressive therapy can be continued indefinitely regardless of CD4 count in patients with severe recurrences of genital herpes or in patients who want to minimize frequency of recurrences, or to reduce the risk of genital ulcer disease in patients with CD4 cell counts <250 cells/mm^3 who are starting antiretroviral therapy. However, continuation of therapy should be reviewed annually, particularly if immune reconstitution has occurred**.**
Herpes labialis/orolabial (cold sores) in HIV-exposed/-positive patients, treatment: Limited data available: Adolescents: Oral: 500 mg twice daily for 5 to 10 days
Herpes zoster (shingles) in HIV- exposed/-positive patients, treatment: Adolescents: Oral:
Acute localized dermatomal lesion: 500 mg 3 times daily for 7 to 10 days; consider longer duration if lesions heal slowly
***Extensive cutaneous lesion or visceral involvement*:** Initial therapy with acyclovir IV may be switched to famciclovir 500 mg 3 times daily to complete a 10- to 14-day course, when formation of new lesions has ceased and signs and symptoms of visceral VZV infection are improving
Varicella infection (chickenpox) in HIV-exposed/-positive patients (uncomplicated cases), treatment: Limited data available: Adolescents: Oral: 500 mg 3 times daily for 5 to 7 days.

Dosage adjustment

Dosing: Renal Impairment: Adult
Herpes zoster:
CrCl ≥60 mL/minute: No dosage adjustment necessary.
CrCl 40 to 59 mL/minute: Administer 500 mg every 12 hours
CrCl 20 to 39 mL/minute: Administer 500 mg every 24 hours
CrCl <20 mL/minute: Administer 250 mg every 24 hours
Hemodialysis: Administer 250 mg after each dialysis session.
Recurrent genital herpes: Treatment:
Single-day regimen:
CrCl ≥60 mL/minute: No dosage adjustment necessary.
CrCl 40 to 59 mL/minute: Administer 500 mg every 12 hours for 1 day
CrCl 20 to 39 mL/minute: Administer 500 mg as a single dose
CrCl <20 mL/minute: Administer 250 mg as a single dose
Hemodialysis: Administer 250 mg as a single dose after a dialysis session.
Recurrent genital herpes: Suppression:
CrCl ≥40 mL/minute: No dosage adjustment necessary.
CrCl 20 to 39 mL/minute: Administer 125 mg every 12 hours
CrCl <20 mL/minute: Administer 125 mg every 24 hours
Hemodialysis: Administer 125 mg after each dialysis session.
Recurrent herpes labialis: Treatment (single-dose regimen):
CrCl ≥60 mL/minute: No dosage adjustment necessary.
CrCl 40 to 59 mL/minute: Administer 750 mg as a single dose
CrCl 20 to 39 mL/minute: Administer 500 mg as a single dose
CrCl <20 mL/minute: Administer 250 mg as a single dose
Hemodialysis: Administer 250 mg as a single dose after a dialysis session.
Recurrent orolabial/genital (mucocutaneous) herpes in patients with HIV:

	CrCl ≥40 mL/minute: No dosage adjustment necessary. CrCl 20 to 39 mL/minute: Administer 500 mg every 24 hours CrCl <20 mL/minute: Administer 250 mg every 24 hours Hemodialysis: Administer 250 mg after each dialysis session. **Dosing: Hepatic Impairment: Adult** No dosage adjustment is necessary **Dosing: Renal Impairment: Pediatric** There are no pediatric specific recommendations available; based on experience in adult patients; dosage adjustment suggested. **Dosing: Hepatic Impairment: Pediatric** There are no pediatric specific recommendations available; experience in adults suggests no dosage adjustment is necessary.
Contra-indications	Hypersensitivity to famciclovir, penciclovir, or any component of the formulation
Adverse Drug Reactions	**10%:** Central nervous system: Headache (9% to 23%) Gastrointestinal: Nausea (11% to 13%) **1% to 10%:** Central nervous system: Fatigue (≤5%), migraine (≤3%), paresthesia (≤3%) Dermatologic: Pruritus (2% to 4%), skin rash (3%) Gastrointestinal: Diarrhea (2% to 8%), flatulence (≤5%), vomiting (≤5%) Genitourinary: Dysmenorrhea (≤8%) Hematologic & oncologic: Neutropenia (3%), leukopenia (1%) Hepatic: Increased serum ALT (3%), increased serum AST (2%), increased serum bilirubin (2%)
Monitoring Parameters	Periodic CBC during long-term therapy; renal function
Drug Interactions	***Risk X: Avoid combination*** Cladribine, Varicella Virus Vaccine, Zoster Vaccine (Live/Attenuated)
Pregnancy and Lactation	**Pregnancy category** B Because there is no published experience with famciclovir during breastfeeding, other agents may be preferred, especially while nursing a newborn or preterm infant.
Administration	**Oral**: May be administered without regard to meals Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Disease-related concerns:*** • ***Renal impairment:*** Use with caution in patients with renal impairment; dosage adjustment required. Acute renal failure has been reported with use of inappropriate high doses in patients with underlying renal disease. Dosage form specific issues***:*** • ***Lactose:*** Tablets contain lactose; do not use with galactose intolerance, severe lactase deficiency, or glucose-galactose malabsorption syndromes. ***Other warnings/precautions:*** • ***Appropriate use:*** Has not been established for use in initial episodes of genital herpes, recurrent episodes of genital herpes in Black and African-American patients, patients with ophthalmic or disseminated zoster, immunocompromised patients (except patients with HIV with orolabial or genital herpes).
Storage	Store at 20°C to 25°C; excursions permitted to 15°C to 30°C Refer to manufacturer PIL if there are specific considerations.

6. Favipiravir

Generic Name	Favipiravir
Dosage form/strengths	Tablets 200 mg
Route of administration	Oral
Pharmacologic category	Antiviral ATC: J05AX27
Indications	Coronavirus disease 2019 (COVID-19)
Dosage Regimen	**Dosing: Adult** 1.6 g twice daily on day 1, followed by 600 mg twice daily for a total duration of 7 to 14 days For mild to moderate COVID-19, some international markets have studied and approved a dose of 1.8 g twice daily on day 1, followed by 800 mg twice daily for a total duration of up to 14 days.
Dosage adjustment	**Dosing: Renal Impairment: Adult** Mild to moderate impairment: There are no specific dosage adjustments recommended. Severe impairment: Use is contraindicated. **Dosing: Hepatic Impairment: Adult** Mild to moderate impairment: There are no specific dosage adjustments recommended. Severe impairment: Use is contraindicated.
Contra-indications	Hypersensitivity to favipiravir or any component of the formulation; severe renal or hepatic impairment; pregnancy; breastfeeding.
Adverse Drug Reactions	**Frequency not defined:** Cardiovascular: Chest pain Endocrine & metabolic: Hyperuricemia Gastrointestinal: Decreased appetite, diarrhea, nausea, vomiting Hematologic & oncologic: Decreased neutrophils Hepatic: Hepatic injury, increased serum transaminases
Monitoring parameters	No data available
Drug Interactions	***Risk D: Consider therapy modification*** Influenza Virus Vaccine (Live/Attenuated)
Pregnancy and Lactation	Based on animal data, use is contraindicated in pregnant patients & breastfeeding
Administration	**Favipiravir** should be taken orally, either with or without **food**. **Favipiravir** tablets should be swallowed whole with water. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • ***Hyperuricemia: C***aution in patients with a history of uric acid metabolism abnormalities***.*** ***Disease-related concerns:*** • ***Gout:*** Use with caution; may increase uric acid.
Storage	Store in a temperature not exceeding 30 ^{0}C, in a dry place Refer to manufacturer PIL if there are specific considerations.

7. Ganciclovir

Generic Name	Ganciclovir
Dosage form/strengths	Powder for injection: 500mg Ophthalmic gel 1.5 mg/gm Ophthalmic drops 0.150 gm/100g
Route of administration	IV, IM, ophthalmic
Pharmacologic action	Antiviral Agent ATC (Systemic): J05AB06 ATC (Ophthamic): S01AD09
Indications	**Cytomegalovirus disease, prophylaxis (transplant patients):** Prevention of cytomegalovirus (CMV) disease in adult transplant recipients at risk for CMV disease. **Cytomegalovirus retinitis (immunocompromised patients**): Treatment of CMV retinitis in immunocompromised adult patients, including patients with AIDS.
Dosage Regimen	**Dosing: Adult** **Cytomegalovirus retinitis (immunocompromised patients):** Immediate sight-threatening lesions (adjacent to the optic nerve or fovea): **IV (alternative agent):** 5 mg/kg/dose every 12 hours for 14 to 21 days followed by chronic maintenance therapy (secondary prophylaxis) Chronic maintenance therapy (alternative agent): **IV:** 5 mg/kg/dose once daily (7 days/week) or 6 mg/kg/dose once daily (5 days/week) for 3 to 6 months until sustained CD4 count >100 cells/mm^3 in response to antiretroviral therapy; discontinue only after consultation with an ophthalmologist **Cytomegalovirus disease prophylaxis in transplant patients: IV:** Hematopoietic cell transplant recipients (allogeneic): 5 mg/kg/dose every 12 hours for 5 to 7 days, then 5 mg/kg/dose every 24 hours until day 100 post-transplant. Solid organ transplant recipients: 5 mg/kg/dose every 24 hours; duration of prophylaxis is dependent on type of transplant, as well as donor and recipient cytomegalovirus (CMV) serostatus **Dosing: Pediatric** **CNS infection, treatment (HIV-exposed/-positive**): Infants and Children: Induction: 5 mg/kg/dose every 12 hours; continue until symptoms improve, followed by chronic maintenance therapy (secondary prophylaxis) Chronic maintenance therapy (secondary prophylaxis): IV: 5 mg/kg/dose once daily; continue maintenance therapy (with ganciclovir, valganciclovir, or foscarnet as appropriate) until patient has been receiving antiretroviral therapy for ≥6 months and achieves CD4 cell count targets for at least 6 months (age <6 years: CD4 percentage ≥15%; age ≥6 years: >100 cells/mm^3). Adolescents: 5 mg/kg/dose every 12 hours in combination with foscarnet until symptoms improve; optimal duration not defined **Cytomegalovirus retinitis (immunocompromised patients [including patients with HIV]):** Induction therapy: 5 mg/kg/dose every 12 hours for 14-21 days; may be increased to 7.5 mg/kg/dose every 12 hours Maintenance therapy: Infants ≥ 3 months and Children: 5 mg/kg/dose as a single daily dose for 5-7 days/week **Secondary prevention in HIV-exposed/-infected patients: Infants and Children:** 5 mg/kg/dose once daily **Prevention in transplant recipients**: Children: Initial: 5 mg/kg/dose every 12 hours for 1-2 weeks,

followed by 5 mg/kg/dose once daily 7 days/week or 6 mg/kg/dose once daily 5 days/week for 100 days

Cytomegalovirus disease, prophylaxis (transplant patients): Note: For patients considered at risk for CMV disease based on donor and recipient CMV serostatus:

Hematopoietic cell transplant recipients (allogeneic) Infants, Children, and Adolescents: Limited data available: IV: 5 mg/kg/dose every 12 hours for 5 to 7 days starting at neutrophil engraftment, then 5 mg/kg/dose every 24 hours until day 100 posttransplant.

***Solid organ transplant recipients*: Infants, Children, and Adolescents: Limited data available: IV:** 5 mg/kg/dose every 24 hours; initiate therapy within 10 days after transplant. Oral valganciclovir typically preferred when appropriate. Total duration of prophylaxis varies depending on organ(s) transplanted, donor and recipient CMV serostatus, and immunosuppressive regimen; typically continued for 3 to 6 months; may be continued for up to 12 months in certain case

Other CMV infections: Children: Initial: 5 mg/kg/dose every 12 hours for 14-21 days; maintenance therapy: 5 mg/kg/dose once daily for 7 days/week or 6 mg/kg/dose once daily for 5 days/week

Dosage adjustment

Dosing: Renal Impairment: Adult

Cl_{cr} (mL/minute)	Initial Treatment (Induction) Dosage	Maintenance Dosage
50–69	2.5 mg/kg every 12 hours	2.5 mg/kg every 24 hours
25–49	2.5 mg/kg every 24 hours	1.25 mg/kg every 24 hours
10–24	1.25 mg/kg every 24 hours	0.625 mg/kg every 24 hours
<10	1.25 mg/kg 3 times weekly	0.625 mg/kg 3 times weekly
Intermittent hemodialysis (IHD) (administer after hemodialysis on dialysis days): Dialyzable (50%): CMV Infection: IV: Induction: 1.25 mg/kg every 3days; Maintenance: 0.625 mg/kg every 3days. **Note:** Dosing dependent on the assumption of 3 times/week, complete IHD sessions		

Dosing: Renal Impairment: Pediatric

Infants, Children and Adolescents: There are no specific pediatric recommendations; based on experience in adult patients, dosage adjustment necessary.

Dosing: Hepatic Impairment:

There are no dosage adjustments data.

Contra-indications

Hypersensitivity to ganciclovir, valganciclovir, acyclovir, or any component of the formulation

Adverse Drug Reactions

Dermatologic: Hyperhidrosis (12%)
Gastrointestinal: Diarrhea (44%), anorexia (14%), vomiting (13%)
Hematologic & oncologic: Thrombocytopenia
Infection: Sepsis (15%), infection (13%)
Ophthalmic: Retinal detachment (11%; relationship to ganciclovir not established)
Renal: Increased serum creatinine
Miscellaneous: Fever (48%)

Monitoring Parameters

CBC with differential and platelet count at baseline and twice weekly, serum creatinine at baseline and once weekly; pregnancy test prior to initiation in females of reproductive potential; frequent

	ophthalmological exams in patients with CMV retinitis.
Drug Interactions	***Risk X: Avoid combination*** Cladribine ***Risk D: Consider therapy modification*** Imipenem ***Risk C: Monitor therapy*** Zidovudine, Tenofovir Products, Probenecid, Mycophenolate, Didanosine, cyclosporine, Amphotericin B
Pregnancy and Lactation	Ganciclovir caused maternal and fetal toxicity, embryofetal mortality, and teratogenic effects in animal studies. It is unknown if ganciclovir is excreted in human breast milk, but the possibility of ganciclovir being excreted in breast milk and causing serious adverse reactions in the breastfed infant cannot be excluded. Therefore, breastfeeding must be discontinued during treatment with ganciclovir
Administration	**Administration: IV** For IV infusion; should not be administered by IM, SubQ, or rapid or bolus IV injection. Administer by slow IV infusion over at least 1 hour. Too rapid infusion can cause increased toxicity due to excessive plasma levels. Flush line well with NS before and after administration. **Preparation for Administration:** Reconstitute 500 mg vial with 10 mL unpreserved sterile water (do **not** use bacteriostatic water; parabens may cause precipitation). Shake vial to dissolve. Typically, dilute in 100 mL D5W or NS to a concentration ≤10 mg/mL for infusion. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Carcinogenic/teratogenic: [US Boxed Warning]: Based on animal data and limited human data, ganciclovir may cause temporary or permanent inhibition of spermatogenesis in males and suppression of fertility in females. Based on animal data, ganciclovir has the potential to cause birth defects and cancers in humans. • Hematologic toxicity: [US Boxed Warning]: Granulocytopenia (neutropenia), anemia, thrombocytopenia, and pancytopenia may occur • Renal toxicity: Increased serum creatinine levels have been reported in elderly patients and transplant patients receiving concomitant nephrotoxic medications (eg, cyclosporine, amphotericin B). Monitor renal function during therapy, especially in elderly patients and those receiving concomitant nephrotoxic agents. ***Special populations:*** • Elderly: Increased serum creatinine levels have been reported; use with caution and closely monitor serum creatinine. ***Other warnings/precautions:*** • Administration: Ensure patients are adequately hydrated. Avoid rapid infusion. Phlebitis and/or pain may occur at injection site despite adequate dilution; infuse solution into veins with adequate blood flow.
Storage	• Store intact vials and premixed solution bags at 25°C. • Reconstituted solution in the vial is stable at room temperature for 12 hours; do not refrigerate or freeze. • Diluted solutions for infusion should be refrigerated and used within 24 hours of preparation; do not freeze. Refer to manufacturer PIL if there are specific considerations.

8. Lamivudine and Zidovudine

Generic Name	Lamivudine and Zidovudine
Dosage form/strengths	Tablets Lamivudine 150 mg ; Zidovudine 300 mg ;
Route of administration	Oral
Pharmacologic category	Antiretroviral, Reverse Transcriptase Inhibitor, Nucleoside (Anti-HIV) ATC: J05AR01
Indications	**HIV-1 infection, treatment:** Treatment of HIV-1 infection in combination with other antiretrovirals.
Dosage Regimen	**Dosing: adult** **HIV-1 infection, treatment:** Oral: One tablet (lamivudine 150 mg/zidovudine 300 mg) twice daily. **Dosing: Pediatric** **Note:** Use in combination with at least one other antiretroviral agent. **HIV-1 Treatment:** Children and Adolescents weighing <30 kg: Not intended for use; product is a fixed-dose combination; safety and efficacy have not been established in these patients Children and Adolescents weighing ≥30 kg: Oral: One tablet twice daily
Dosage adjustment	**Dosing: Renal Impairment:** CrCl ≥50 mL/minute: No dosage adjustment necessary. CrCl <50 mL/minute: Use is not recommended (use dose-adjusted individual components). **Dosing: Hepatic Impairment:** Use is not recommended (use dose-adjusted individual components).
Contra-indications	Hypersensitivity to lamivudine or zidovudine, or any component of the formulation. Neutrophil count <750/mm^3 or hemoglobin <7.5 g/dL (4.65 mmol/L)
Adverse Drug Reactions	Refer to single drug adverse effects
Monitoring Parameters	Amylase, bilirubin, signs and symptoms of pancreatitis. Monitor CBC with differential and platelet count at least every 2 weeks, liver function tests (including signs/symptoms of hepatomegaly), MCV, serum creatinine kinase, viral load, and CD4 count; observe for appearance of opportunistic infections; signs of muscle weakness or pain; blood lactate levels and signs of acidosis
Drug Interactions	***Risk X: Avoid combination*** Amodiaquine BCG (Intravesical) Cladribine Dipyrone Emtricitabine Stavudine ***Risk D: Consider therapy modification*** Clarithromycin Deferiprone Doxorubicin Ribavirin Sorbitol Tolvaptan ***Risk C: Monitor therapy*** Teriflunomide Trimethoprim Acemetacin Acyclovir Valacyclovir Cabozantinib Clozapine Dexketoprofen Fluconazole Ganciclovir Valganciclovir Interferons Levomethadone Mesalamine Methadone Nitisinone Orlistat Pretomanid Probenecid Promazine Protease Inhibitors Raltegravir Rifamycin Derivatives Except: Rifabutin Tenoxicam Valproate Products
Pregnancy and Lactation	**Pregnancy factor C** Lamivudine is allowed during breastfeeding, use caution due to lackof long time safety data. Zidovudine has been well studied during breastfeeding. Milk levels are low and most breastfed

	infants do not have detectable blood levels. Some breastfed infants have developed anemia during maternal therapy.
Administration	Administer without regard to food Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hematologic toxicity: **[US Boxed Warning]: Zidovudine is associated with hematologic toxicity, including neutropenia and severe anemia.** Use with caution in patients with bone marrow compromise (granulocytes <1,000 cells/mm^3 or hemoglobin <9.5 g/dL). • Immune reconstitution syndrome: Patients may develop immune reconstitution syndrome resulting in the occurrence of an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (eg, Graves disease, polymyositis, Guillain-Barré syndrome) later in therapy; further evaluation and treatment may be required. • Lactic acidosis/hepatomegaly: [US Boxed Warning]: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues and other antiretrovirals. Female gender and obesity may increase the risk for development. Suspend treatment in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or hepatotoxicity (transaminase elevation may/may not accompany hepatomegaly and steatosis). • Lipoatrophy: Zidovudine may cause loss of subcutaneous fat, especially in the face, limbs, and buttocks. Lipoatrophy incidence and severity are related to cumulative exposure and may be only partially reversible; improvement may take months to years after switching to a regimen that does not contain zidovudine. Monitor patients for signs of lipoatrophy and consider switching to a non-zidovudine-containing regimen if lipoatrophy occurs. • Myopathy: [US Boxed Warning]: Prolonged use of zidovudine has been associated with symptomatic myopathy. ***Disease-related concerns:*** • Chronic hepatitis B: [US Boxed Warning]: Severe acute exacerbations of hepatitis B have been reported in patients coinfected with HBV and HIV-1 when therapy is discontinued; monitor patients with clinical and laboratory follow-up for at least several months after treatment discontinuation. Emergence of hepatitis B virus lamivudine-resistant variants has been reported in patients with concurrent HBV infection who received a lamivudine-containing regimen for HIV-1 treatment.
Storage	Store between 2°C and 30°C

9. Ledipasvir and Sofosbuvir

Generic Name	Ledipasvir and Sofosbuvir
Dosage form/strengths	Tablets: Sofosbuvir 400 mg; Ledipasvir 90 mg, Sofosbuvir 400 mg; Ledipasvir 180 mg
Route of administration	*Oral*
Pharmacologic action	Antihepaciviral, Polymerase Inhibitor (Anti-HCV); NS5A Inhibitor ATC: J05AP51
Indications	**Chronic hepatitis C**: Treatment of chronic hepatitis C virus genotype 1, 4, 5, or 6 infection in adult and pediatric patients ≥3 years of age, without cirrhosis or with compensated cirrhosis; genotype 1 in adult patients with decompensated cirrhosis, in combination with ribavirin; and genotype 1 or 4 in adult liver transplant patients without cirrhosis or with compensated cirrhosis, in combination with ribavirin.
Dosage Regimen	**Dosing: Adult** **Note:** Compensated cirrhosis is defined as Child-Pugh class A and decompensated cirrhosis is defined as Child-Pugh class B or C. **Chronic hepatitis C infection: Oral: According to.** ***Genotype 1:*** – *Treatment-naive patients without cirrhosis or with compensated cirrhosis or peginterferon/ribavirin treatment–experienced patients without cirrhosis:* Ledipasvir 90 mg/sofosbuvir 400 mg once daily for 12 weeks (8 weeks in treatment-naive patients without cirrhosis who are HIV uninfected and have hepatitis C virus RNA <6 million units/mL) – *Peginterferon/ribavirin treatment–experienced patients with compensated cirrhosis (alternative regimen):* Ledipasvir 90 mg/sofosbuvir 400 mg once daily with concomitant ribavirin for 12 weeks. – *NS3 protease inhibitor + peginterferon/ribavirin treatment–experienced patients:* *Without cirrhosis:* Ledipasvir 90 mg/sofosbuvir 400 mg once daily for 12 weeks. *With compensated cirrhosis (alternative regimen):* Ledipasvir 90 mg/sofosbuvir 400 mg once daily with concomitant ribavirin for 12 weeks. – *Non-NS5A inhibitor, sofosbuvir-containing regimen–experienced patients without cirrhosis (except in cases of simeprevir failure) (alternative regimen):* Ledipasvir 90 mg/sofosbuvir 400 mg once daily with concomitant ribavirin for 12 weeks. *Decompensated cirrhosis:* Ledipasvir 90 mg/sofosbuvir 400 mg once daily with concomitant ribavirin for 12 weeks; if ribavirin ineligible, ledipasvir 90 mg/sofosbuvir 400 mg once daily for 24 weeks. *Decompensated cirrhosis in patients with prior sofosbuvir- or NS5A inhibitor–based treatment failure:* Ledipasvir 90 mg/sofosbuvir 400 mg once daily with concomitant ribavirin for 24 weeks. – *Liver transplant recipients (treatment-naive and treatment-experienced) without cirrhosis or with compensated cirrhosis:* Ledipasvir 90 mg/sofosbuvir 400 mg once daily for 12 weeks. ***Genotype 4:*** – *Treatment-naive patients without cirrhosis or with compensated cirrhosis and peginterferon/ribavirin treatment–experienced patients without cirrhosis:* Ledipasvir 90

mg/sofosbuvir 400 mg once daily for 12 weeks.

Note: An 8-week duration may be considered in treatment-naive patients with favorable baseline characteristics (eg, no cirrhosis, HCV RNA <6 million units/mL, absence of genotype 4r).

- *Peginterferon/ribavirin treatment–experienced patients with compensated cirrhosis (alternative regimen):* Ledipasvir 90 mg/sofosbuvir 400 mg once daily with concomitant ribavirin for 12 weeks.
- *Liver transplant recipients (treatment naive and treatment experienced) without cirrhosis or with compensated cirrhosis:* Ledipasvir 90 mg/sofosbuvir 400 mg once daily with concomitant ribavirin for 12 weeks.

Genotype 5 or 6:

- *Treatment-naive and peginterferon/ribavirin treatment–experienced patients without cirrhosis or with compensated cirrhosis:* Ledipasvir 90 mg/sofosbuvir 400 mg once daily for 12 weeks.

  Note: Not recommended for treatment-naive patients with genotype 6e if subtype is known.
- *Decompensated cirrhosis in patients with sofosbuvir- or NS5A inhibitor–based treatment failure:* Ledipasvir 90 mg/sofosbuvir 400 mg once daily with concomitant ribavirin for 24 weeks.
- *Liver transplant recipients (treatment-naive and treatment-experienced) without cirrhosis or with compensated cirrhosis:* Ledipasvir 90 mg/sofosbuvir 400 mg once daily for 12 weeks.

Dosing: Pediatric

Note: Prior to initiating therapy, test patient for evidence of hepatitis B infection (current or prior).

Chronic hepatitis C infection (monoinfection or co-infected with HIV-1):

Children ≥3 years and Adolescents:

- 17 to <35 kg: tablets: Oral: 45 mg ledipasvir/200 mg sofosbuvir once daily.
- ≥35 kg: tablets: Oral: 90 mg ledipasvir/400 mg sofosbuvir once daily.
- Duration of therapy dependent upon multiple factors (eg, genotype, hepatic function [cirrhosis/compensation], previous treatment and response).

Note: Treatment-experienced patients are defined as those who have failed an interferon-based regimen.

Genotype 1*:*

- Treatment-naive patients without cirrhosis or with compensated cirrhosis (Child-Pugh class A) or treatment-experienced patients without cirrhosis: 12 weeks.
- Treatment-experienced patients with compensated cirrhosis (Child-Pugh class A): 24 weeks.
- Treatment-naive or treatment-experienced with decompensated cirrhosis (Child-Pugh class B or C): 12 weeks in combination with ribavirin.

Genotype 1 or 4*:* Treatment-naive or treatment-experienced liver transplant recipients without cirrhosis or with compensated cirrhosis (Child-Pugh class A): 12 weeks in combination with ribavirin.

Genotype 4, 5, or 6: Treatment-naive and treatment-experienced patients without cirrhosis or with compensated cirrhosis (Child-Pugh class A): 12 weeks.

Dosage

Dosing: Renal Impairment:

adjustment	Mild, moderate, or severe impairment: No dosage adjustment necessary. End-stage renal disease requiring hemodialysis: No dosage adjustment necessary. **Dosing: Hepatic Impairment:** Mild, moderate, or severe impairment: No dosage adjustment necessary.
Contra-indications	If ledipasvir/sofosbuvir is administered with ribavirin, the contraindications to ribavirin also apply. Hypersensitivity to any component of the formulation.
Adverse Drug Reactions	**>10%:** Nervous system: Headache (11% to 29%), fatigue (10% to 18%) Neuromuscular & skeletal: Asthenia (18% to 31%) **1% to 10%:** Gastrointestinal: Nausea, increased serum lipase, diarrhea Hepatic: Hyperbilirubinemia Nervous system: Irritability, insomnia, dizziness, depression Neuromuscular & skeletal: Myalgia, increased serum creatine kinase Respiratory: Cough, dyspnea
Monitoring Parameters	– Baseline (obtain any time prior to treatment initiation) quantitative hepatitis C virus (HCV) RNA; HCV genotype and subtype (if a non–pan-genotypic direct-acting antiviral [DAA] will be prescribed); staging of fibrosis. Baseline (within 6 months prior to treatment initiation) CBC, INR, hepatic function (albumin, total and direct bilirubin, ALT, AST, alkaline phosphatase), calculated GFR; baseline (obtain any time prior to treatment initiation). Before initiating DAA therapy, serum pregnancy test (women of childbearing age) and assessment for HIV coinfection. – Hepatitis B virus (HBV) surface antigen, HBV core antibody and HBV surface antibody prior to initiation. If used in combination with amiodarone (or in patients who discontinued amiodarone just prior to initiating ledipasvir/sofosbuvir), inpatient cardiac monitoring for the first 48 hours of coadministration, then outpatient or self-monitoring of heart rate daily through at least the first 2 weeks of treatment. – In patients with serologic evidence of HBV infection, monitor for clinical and laboratory signs of hepatitis flare or HBV reactivation during treatment and during posttreatment follow-up. – During treatment, monitor CBC, serum creatinine, calculated GFR, hepatic function panel as clinically indicated. Quantitative HCV viral load testing at ≥12 weeks after completion of therapy. – In patients with diabetes, monitor blood glucose and for signs/symptoms of hypoglycemia; in patients taking warfarin, monitor INR during and post-therapy.
Drug Interactions	***Risk X: Avoid combination*** Amiodarone Asunaprevir Bilastine Doxorubicin Elagolix Elagolix, Estradiol, And Norethindrone Grazoprevir Modafinil Oxcarbazepine Ozanimod Pazopanib P-Glycoprotein/ABCB1 Inducers Phenobarbital Primidone Revefenacin Rifabutin Rifapentine Rimegepant Rosuvastatin Simeprevir Tipranavir Topotecan Vincristine Voxilaprevir ***Risk D: Consider therapy modification*** Afatinib Alpelisib Antacids Berotralstat Betrixaban Cladribine Colchicine Digoxin Eluxadoline Histamine H2 Receptor Antagonists Lefamulin Proton Pump Inhibitors Relugolix Sirolimus Tenofovir Disoproxil Fumarate Ubrogepant Venetoclax
Pregnancy and Lactation	Pregnancy category: Not assigned. Risk summary: No data available on use of this drug in pregnant women to inform a drug-

	related risk. As a precaution, it is preferable to avoid use of this drug during pregnancy. It is not known if ledipasvir or sofosbuvir are present in breast milk. Because it is 99.8% bound to maternal plasma proteins, amounts in breastmilk are likely to be very low. If ledipasvir alone or in combination with sofosbuvir is required by the mother, it is not a reason to discontinue breastfeeding
Administration	Tablets: Administer with or without food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Disease-related concerns:*** • Diabetes: Rapid reduction in hepatitis C viral load during direct-acting antiviral (DAA) therapy for hepatitis C may lead to improvement in glucose metabolism in patients with diabetes, potentially resulting in symptomatic hypoglycemia if antidiabetic agents are continued at the same dose. Monitor for changes in glucose tolerance and inform patients of the risk of hypoglycemia during DAA therapy, particularly within the first 3 months. Modification of antidiabetic therapy may be necessary. • Hepatitis B virus reactivation: [US Boxed Warning]: Hepatitis B virus (HBV) reactivation has been reported in hepatitis C virus (HCV)/HBV coinfected patients who were receiving or had completed treatment with HCV direct-acting antivirals and were not receiving HBV antiviral therapy; some cases have resulted in fulminant hepatitis, hepatic failure, and death. Test all patients for evidence of current or prior HBV infection prior to initiation of ledipasvir/sofosbuvir; monitor HCV/HBV co-infected patients for hepatitis flare or HBV reactivation during treatment and post-treatment follow-up. Initiate treatment for HBV infection as clinically indicated. ***Concurrent drug therapy issues:*** • Amiodarone: Symptomatic bradycardia (some requiring pacemaker intervention) and fatal cardiac arrest has occurred in patients receiving amiodarone and ledipasvir/sofosbuvir. The risk of bradycardia may be increased in patients taking beta blockers or patients with underlying cardiac comorbidities and/or advanced liver disease. Bradycardia generally resolves following discontinuation of ledipasvir/sofosbuvir.
Storage	Tablets: Store below 30°C. Dispense in original packaging. Refer to manufacturer PIL if there are specific considerations.

10. Ombitasvir, Papritaprevir and Ritonavir

Generic Name	Ombitsavir + Papritaprevir + Ritonavir
Dosage form/strengths	Ritonavir 50 mg ; Ombitasvir 12.5 mg ; Papritaprevir 75 mg tablets
Route of administration	Oral
Pharmacologic category	Antiviral ATC: J05AP53
Indications	-Treatment of chronic hepatitis C (CHC) in adults. -For Hepatitis C virus (HCV) genotype specific activity including the following genotypes: - Genotype 1b, without cirrhosis or with compensated cirrhosis - Genotype 1a, without cirrhosis - Genotype 1a, with compensated cirrhosis - Genotype 4, without cirrhosis or with compensated cirrhosis
Dosage Regimen	-Adults: -Two 12.5mg / 75mg / 50mg tablets once daily. -It should be used in combination with other medicinal products for the treatment of HCV
Dosage adjustment	**-Renal Impairment:** No dose adjustment required for patients with mild, moderate, or severe renal impairment, or end-stage-renal disease on dialysis **-Hepatic impairment:** No dose adjustment required in patients with mild hepatic impairment (Child-Pugh A). -Contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B or C)
Contra-indications	- Hypersensitivity to the active substances or to any of the drug components - Moderate to severe hepatic impairment (Child-Pugh B or C) - Use of ethinyloestradiol-containing medicinal products such as those contained in most combined oral contraceptives or contraceptive vaginal rings - Medicinal products that are highly dependent on CYP3A for clearance and for which elevated plasma levels are associated with serious events including the following: -CYP3A4 substrates: ➢ alfuzosin hydrochloride, amiodarone, disopyramide, dronedarone, quinidine, ranolazine, astemizole, terfenadine, cisapride ➢ colchicine in patients with renal or hepatic impairment ➢ ergotamine, dihydroergotamine, ergonovine, methylergometrine ➢ fusidic acid, lomitapide, lovastatin, simvastatin, atorvastatin, lurasidone, oral midazolam, triazolam, pimozid, quetiapine, salmeterol, sildenafil (when used for the treatment of pulmonary arterial hypertension), ticagrelor - Medicinal products that are strong or moderate enzyme inducers is expected to decrease ombitasvir, paritaprevir, and ritonavir plasma concentrations and reduce their therapeutic effect including the following: -carbamazepine, phenytoin, phenobarbital, efavirenz, nevirapine, etravirine, apalutamide, enzalutamide, mitotane, rifampicin, St. John's Wort (Hypericum perforatum) - Medicinal products that are strong inhibitors of CYP3A4 is expected to increase paritaprevir plasma concentrations including the following: -Cobicistat , indinavir, lopinavir/ritonavir, saquinavir, tipranavir, itraconazole, ketoconazole, posaconazole, voriconazole , clarithromycin, telithromycin , conivaptan
Adverse Drug Reactions	-Fatigue, nausea, pruritus, other skin reactions, insomnia and asthenia

Monitoring Parameters	- Clinical signs and symptoms of hepatic decompensation (such as ascites, hepatic encephalopathy, variceal haemorrhage). - Direct bilirubin levels should be performed at baseline, during the first 4 weeks of starting treatment and as clinically indicated thereafter.
Drug Interactions	***Risk X: Avoid combination:*** Alfuzosin , Amiodarone ,Disopyramide, Dronedarone , Quinidine ,Ranolazine , Clarithromycin, Telithromycin , Fusidic Acid , Apalutamide , Enzalutamide, Mitotane , Carbamazepine , Phenobarbital , Phenytoin , Conivaptan , Ketoconazole , Itraconazole , Posaconazole , Voriconazole , Astemizole , Terfenadine , Lomitapide , Rifampicin , Lurasidone , Pimozide , Quetiapine , Ticagrelor , Ethinyloestra diol/ norgestimate , Ergotamine Dihydroergot amine , Ergonovine Methylergom etrine , Cisapride , St. John's Wort (hypericum perforatum) , Lopinavir / ritonavir , Indinavir Saquinavir Tipranavir , Efavirenz/ emtricitabine/ tenofovir disoproxil fumarate , Nevirapine etravirine , Cobicistatcontaining regimens , Lovastatin , Simvastatin , atorvastatin , Salmeterol , Sildenafil (when used for treatment of pulmonary hypertension) , Oral midazolam Triazolam, Colchicine (in patients with renal or hepatic impairment) ***Risk D: Consider therapy modification*** Abemaciclib Ado-Trastuzumab Emtansine Afatinib Alfentanil Alitretinoin (Systemic) Almotriptan Alpelisib Amiodarone Apixaban Aripiprazole Aripiprazole Lauroxil Atogepant Avacopan Axitinib Bedaquiline Berotralstat Brexpiprazole Brigatinib Brincidofovir Bromocriptine Budesonide Buspirone Cabazitaxel Cabozantinib Candesartan Cariprazine Ceritinib Cilostazol Cladribine Clarithromycin Copanlisib Crizotinib Cyclosporine (Systemic) Daclatasvir Darifenacin Darunavir Dasatinib Deflazacort Delamanid Digoxin Docetaxel Duvelisib Elexacaftor, Tezacaftor, And Ivacaftor Eliglustat Eluxadoline Encorafenib Entrectinib Erdafitinib Erlotinib Eszopiclone Fedratinib Felodipine Fentanyl Fesoterodine Fexinidazole Fluticasone (Oral Inhalation) Gilteritinib Glasdegib Guanfacine Halofantrine Hydrocodone Ibrexafungerp Idelalisib Iloperidone Irinotecan Products Istradefylline Ivacaftor Ivosidenib Ixabepilone Ketoconazole (Systemic) Lapatinib Larotrectinib Levomilnacipran Losartan Manidipine Maraviroc Midostaurin Mifepristone Mirodenafil Nifedipine Nilotinib Olaparib Osilodrostat Palbociclib Panobinostat Pemigatinib Pimavanserin Ponatinib Pralsetinib Pravastatin Quetiapine Relugolix Relugolix, Estradiol, And Norethindrone Riociguat Ruxolitinib (Systemic) Saxagliptin Selpercatinib Selumetinib Sildenafil Solifenacin Sufentanil Sunitinib Tadalafil Temsirolimus Tezacaftor And Ivacaftor Thioridazine Thiotepa Tofacitinib Tolterodine Toremifene Trazodone Triamcinolone (Systemic) Upadacitinib Valbenazine Valsartan Vardenafil Vemurafenib Venetoclax Vilazodone Vincristine Voriconazole Zanubrutinib Zopiclone
Pregnancy and Lactation	-Potential risk for humans is unknown. Viekirax should not be used during pregnancy or in women of childbearing potential not using effective contraception. Ritonavir is present in breast milk; it is not known if ombitasvir or paritaprevir are present in breast milk. A decision should be made to discontinue breastfeeding or discontinue the drug, taking into account the importance of the drug to the mother.
Administration	-Take with food without regard to fat and calorie content. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	- Watch for early warning signs of liver inflammation, such as fatigue, weakness, lack of appetite, nausea and vomiting, as well as later signs such as jaundice and discoloured faeces - Efficacy of Viekirax has not been established in patients with HCV genotypes 2, 3, 5 and 6; therefore, it should not be used to treat patients infected with these genotypes. - HIV co-infected patients without suppressive antiretroviral therapy should not be treated with the drug. - Diabetics may experience improved glucose control, potentially resulting in symptomatic hypoglycaemia, after initiating HCV direct acting antiviraltreatment. Glucose levels of diabetic

	patients initiating direct acting antiviraltherapy should be closely monitored, particularly within the first 3 months, and their diabetic medicinal productsmodified when necessary.
Storage	Store at or below 30°C Refer to manufacturer PIL if there are specific considerations.

11. Oseltamivir

Generic Name	Oseltamivir
Dosage form/strengths	Capsule 75mg Powder (or Granules) for Oral Suspension 12mg/ml
Route of administration	*Oral*
Pharmacologic category	Antiviral Agent; Neuraminidase Inhibitor ATC: J05AH02
Indications	**Influenza, seasonal, prophylaxis:** Prophylaxis of influenza (A or B) infection in patients ≥1 year of age. **Influenza, seasonal, treatment:** Treatment of uncomplicated acute illness due to influenza (A or B) infection in patients ≥2 weeks of age who have been symptomatic for no more than 48 hours. **Note:** The Advisory Committee on Immunization Practices (ACIP) recommends that treatment and prophylaxis be given to children <1 year of age when indicated.
Dosage Regimen	**Dosing: Adult** **Influenza, seasonal, prophylaxis: Oral:** 75 mg once daily Continue for 1 week after last exposure (if previously vaccinated) or 2 weeks (if unvaccinated). **Preexposure prophylaxis:** Only during widespread outbreaks for persons at very high risk for influenza complications (eg, severely immunocompromised patients) not protected by vaccination. Continue for the duration of influenza activity or for 2 weeks following vaccination. **Influenza, seasonal, treatment: Oral:** 75 mg twice daily. **Note:** Higher doses (150 mg twice daily) are **not** currently recommended even in severely ill or immunocompromised patients. ***Duration of therapy:*** Usual duration: 5 days; a longer duration can be considered in severely ill or immunocompromised patients. **Dosing: Pediatric** **Influenza, treatment: Note:** Treatment should ideally begin within 48 hours of illness onset; however, initiation after 48 hours is recommended for patients with severe, complicated, or progressive illness; hospitalized patients; or those at increased risk for complications (see **Use** for additional information). Initiate as early as possible in any hospitalized patient with suspected/confirmed influenza. The usual duration of therapy is 5 days; a longer duration may be necessary in severely ill or immunocompromised patients. Infants ≤8 months: Oral: 3 mg/kg/dose twice daily Infants ≥9 months: Oral: 3.5 mg/kg/dose twice daily Children and Adolescents: ≤15 kg: Oral: 30 mg twice daily. >15 to 23 kg: Oral: 45 mg twice daily. >23 to 40 kg: Oral: 60 mg twice daily. >40 kg: Oral: 75 mg twice daily. **Influenza, prophylaxis:** Infants ≥9 months: Limited data available: Oral: 3.5 mg/kg/dose once daily; some experts still recommend 3 mg/kg/dose once daily. Children and Adolescents:

	≤15 kg: Oral: 30 mg once daily. >15 kg to 23 kg: Oral: 45 mg once daily. >23 kg to 40 kg: Oral: 60 mg once daily. >40 kg: Oral: 75 mg once daily.
Dosage adjustment	**Dosing: Renal Impairment: Adult** **Influenza, seasonal, treatment:** CrCl >60 mL/minute: No dosage adjustment necessary CrCl >30 to 60 mL/minute: 30 mg twice daily CrCl >10 to 30 mL/minute: 30 mg once daily ESRD not undergoing dialysis: Use is not recommended (has not been studied) **Influenza, seasonal, prophylaxis:** CrCl >60 mL/minute: No dosage adjustment necessary CrCl >30 to 60 mL/minute: 30 mg once daily CrCl >10 to 30 mL/minute: 30 mg every other day ESRD not undergoing dialysis: Use is not recommended (has not been studied) **Dosing: Renal Impairment: Pediatric** Children and Adolescents: Treatment: Limited data available Intermittent hemodialysis (IHD): Fixed dosing: ≤15 kg: 7.5 mg after each hemodialysis session. >15 kg to ≤23 kg: 10 mg after each hemodialysis session. >23 kg to ≤40 kg: 15 mg after each hemodialysis session. >40 kg: 30 mg after each hemodialysis session. Prophylaxis: There are no pediatric specific recommendations; based on experience in adult patients, dosage adjustment suggested. **Dosing: Hepatic Impairment: Adult** Mild-to-moderate impairment: No dosage adjustment necessary. Severe impairment: No dosage adjustment data.
Contra-indications	Hypersensitivity to oseltamivir or any component of the formulation
Adverse Drug Reactions	**>10%:** Gastrointestinal: Vomiting (2% to 16%) Nervous system: Headache (adolescents and adults: 2% to 17%) **1% to 10%:** Gastrointestinal: Nausea Nervous system: Pain
Monitoring Parameters	signs or symptoms of unusual behavior, including attempts at self-injury, confusion, and/or delirium Critically ill patients: Repeat rRT-PCR or viral culture may help to determine on-going viral replication
Drug Interactions	***Risk X: Avoid combination*** Dichlorphenamide ***Risk D: Consider therapy modification*** Influenza Virus Vaccine (Live/Attenuated)
Pregnancy and	Pregnancy Category C

Lactation	Limited data indicate that oseltamivir and its active metabolite are poorly excreted into breastmilk. Maternal dosages of 150 mg daily produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. Infants over 1 year of age can receive oseltamivir directly in doses much larger than those in breastmilk.
Administration	**Administration: Pediatric** Oral: May administer with or without food; may decrease stomach upset if administered with food. • Capsules: May be opened and mixed with sweetened liquid (eg, chocolate syrup, light brown sugar [dissolved in water]). • Oral suspension: Shake suspension well before use; measure dose in an appropriately sized calibrated oral syringe that provides accurate measurement of prescribed dose. **Preparation of 6 mg/mL Oral Suspension** If the commercially prepared oral suspension is not available, compounding information to prepare a **6 mg/mL** suspension in emergency situations is: 1. Place the specified amount of water into a polyethyleneterephthalate (PET) or glass bottle. 2. Carefully separate the capsule body and cap and pour the contents of the required number of 75 mg capsules into the PET or glass bottle. 3. Gently swirl the suspension to ensure adequate wetting of the powder for at least 2 minutes. 4. Slowly add the specified amount of vehicle to the bottle. 5. Close the bottle using a child-resistant cap and shake well for 30 seconds to completely dissolve the active drug. 6. Label “Shake Well Before Use.” Stable for 35 days at 2°C to 8°C or 5 days at 25° C. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Disease-related concerns:*** • Cardiovascular disease: Use with caution in patients with chronic cardiac disease. • Hepatic impairment: Use with caution in patients with severe hepatic impairment; safety and efficacy have not been established. • Renal impairment: Use with caution; dosage adjustment is required for patients with renal impairment. Not recommended for patients with end stage renal disease (ESRD) not undergoing dialysis. • Respiratory disease: Use with caution in patients with respiratory disease. ***Dosage form specific issues:*** • Benzyl alcohol and derivatives: Some dosage forms may contain sodium benzoate/benzoic acid; benzoic acid (benzoate) is a metabolite of benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates; the “gasping syndrome” consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction, hypotension, and cardiovascular collapse; avoid or use dosage forms containing benzyl alcohol derivative with caution in neonates. • Sorbitol: Oral suspension contains sorbitol (delivers ~2 g sorbitol per 75 mg dose) which is greater than the maximum daily limit for patients with hereditary fructose intolerance; may cause diarrhea and dyspepsia; use with caution. ***Other warnings/precautions:*** • Appropriate use: Oseltamivir is not a substitute for the influenza virus vaccine. It has not been shown to prevent primary or concomitant bacterial infections that may occur with

	influenza virus. Antiviral treatment should begin within 48 hours of symptom onset. However, the CDC recommends that treatment may still be beneficial and should be started in hospitalized patients with severe, complicated or progressive illness if >48 hours. Treatment should not be delayed while awaiting results of laboratory tests for influenza. Nonhospitalized persons who are not at high risk for developing severe or complicated illness and who have a mild disease are not likely to benefit if treatment is started >48 hours after symptom onset. Nonhospitalized persons who are already beginning to recover do not need treatment.
Storage	**Capsules**: Store at 25°C; excursions permitted to 15°C to 30°C. **Oral suspension**: Store powder for suspension at 25°C; excursions permitted to 15°C to 30°C. Once reconstituted, store oral suspension under refrigeration at 2°C to 8°C or at room temperature; do not freeze. Use within 10 days of preparation if stored at room temperature or within 17 days of preparation if stored under refrigeration. Refer to manufacturer PIL if there are specific considerations.

12. Ribavirin

Generic Name	Ribavirin
Dosage form/strengths	Capsule 200mg, 400mg Tablets 200mg, 400mg, 500mg, 600mg Oral Syrup 100mg/5ml
Route of administration	*Oral*
Pharmacologic category	Antihepaciviral, Nucleoside (Anti-HCV) ATC: J05AP01
Indications	**Hepatitis C virus infection, chronic**: Ribavirin, in combination with direct-acting antivirals, is recommended in the AASLD/IDSA guidelines as part of an antiviral regimen for certain clinical scenarios. Hepatitis C treatment guidelines are frequently changing with the advent of new treatment therapies and information; consult current clinical practice guidelines for the most recent treatment recommendations.
Dosage Regimen	**Dosing: Adult** **Hepatitis C virus infection, chronic: according to** (AASLD/IDSA 2020) *Weight-based ribavirin:* <75 kg: 1 g/day in 2 divided doses. ≥75 kg: 1.2 g/day in 2 divided doses. *Low initial dose ribavirin:* 600 mg; increase as tolerated (maximum dose: 1 g/day [<75 kg] or 1.2 g/day [≥75 kg]). Dosing regimen, concomitant therapy, and duration is dependent on HCV genotype and treatment status (treatment-naive or treatment-experienced), as well as other factors (eg, presence and type of cirrhosis). Combination therapy with peginterferon is **not** recommended in HCV treatment guidelines. **Dosing: Pediatric** **Hepatitis C monoinfection, chronic:** **Note**: Combination therapy with interferon or peginterferon is **not** recommended; refer to current AASLD/IDSA clinical practice guidelines for most recent treatment recommendations. Children ≥3 years and Adolescents: Oral: Children ≥3 years and Adolescents: Oral: <47 kg: 15 mg/kg/day in 2 divided doses. 47 to 59 kg: 400 mg twice daily. 60 to 73 kg: 400 mg in the morning; 600 mg in the evening. >73 kg: 600 mg twice daily. • Discontinue treatment If: Hemoglobin <8.5 g/dL, WBC <1,000 mm^3, neutrophils <500 mm^3 , Platelets <25 x 10^9/L for adults or 50 x 10^9/L in children
Dosage adjustment	**Dosing: Renal Impairment:** **Hepatitis C monoinfection, chronic:** Capsules/solution: Oral: *Baseline*: CrCl ≥50 mL/minute: No dosage adjustments are recommended. CrCl <50 mL/minute: Use is contraindicated. *During therapy*: Serum creatinine >2 mg/dL: Permanently discontinue treatment.

	tablets: CrCl >50 mL/minute: No dosage adjustments necessary. CrCl 30 to 50 mL/minute: Alternate 200 mg and 400 mg every other day. CrCl <30 mL/minute: 200 mg once daily. ESRD requiring hemodialysis: 200 mg once daily. **Dosing: Hepatic Impairment:** **Hepatitis C, chronic:** Hepatic decompensation (Child-Pugh class B and C): Oral tablets: Use contraindicated. **Dosing adjustment for toxicity:** *Patient **without** cardiac history:* • Dose modifications in adults with Hemoglobin 8.5 to <10 g/dL: First reduction: ≤105 kg: Decrease by 200 mg daily; >105 kg: Decrease by 400 mg daily Second reduction: Decrease by an additional 200 mg daily (not weight-based) Oral tablets: Decrease dose to 600 mg daily (200 mg in the morning, 400 mg in the evening) *Patient **with** stable cardiac history:* Hemoglobin has decreased ≥2 g/dL during any 4-week period of treatment: Oral capsules, solution: Decrease dose by 200 mg daily; decrease peginterferon alfa-2b dose by 50%. If hemoglobin <8.5 g/dL any time after dose reduction or <12 g/dL after 4 weeks of dose reduction, permanently discontinue treatment. Oral tablets: Decrease dose to 600 mg daily (200 mg in the morning, 400 mg in the evening). If hemoglobin <8.5 g/dL any time after dose reduction or <12 g/dL after 4 weeks of dose reduction, permanently discontinue treatment. Hemoglobin <8.5 g/dL: Oral capsules, solution, tablets: Permanently discontinue treatment. WBC <1,000 mm^3, neutrophils <500 mm^3: Oral capsules, solution: Permanently discontinue treatment. Platelets <25 x 10^9/L: Oral capsules, solution: Permanently discontinue treatment.
Contra-indications	Hypersensitivity to ribavirin or any component of the formulation; women who are pregnant or may become pregnant; males whose female partners are pregnant; patients with hemoglobinopathies (eg, thalassemia major, sickle cell anemia); concomitant use with didanosine Patients with a CrCl <50 mL/minute
Adverse Drug Reactions	**>10%:** Dermatologic: Alopecia (17% to 36%; children and adolescents: 17% to 23%), dermatitis (13% to 16%), dermatologic disorder (children and adolescents: 47%), diaphoresis (4% to 11%), pruritus (13% to 29%; children and adolescents: 11% to 12%), skin rash (5% to 34%; children and adolescents: 15% to 17%), xeroderma (10% to 24%) Endocrine & metabolic: Growth retardation (children and adolescents: <3rd percentile height decrease: 70%, >15 percentile height or weight decrease: 11% to 43%, >30 percentile height decrease: ≤13%), hyperuricemia (33% to 38%), weight loss (10% to 29%; children and adolescents: 19%) Gastrointestinal: Abdominal pain (8% to 21%), anorexia (21% to 32%; children and adolescents: 29% to 51%), decreased appetite (children and adolescents: 11% to 22%), diarrhea (10% to 22%), dyspepsia (5% to 16%; children and adolescents: <1%), gastrointestinal disease (children and adolescents: 49% to 56%), nausea (≤47%; children and adolescents: 18% to 33%), upper abdominal pain (children and adolescents: 12%), vomiting (≤29%; children and adolescents: 27% to 42%), xerostomia (4% to 12%)

	Hematologic & oncologic: Anemia (11% to 35%), hemolytic anemia (10% to 13%), lymphocytopenia (12% to 14%), neutropenia (8% to 40%; severe neutropenia (children and adolescents: 1%) Hepatic: Hyperbilirubinemia (10% to 14%) Infection: Viral infection (12%) Local: Erythema at injection site (children and adolescents: 29%), inflammation at injection site (13% to 25%; children and adolescents: 14%), injection site reaction (5% to 58%; children and adolescents: 19% to 45%) Nervous system: Anxiety (≤47%), chills (23% to 39%; children and adolescents: 21%), depression (≤40%, severe depression: <1%; children and adolescents: 1% to 13%), dizziness (13% to 26%), emotional lability (≤47%; children and adolescents: 16%), fatigue (≤68%; children and adolescents: 25% to 58%), headache (41% to 69%; severe headache: children and adolescents: 1%), insomnia (26% to 41%; children and adolescents: 9% to 14%), irritability (≤47%; children and adolescents: 10% to 24%), lack of concentration (10% to 21%; children and adolescents: 5%), nervousness (≤38%; children and adolescents: 3% to 7%), pain (9% to 13%), right upper quadrant pain (6% to 12%), rigors (25% to 48%; children and adolescents: 25%) Neuromuscular & skeletal: Arthralgia (21% to 34%; children and adolescents: 15% to 17%), asthenia (≤68%; children and adolescents: 5% to 15%), musculoskeletal pain (19% to 21%; children and adolescents: 21% to 35%), myalgia (22% to 64%; children and adolescents: 17% to 32%) Respiratory: Cough (7% to 23%), dyspnea (13% to 26%; children and adolescents: 5%), flu-like symptoms (15% to 16%; children and adolescents: 31% to 91%), pharyngitis (12% to 13%), sinusitis (5% to 12%; children and adolescents: <1%), upper respiratory tract infection (children and adolescents: 60%) Miscellaneous: Fever (21% to 55%; children and adolescents: 61% to 80%; high fever: children and adolescents: 4%) **1% to 10%:** Cardiovascular: Chest pain, flushing Dermatologic: Eczema Endocrine & metabolic: Hypothyroidism, menstrual disease Gastrointestinal: Constipation, decompensated liver disease, dysgeusia Hematologic & oncologic: Leukopenia, thrombocytopenia Hepatic: Hepatomegaly, increased serum alanine aminotransferase Infection: Bacterial infection, fungal infection Local: Pain at injection site Nervous system: Aggressive behavior, agitation, hostility, malaise, memory impairment, mood changes, suicidal ideation Neuromuscular & skeletal: Back pain, limb pain Ophthalmic: Blurred vision, conjunctivitis Respiratory: Dyspnea on exertion, rhinitis
Monitoring Parameters	– Pretreatment hematological and biochemical tests are recommended for all patients; dental exam, ECG (if preexisting cardiac abnormalities or disease) and ophthalmic exam (also periodically during treatment for those with preexisting ophthalmologic disorders) are also recommended. In adults, hematologic tests should be performed at treatment weeks 2 and 4, biochemical tests at week 4, and TSH every 12 weeks. – Pregnancy testing: Evaluate pregnancy status prior to use in females of reproductive potential. A negative pregnancy test is required immediately before initiation, periodically

	during therapy, and during the 6 months after treatment is discontinued. – Growth velocity and weight should also be monitored during and periodically after treatment discontinuation. – Serum HCV RNA (pretreatment, week 12 and week 24, and 24 weeks after completion of therapy). – Baseline values used in adult clinical trials in combination with alfa interferons: ✓ Platelet count ≥90,000/mm^3 (75,000/mm^3 for cirrhosis or 70,000/mm^3 for coinfection with HIV) ✓ ANC ≥1,500/mm^3 ✓ Hemoglobin ≥12 g/dL for women and ≥13 g/dL for men (11 g/dL for HIV coinfected women and 12 g/dL for HIV coinfected men) ✓ TSH and T_4 within normal limits or adequately controlled ✓ $CD4^+$ cell count ≥200 cells/microL or $CD4^+$ cell count 100 to 200 cells/microL and HIV-1 RNA <5,000 copies/mL for coinfection with HIV
Drug Interactions	• ***Risk X: Avoid combination*** Cladribine Didanosine • ***Risk D: Consider therapy modification*** Azathioprine Influenza Virus Vaccine (Live/Attenuated) Zidovudine
Pregnancy and Lactation	**Pregnancy category** X There are no data on the excretion of ribavirin into human milk. Due to the potential for serious adverse reactions in nursing infants, a decision should be made to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.
Administration	**Administration: Oral** Capsule: Administer with food. Capsule should not be opened, crushed, or broken. Solution: Administer with food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hemolytic anemia: [US Boxed Warning]: Hemolytic anemia has been reported with ribavirin therapy; anemia associated with ribavirin may worsen underlying cardiac disease and lead to fatal and nonfatal myocardial infarctions. Avoid use in patients with significant/unstable cardiac disease. ***Disease-related concerns:*** • Hepatic impairment: Risk of hepatic decompensation in chronic hepatitis C patients treated with combination therapy; monitor hepatic function closely and discontinue therapy immediately if evidence of hepatic decompensation is observed. • Hepatitis C: Appropriate use: [US Boxed Warning]: Ribavirin monotherapy is not effective for chronic hepatitis C infection and should not be used alone for hepatitis C. • Renal impairment: Use with caution in patients with renal impairment; dosage adjustment or discontinuation may be required. ***Concurrent drug therapy issues:*** *Combination therapy with alfa interferons:* • Autoimmune/infectious disorders: Have occurred with combination therapy; use with caution in patients with autoimmune disease or severe infection. • Bone marrow suppression: Pancytopenia has occurred with combination therapy and concomitant use of azathioprine; onset occurs within 3 to 7 weeks; discontinue combination therapy and azathioprine if pancytopenia occurs; may be reversible (usually within 4 to 6 weeks).

• Dental and periodontal disorders: Have been reported with combination therapy; patients should be instructed to brush teeth twice daily and have regular dental exams. Xerostomia may contribute to and/or exacerbate dental disorders.
• Dermatologic reactions: Severe cutaneous reactions, including Stevens-Johnson syndrome and exfoliative dermatitis have been reported (rarely) with combination therapy; discontinue immediately with signs or symptoms of severe skin reactions.
• Diabetes: Has occurred with combination therapy; monitor blood sugars closely.
• Hypersensitivity reactions: Acute hypersensitivity reactions (eg, anaphylaxis, angioedema, bronchoconstriction, and urticaria) have been observed with combination therapy; discontinue immediately with signs or symptoms of severe hypersensitivity reactions.
• Ophthalmologic disorders: Serious disorders (eg, retinopathy, macular edema, retinal artery/vein thrombosis, optic neuritis, retinal detachment) have occurred with combination therapy. All patients require an eye exam at baseline; those with preexisting ophthalmologic disorders (eg, diabetic or hypertensive retinopathy) require periodic follow up. Discontinue therapy in patients with new or worsening ophthalmologic disorders.
• Pancreatitis: Has occurred with combination therapy; interrupt therapy if pancreatitis is suspected and discontinue if confirmed.
• Psychiatric disorders: Severe psychiatric events have occurred including depression and suicidal/homicidal ideation during combination therapy. Suicidal ideation or attempts occurred more often in pediatric patients versus reports in adults during treatment and off-therapy follow-up (2.4% vs 1%). Avoid use in patients with a psychiatric history; discontinue if severe psychiatric symptoms occur.
• Pulmonary events: Pulmonary symptoms (eg, dyspnea, pulmonary infiltrates, pneumonitis, pulmonary hypertension, and pneumonia [rarely fatal]) have been associated with combination therapy; use with caution in patients with pulmonary disease, including sarcoidosis (exacerbation reported).

Special populations:

• Elderly: Use with caution in the elderly; may be more susceptible to adverse effects such as anemia. Monitor renal function closely.
• Pediatric: In combination therapy with alfa interferons, ribavirin may cause a reduction in growth velocity in pediatric and adolescent patients 5 to 17 years of age for the length of treatment. Following treatment, rebound growth and weight gain occurred in most patients; however, a small percentage did not. Long-term data indicate that combination therapy may inhibit growth resulting in reduced adult height in some patients. Growth should be closely monitored in pediatric patients during therapy and post-treatment for growth catch-up.
• Pregnancy: [US Boxed Warning]: Use is contraindicated in pregnant females or male partners of pregnant females. Significant teratogenic and/or embryocidal effects have been observed in all animal studies. Avoid pregnancy in female patients and female partners of male patients during therapy; use effective contraceptive measures during treatment and for at least 6 months after completion of therapy.

Dosage form specific issues:

• Benzyl alcohol and derivatives: Some dosage forms may contain sodium benzoate/benzoic acid which is a metabolite of benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates;

Other warnings/precautions:

• Appropriate use: Safety and efficacy have not been established in patients who have failed previous interferon therapy, received organ transplants, or been coinfected with hepatitis B or HIV. The combination of peginterferon and ribavirin, even with additional

	preferred HCV antiviral agent(s), is **not** recommended for hepatitis C virus (HCV) (regardless of genotype) in HCV adult treatment guidelines (treatment-naive or treatment-experienced); consult current clinical practice guidelines for details on appropriate use.
Storage	Store at 25°C; excursions permitted between 15°C and 30°C. Solution may also be refrigerated at 2°C to 8°C. Refer to manufacturer PIL if there are specific considerations.

13. Simeprevir

Generic Name	Simeprevir
Dosage form/strengths	Capsule 150 mg
Route of administration	*Oral*
Pharmacologic category	Antihepaciviral, NS3/4A Protease Inhibitor (Anti-HCV) ATC: J05AP05
Indications	**Chronic hepatitis C:** Treatment of genotype 1 chronic hepatitis C in combination with sofosbuvir in adults without cirrhosis Limitations of use: Not recommended for use in patients who have previously failed a simeprevir-containing regimen or another regimen containing HCV protease inhibitors.
Dosage Regimen	**Dosing: Adult** **Chronic hepatitis C, genotype 1 (without cirrhosis or with compensated cirrhosis [Child-Pugh class A]): Oral:** 150 mg once daily in combination with sofosbuvir for 12 weeks (without cirrhosis) or 24 weeks (with compensated cirrhosis). **Note:** The American Association for the Study of Liver Diseases/Infectious Diseases Society of America guidelines for testing, managing, and treating hepatitis C no longer include simeprevir as a component of recommended treatment regimens for HCV infection
Dosage adjustment	**Dosing: Renal Impairment: Adult** CrCl >30 mL/minute: No dosage adjustment necessary. CrCl ≤30 mL/minute: There are no dosage adjustments data. Dialysis is unlikely to result in significant removal of simeprevir. **Dosing: Hepatic Impairment: Adult** Mild impairment (Child-Pugh class A): No dosage adjustment necessary. Moderate or severe impairment (Child-Pugh class B or C): Use is not recommended.
Contra-indications	Hypersensitivity to simeprevir or any component of the formulation When administered with ribavirin and peginterferon alfa, the contraindications to ribavirin and peginterferon alfa also apply. See Ribavirin and Peginterferon Alfa monographs.
Adverse Drug Reactions	**>10%:** Central nervous system: Headache (with sofosbuvir 7% to 49%), fatigue (with sofosbuvir 10% to 47%), insomnia (with sofosbuvir 14%), dizziness (with sofosbuvir 5% to 10%) Dermatologic: Skin photosensitivity (with sofosbuvir ≤5% to ≤34%; grade 3: ≤1%; with Peg-IFN-alfa and RBV ≤28%; grade 3: <1%), skin rash (with sofosbuvir ≤5% to ≤34%; grade 3: ≤1%; with Peg-IFN-alfa and RBV ≤28%; including erythema, eczema, maculopapular rash, urticaria, toxic skin eruption, dermatitis exfoliative, cutaneous vasculitis; grade 3: ≤1%), pruritus (with Peg-IFN-alfa and RBV 22%; with sofosbuvir 11%) Endocrine & metabolic: Increased amylase (with sofosbuvir) Gastrointestinal: Nausea (with sofosbuvir 4% to 40%; with Peg-IFN-alfa and RBV 22%), diarrhea (with sofosbuvir 5% to 18%) Hepatic: Increased serum bilirubin (<66%), hyperbilirubinemia (with sofosbuvir) Neuromuscular & skeletal: Myalgia (16%) Respiratory: Dyspnea (12%) **1% to 10%:** Gastrointestinal: Increased serum lipase

	Hepatic: Increased serum alkaline phosphatase
Monitoring Parameters	• Baseline CBC, INR, hepatic function (albumin, total and direct bilirubin, ALT, AST, alkaline phosphatase), calculated GFR; baseline hepatitis C virus (HCV) genotype and subtype, quantitative HCV viral load. • During treatment, monitor CBC, serum creatinine, calculated GFR, hepatic function panel (after 4 weeks of therapy and as clinically indicated); quantitative HCV viral load testing (after 4 weeks of therapy and at 12 weeks after completion of therapy). If quantitative HCV viral load is detectable at treatment week 4, repeat testing is recommended after 2 additional weeks of treatment (treatment week 6). • Screen patients infected with HCV genotype 1a for the presence of virus with the NS3 Q80K polymorphism prior to the initiation of treatment. • Hepatitis B surface antigen and hepatitis B core antibody prior to initiation; in patients with serologic evidence of hepatitis B virus (HBV) infection, monitor for clinical and laboratory signs of hepatitis flare or HBV reactivation during treatment and during posttreatment follow-up.
Drug Interactions	***Risk X: Avoid combination*** Abametapir Aminolevulinic Acid (Systemic) Asunaprevir Bilastine Cisapride Conivaptan Cyclosporine CYP3A4 Inducers CYP3A4 Inhibitors Delavirdine Dexamethasone (Systemic) Doxorubicin Elagolix Elagolix, Estradiol, And Norethindrone Erythromycin (Systemic) Grazoprevir Idelalisib Milk Thistle Nevirapine Ozanimod Pazopanib Protease Inhibitors Revefenacin Rimegepant St John's Wort Topotecan Vincristine (Liposomal) Voxilaprevir ***Risk D: Consider Therapy Modification*** Afatinib Alpelisib Betrixaban Cladribine Colchicine Digoxin Eluxadoline Relugolix Rosuvastatin Stiripentol Tizanidine Ubrogepant Venetoclax
Pregnancy and Lactation	– FDA pregnancy category: Not assigned. No data available on use of this drug in pregnant women to inform a drug-related risk; findings in animal studies suggest potential risk to the fetus It is not known if simeprevir is present in breast milk. The decision to continue or discontinue breastfeeding during therapy should take into account the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother.
Administration	**Administration: Oral** Administer with food. Swallow capsules whole; do not chew, crush, break, cut, or dissolve the capsule. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hepatic decompensation/failure: Hepatic decompensation and failure (including fatal cases) have been reported in patients treated with simeprevir in combination with peginterferon alfa and ribavirin or sofosbuvir. Most cases occurred in patients with advanced and/or decompensated cirrhosis. Monitor hepatic function at baseline and as clinically indicated; closely monitor patients who experience an increase in total bilirubin >2.5 times the ULN. Discontinue treatment if elevated bilirubin accompanied by liver transaminase increases or clinical signs or symptoms of hepatic decompensation occur. • Photosensitivity: Photosensitivity reactions, including serious reactions resulting in hospitalization, have been reported when used in combination with peginterferon alfa and ribavirin. Most frequently occurs within the first 4 weeks of treatment. Avoid excessive sunlight, tanning devices, and take precautions to limit exposure (eg, loose

	fitting clothing, sunscreen). Discontinue use if photosensitivity occurs and monitor until the reaction resolves. If therapy is to be continued in a patient who has experienced photosensitivity, expert consultation is advised. • Skin reactions: Rash has been typically observed within first 4 weeks of therapy initiation, but can occur at any time during treatment. Severe rashes and rash requiring discontinuation have occurred in combination with peginterferon alfa and ribavirin. If a patient experiences a mild to moderate rash, follow for progression and/or development of mucosal signs (eg, oral lesions, conjunctivitis) or systemic symptoms. If rash becomes severe, discontinue simeprevir and monitor for rash resolution. • Sulfa allergy: Contains a sulfonamide moiety. Discontinue if signs of hypersensitivity are noted. ***Disease-related concerns:*** • Diabetes: Rapid reduction in hepatitis C viral load during direct-acting antiviral (DAA) therapy for hepatitis C may lead to improvement in glucose metabolism in patients with diabetes, potentially resulting in symptomatic hypoglycemia if antidiabetic agents are continued at the same dose. Monitor for changes in glucose tolerance and inform patients of the risk of hypoglycemia during DAA therapy, particularly within the first 3 months. Modification of antidiabetic therapy may be necessary. • Hepatic impairment: Not recommend in patients with moderate or severe hepatic impairment (Child-Pugh class B or C). • Hepatitis B virus reactivation: [US Boxed Warning]: Hepatitis B virus (HBV) reactivation has been reported in hepatitis C virus (HCV)/HBV co-infected patients who were receiving or had completed treatment with HCV direct-acting antivirals and were not receiving HBV antiviral therapy; some cases have resulted in fulminant hepatitis, hepatic failure, and death. Test all patients for evidence of current or prior HBV infection prior to initiation of simeprevir; monitor HCV/HBV co-infected patients for hepatitis flare or HBV reactivation during treatment and post-treatment follow-up. Initiate treatment for HBV infection as clinically indicated. ***Concurrent drug therapy issues:*** • Amiodarone: Symptomatic bradycardia (some requiring pacemaker intervention) has occurred in patients receiving amiodarone and a sofosbuvir-containing regimen. The risk of bradycardia may be increased in patients taking beta blockers or patients with underlying cardiac comorbidities and/or advanced liver disease. Bradycardia generally resolves following discontinuation of HCV treatment. ***Other warnings/precautions:*** • Appropriate use: Do not use as monotherapy; use only as part of a multiple-drug regimen for treatment of HCV; consult current HCV treatment guidelines for guidance. • Resistance: Reduced sustained virologic response (SVR) rates of simeprevir in combination with sofosbuvir were observed in patients infected with hepatitis C genotype 1a with an NS3 Q80K polymorphism compared to patients without the polymorphism; consider alternative therapy in these patients. Patients with compensated cirrhosis and hepatitis C genotype 1a should be evaluated for the presence of the Q80K polymorphism; alternative regimens should be used if Q80K variant is present.
Storage	Store below 30°C. Store in the original bottle. Protect from light. Refer to manufacturer PIL if there are specific considerations.

14. Sofosbuvir

Generic Name	Sofosbuvir
Dosage form/strengths	Tablets 400 mg
Route of administration	*Oral*
Pharmacologic category	Antihepaciviral, Polymerase Inhibitor (Anti-HCV); NS5B RNA Polymerase Inhibitor ATC: J05AP08
Indications	**Chronic hepatitis C:** Treatment of genotype 1, 2, 3, or 4 chronic hepatitis C virus (HCV) infection in adults and genotype 2 or 3 chronic HCV infection in pediatric patients ≥3 years of age, without cirrhosis or with compensated cirrhosis, as a component of a combination antiviral treatment regimen.
Dosage Regimen	**Dosing: Adult** *Genotype 3, peginterferon + ribavirin treatment–experienced patients with compensated cirrhosis (Child-Pugh class A) (alternative agent):* **Oral:** 400 mg once daily with concomitant elbasvir/grazoprevir for 12 weeks. *All genotypes, patients with prior glecaprevir/pibrentasvir or sofosbuvir/velpatasvir/voxilaprevir treatment failure, without cirrhosis or with compensated cirrhosis (Child-Pugh class A):* **Oral:** 400 mg once daily in combination with ribavirin and glecaprevir/pibrentasvir for 16 weeks **Dosing: Pediatric** **Note:** Prior to initiating therapy, test patient for evidence of hepatitis B infection (current or prior). **Chronic hepatitis C infection (monoinfection or coinfected with HIV-1); treatment-naive or treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh class A):** **Note:** Use in combination with ribavirin. Children ≥3 years and Adolescents: Patient weight: 17 to <35 kg: tablets: Oral: 200 mg once daily. ≥35 kg: tablets: Oral: 400 mg once daily. Treatment duration based on genotype: Genotype 2: 12 weeks. Genotype 3: 24 weeks.
Dosage adjustment	**Dosing: Renal Impairment: Adult** Adults, Adolescents and Children ≥3 years: eGFR ≥30 mL/minute: No dosage adjustment necessary. eGFR <30 mL/minute: There are no dosage recommendations available. safety and efficacy not established in such patients. Predominant metabolite accumulates (up to 20-fold) in impaired renal function. **Dosing: Hepatic Impairment: Adult** Mild, moderate, or severe impairment (Child-Pugh class A, B, or C): No dosage adjustment necessary
Contra-indications	When administered with ribavirin and peginterferon alfa, the contraindications to ribavirin and peginterferon alfa also apply. See Ribavirin and Peginterferon Alfa monographs.

Adverse Drug Reactions	**>10%:** Dermatologic: Pruritus (11% to 27%), skin rash (8% to 18%) Gastrointestinal: Decreased appetite (18%), diarrhea (9% to 12%), nausea (22% to 34%) Hematologic & oncologic: Anemia (6% to 21%), neutropenia (<1% [interferon-free regimen] to 17% [interferon-containing regimen]) Nervous system: Chills (2% to 17%), fatigue (30% to 59%), headache (24% to 36%), insomnia (15% to 25%), irritability (10% to 13%) Neuromuscular & skeletal: Asthenia (5% to 21%), myalgia (6% to 14%) Respiratory: Flu-like symptoms (6% to 16%) Miscellaneous: Fever (4% to 18%) **1% to 10%:** Gastrointestinal: Increased serum lipase Hematologic & oncologic: Thrombocytopenia Hepatic: Increased serum bilirubin Renal: Increased creatine phosphokinase in blood specimen
Monitoring Parameters	• Baseline CBC, INR, hepatic function (albumin, total and direct bilirubin, ALT, AST, alkaline phosphatase), calculated GFR; baseline (obtain any time prior to treatment initiation) HCV genotype and subtype, quantitative HCV viral load. • During treatment, monitor CBC, serum creatinine, calculated GFR, hepatic function panel (after 4 weeks of therapy and as clinically indicated); quantitative HCV viral load testing (after 4 weeks of therapy and at 12 weeks after completion of therapy). If quantitative HCV viral load is detectable at treatment week 4, repeat testing is recommended after 2 additional weeks of treatment (treatment week 6). If used in combination with amiodarone and another direct acting antiviral (DAA) (or in patients who discontinued amiodarone just prior to initiating sofosbuvir in combination with a DAA), inpatient cardiac monitoring for the first 48 hours of coadministration, then daily outpatient or self monitoring of heart rate through at least the first 2 weeks of treatment. • Hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc) prior to initiation; in patients with serologic evidence of hepatitis B virus (HBV) infection, monitor for clinical and laboratory signs of hepatitis flare or HBV reactivation during treatment and during post-treatment follow-up. • In patients with diabetes, monitor blood glucose and for signs/symptoms of hypoglycemia
Drug Interactions	***Risk X: Avoid Combination*** Modafinil Oxcarbazepine P-Glycoprotein /ABCB1 Inducers Phenobarbital Primidone Rifapentine Tipranavir ***Risk D: Consider therapy modification*** Amiodarone
Pregnancy and Lactation	Pregnancy Category B It is not known if sofosbuvir is present in breast milk. The decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother. According to some authorities: Breastfeeding is not recommended during use of this drug.

Administration	**Administration: Oral** Tablets: Administer with or without food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Disease-related concerns:*** • Diabetes: Rapid reduction in hepatitis C viral load during direct-acting antiviral (DAA) therapy for hepatitis C may lead to improvement in glucose metabolism in patients with diabetes, potentially resulting in symptomatic hypoglycemia if antidiabetic agents are continued at the same dose. Monitor for changes in glucose tolerance and inform patients of the risk of hypoglycemia during DAA therapy, particularly within the first 3 months. Modification of antidiabetic therapy may be necessary. • Hepatitis B virus reactivation: [US Boxed Warning]: Hepatitis B virus (HBV) reactivation has been reported in hepatitis C virus (HCV)/HBV co-infected patients who were receiving or had completed treatment with HCV direct-acting antivirals and were not receiving HBV antiviral therapy; some cases have resulted in fulminant hepatitis, hepatic failure, and death. Test all patients for evidence of current or prior HBV infection prior to initiation of sofosbuvir; monitor HCV/HBV co-infected patients for hepatitis flare or HBV reactivation during treatment and post-treatment follow-up. Initiate treatment for HBV infection as clinically indicated. ***Concurrent drug therapy issues:*** • Amiodarone: Symptomatic bradycardia (some requiring pacemaker intervention) has occurred in patients receiving amiodarone and a sofosbuvir-containing regimen. The risk of bradycardia may be increased in patients taking beta blockers or patients with underlying cardiac comorbidities and/or advanced liver disease. Bradycardia generally resolves following discontinuation of HCV treatment. ***Special populations:*** • Hepatic impairment: Safety and efficacy have not been established in patients with decompensated cirrhosis. ***Other warnings/precautions:*** • Appropriate use: Do not use as monotherapy; use only as part of a multiple drug regimen for treatment of HCV; consult current HCV treatment guidelines for guidance.
Storage	Tablets: Store below 30°C. Dispense only in original packaging. Refer to manufacturer PIL if there are specific considerations.

15. Sofosbuvir and Velpatasvir

Generic Name	Sofosbuvir and Velpatasvir
Dosage form/strengths	Tablets: Sofosbuvir 400 mg ; velpatasvir 100 mg
Route of administration	Oral
Pharmacologic category	Antihepaciviral, NS5A Inhibitor; Antihepaciviral, Polymerase Inhibitor (Anti-HCV); NS5B RNA Polymerase Inhibitor ATC: J05AP55
Indications	**Chronic hepatitis C**: Treatment of chronic hepatitis C virus genotype 1, 2, 3, 4, 5, or 6 infection in adults and pediatric patients ≥3 years of age without cirrhosis or with compensated cirrhosis or in combination with ribavirin in patients with decompensated cirrhosis.
Dosage Regimen	**Dosing: Adult** **Chronic hepatitis C: Oral:** **Note:** One tablet contains sofosbuvir 400 mg/velpatasvir 100 mg. Compensated cirrhosis is defined as Child-Pugh class A and decompensated cirrhosis is defined as Child-Pugh class B or C. **Genotype 4, 5, or 6:** • Treatment naive or peginterferon/ribavirin experienced without cirrhosis or with compensated cirrhosis: One tablet once daily for 12 weeks. • With decompensated cirrhosis: One tablet once daily with concomitant ribavirin for 12 weeks (if ribavirin ineligible, one tablet once daily for 24 weeks). ○ *Prior treatment failure with sofosbuvir- or NS5A-based regimens:* One tablet once daily with concomitant ribavirin for 24 weeks. • Post kidney transplantation, treatment-naive or nondirect-acting antiviral-experienced patients without cirrhosis or with compensated cirrhosis: One tablet once daily for 12 weeks. • Post liver transplantation: ○ *Treatment-naive and -experienced patients without cirrhosis or with compensated cirrhosis*: One tablet once daily for 12 weeks; in patients with compensated cirrhosis, consider adding ribavirin. ○ *Treatment-naive and -experienced patients with decompensated cirrhosis*: One tablet once daily with concomitant ribavirin for 12 weeks (treatment naive) or 24 weeks (treatment experienced). **Hepatitis C virus-uninfected recipients of organs from hepatitis C virus-viremic donors: Oral:** One tablet once daily for 12 weeks **Dosing: Pediatric** **Chronic hepatitis C virus infection:** Children ≥3 years and Adolescents: ○ <17 kg: Oral pellets: Oral: Sofosbuvir 150 mg/velpatasvir 37.5 mg once daily. ○ 17 to <30 kg: Oral pellets, tablet: Oral: Sofosbuvir 200 mg/velpatasvir 50 mg once daily. ○ ≥30 kg: Oral pellets, tablet: Oral: Sofosbuvir 400 mg/velpatasvir 100 mg once daily. Duration of therapy dependent upon multiple factors (eg, genotype, hepatic function [cirrhosis/compensation], previous treatment and response). **Note:** Treatment-experienced patients are defined as those who have failed an interferon-based regimen. • *Genotype 1, 2, 3, 4, 5, or 6:* ○ Treatment-naive or treatment-experienced patients without cirrhosis or with

	compensated cirrhosis (Child-Pugh class A), including patients post-liver transplantation: 12 weeks. ○ Treatment-naive or treatment-experienced patients with decompensated cirrhosis (Child-Pugh class B or C): 12 weeks in combination with ribavirin.
Dosage adjustment	**Dosing: Renal Impairment:** No dosage adjustment necessary. **Dosing: Hepatic Impairment:** No dosage adjustment necessary. **Note:** Safety data in pediatric patients with renal impairment unavailable.
Contra-indications	Hypersensitivity to sofosbuvir, velpatasvir, or any component of the formulation.
Adverse Drug Reactions	**>10%:** Nervous system: Fatigue (15%), headache (22%) **1% to 10%:** Cardiovascular: Increased serum creatine kinase (≥10X ULN: 1% to 2%) Dermatologic: Skin rash (2%) Gastrointestinal: Increased serum lipase (>3X ULN: 3% to 6%), nausea (9%) Nervous system: Depressed mood (1%), insomnia (5%), irritability (≥5%) Neuromuscular & skeletal: Asthenia (5%) **Postmarketing**: Infection: Reactivation of HBV (including fulminant hepatitis and hepatic failure)
Monitoring Parameters	• Baseline (at any time prior to starting therapy) quantitative hepatitis C virus (HCV) viral load and HCV genotype and subtype (if non–pan-genotypic direct-acting antiviral [DAA] will be prescribed); repeat quantitative HCV viral load testing ≥12 weeks after completion of therapy. • Baseline (within 6 months prior to starting DAA therapy) CBC, INR, hepatic function panel (albumin, total and direct bilirubin, ALT, AST, and alkaline phosphatase), and calculated GFR; repeat hepatic function panel as clinically indicated. • Presence of HIV coinfection and serum pregnancy test (women of childbearing age) prior to initiation of therapy. Hepatitis B virus (HBV) surface antigen, HBV core antibody, and HBV surface antibody prior to initiation. In patients with serologic evidence of HBV infection, monitor for clinical and laboratory signs of hepatitis flare or HBV reactivation during treatment and during post treatment follow-up. • In patients with diabetes, monitor blood glucose and for signs/symptoms of hypoglycemia; in patients taking warfarin, monitor INR during and post-therapy.
Drug Interactions	***Risk X: Avoid combination*** Asunaprevir, Bilastine, CYP2B6 Inducers, CYP3A4 Inducers, CYP3A4 Inducers, Doxorubicin (Conventional), Elagolix, Elbasvir and Grazoprevir, Modafinil, Oxcarbazepine, Pazopanib P-Glycoprotein/ABCB1 Inducers, Phenobarbital, Primidone, Revefenacin, Rifabutin, Rifapentine, Rimegepant, Tipranavir, Topotecan, Vincristine (Liposomal), Voxilaprevir Phenobarbital Primidone Revefenacin Rifabutin Rifapentine Rimegepant Tipranavir Topotecan Vincristine (Liposomal) ***Risk D: Consider therapy modification*** Afatinib, Alpelisib, Amiodarone, Antacids, Atogepant, Berotralstat, Betrixaban, Brincidofovir, Cladribine, Colchicine, Digoxin, Eluxadoline, Inhibitors Of The Proton Pump (Ppis And Pcabs) Lefamulin, Relugolix, Rosuvastatin, Sirolimus, Ubrogepant, Venetoclax
Pregnancy and Lactation	Pregnancy category B It is not known if sofosbuvir or velpatasvir are present in breast milk. The decision to continue or

	discontinue breastfeeding during therapy should take into account the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother.
Administration	**Administration: Oral** Administer with or without food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Disease-related concerns:*** • ***Diabetes:*** Rapid reduction in hepatitis C viral load during direct-acting antiviral (DAA) therapy for hepatitis C may lead to improvement in glucose metabolism in patients with diabetes, potentially resulting in symptomatic hypoglycemia if antidiabetic agents are continued at the same dose. Monitor for changes in glucose tolerance and inform patients of the risk of hypoglycemia during DAA therapy, particularly within the first 3 months. Modification of antidiabetic therapy may be necessary. • ***Hepatitis B virus reactivation: [US Boxed Warning]:*** Hepatitis B virus (HBV) reactivation has been reported in hepatitis C virus (HCV)/HBV co-infected patients who were receiving or had completed treatment with HCV direct-acting antivirals and were not receiving HBV antiviral therapy; some cases have resulted in fulminant hepatitis, hepatic failure, and death. Test all patients for evidence of current or prior HBV infection prior to initiation of ledipasvir/sofosbuvir; monitor HCV/HBV co-infected patients for hepatitis flare or HBV reactivation during treatment and post-treatment follow-up. Risk of HBV reactivation may be increased in patients receiving certain immunosuppressants or chemotherapeutic agents. ***Concurrent drug therapy issues:*** • ***Amiodarone:*** Symptomatic bradycardia (some requiring pacemaker intervention) has occurred in patients receiving amiodarone and a sofosbuvir-containing regimen. A fatal cardiac arrest was reported in a patient taking amiodarone with sofosbuvir/ledipasvir. Coadministration of amiodarone and sofosbuvir/velpatasvir is not recommended. However, if patients have no treatment alternatives, patients should have inpatient cardiac monitoring for the first 48 hours, followed by daily outpatient or self-monitoring of heart rate for at least the first 2 weeks of treatment. Patients should seek medical attention immediately if they experience fainting or near-fainting, dizziness, lightheadedness, malaise, weakness, excessive tiredness, shortness of breath, chest pains, confusion or memory problems.
Storage	Store below 30°C. Dispense in original container. Refer to manufacturer PIL if there are specific considerations.

16. Sofosbuvir, Velpatasvir and Voxilaprevir

Generic Name	Sofosbuvir, Velpatasvir and Voxilaprevir
Dosage form/strengths	Tablet: Sofosbuvir 400 mg ; velpatasvir 100 mg ; Voxilaprevir 100 mg ;
Route of administration	Oral
Pharmacologic category	Antihepaciviral, Polymerase Inhibitor (Anti-HCV); NS3/4A Inhibitor; NS5A Inhibitor; NS5B RNA Polymerase Inhibitor ATC: J05AP56
Indications	**Chronic hepatitis C:** Treatment of adults with chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis (Child-Pugh class A) who have genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor or who have genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibiton
Dosage Regimen	**Dosing: Adult** **Chronic hepatitis C:** **Note:** Compensated cirrhosis is defined as Child-Pugh class A *Genotype 4, 5 or 6:* • Direct-acting antiviral–experienced without cirrhosis or with compensated cirrhosis: **Oral:** One tablet once daily for 12 weeks. • Prior sofosbuvir/velpatasvir/voxilaprevir treatment failure without cirrhosis or with compensated cirrhosis: **Oral:** One tablet once daily in combination with ribavirin for 24 weeks. • Liver or kidney transplant recipients, direct-acting antiviral–experienced without cirrhosis or with compensated cirrhosis (off-label use): **Oral:** One tablet once daily for 12 weeks. For patients with cirrhosis and multiple negative baseline characteristics, consider adding concomitant ribavirin.
Dosage adjustment	**Dosing: Renal Impairment:** No dosage adjustment necessary. **Dosing: Hepatic Impairment:** No dosage adjustment necessary. Hepatotoxicity during treatment: Hepatic decompensation/failure: Discontinue use.
Contra-indications	Concurrent use with rifampin Additional contraindications: Hypersensitivity to sofosbuvir, velpatasvir, voxilaprevir, or any component of the formulation; concurrent use with dabigatran, phenobarbital, phenytoin, rosuvastatin, or St John's wort
Adverse Drug Reactions	**>10%:** Central nervous system: Headache (21% to 23%), fatigue (17% to 19%) Gastrointestinal: Diarrhea (13% to 14%), nausea (10% to 13%) Hepatic: Increased serum bilirubin (4% to 13%) **1% to 10%:** Central nervous system: Insomnia (3% to 6%), depression (≤1%) Dermatologic: Skin rash (2%) Gastrointestinal: Increased serum lipase (2%) Neuromuscular & skeletal: Asthenia (4% to 6%)

	Frequency not defined: Infection: Reactivation of HBV
Monitoring Parameters	**Baseline** (obtain any time prior to treatment initiation) quantitative hepatitis C virus RNA; HCV genotype and subtype (if a non-pan-genotypic direct-acting antiviral [DAA] will be prescribed); staging of fibrosis. **Baseline** (within 6 months prior to starting antiviral therapy) CBC, INR, hepatic function panel (albumin, total and direct bilirubin, ALT, AST, and alkaline phosphatase), and calculated GFR. **Before initiating DAA therapy**, serum pregnancy test (women of childbearing age) and assessment for HIV coinfection. Hepatitis B virus (HBV) surface antigen, HBV core antibody, and HBV surface antibody prior to initiation. **During treatment**, monitor CBC, serum creatinine, calculated GFR, hepatic function panel (as clinically indicated). Quantitative HCV viral load testing (at ≥12 weeks after completion of therapy). In patients with serologic evidence of HBV infection, monitor for clinical and laboratory signs of hepatitis flare or HBV reactivation during treatment and during post-treatment follow-up. In patients with diabetes, monitor blood glucose and for signs/symptoms of hypoglycemia; in patients taking warfarin, monitor INR during and post-therapy. If used in combination with amiodarone (or in patients who discontinued amiodarone just prior to initiating sofosbuvir/velpatasvir), inpatient cardiac monitoring for the first 48 hours of coadministration, then outpatient or self-monitoring of heart rate daily through at least the first 2 weeks of treatment.
Drug Interactions	***Risk X: Avoid Combination*** Asunaprevir Atazanavir BCRP/ABCG2 Substrates Bilastine CYP2B6 Inducers CYP3A4 Inducers Doxorubicin (Conventional) Elagolix Elbasvir and Grazoprevir Lopinavir Modafinil Oxcarbazepine Pazopanib P-Glycoprotein/ABCB1 Inducers Phenobarbital Pitavastatin Primidone Revefenacin Rifabutin Rifampin Rifapentine Rimegepant Rosuvastatin Tipranavir Topotecan Vincristine (Liposomal) Voxilaprevir ***Risk D: Consider Therapy Modification*** Afatinib Alpelisib Amiodarone Antacids Atogepant Atorvastatin Betrixaban Brincidofovir Cladribine Colchicine Digoxin HMG-Coa Reductase Inhibitors (Statins) Inhibitors Of The Proton Pump (PPIs And PCABs) Lefamulin Relugolix Sirolimus Venetoclax
Pregnancy and Lactation	This drug should be used during pregnancy only if the benefit outweighs the risk to the fetus. No adequate data available on use of this drug in pregnant women to inform a drug-related risk. It is not known if sofosbuvir, velpatasvir, or voxilaprevir are present in human breast milk. The decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother.
Administration	**Administration: Oral:** Administer with food. Refer to manufacturer PIL if there are specific considerations.
Warnings /Precautions	***Concerns related to adverse effects:*** • ***Hepatitis B virus reactivation: [US Boxed Warning]:*** Hepatitis B virus (HBV) reactivation has been reported in hepatitis C virus (HCV)/HBV co-infected patients who were receiving or had completed treatment with HCV direct-acting antivirals and were not receiving HBV antiviral therapy; some cases have resulted in fulminant hepatitis, hepatic failure, and death. Test all patients for evidence of current or prior HBV infection prior to initiation of sofosbuvir/velpatasvir/voxilaprevir; monitor HCV/HBV co-infected patients for hepatitis flare or HBV reactivation during treatment and post-treatment follow-up. Initiate treatment for HBV infection as clinically indicated. Risk of HBV reactivation may be increased in patients receiving certain immunosuppressants or chemotherapeutic agents. ***Disease-related concerns:*** • ***Diabetes:*** Rapid reduction in hepatitis C viral load during direct-acting antiviral (DAA) therapy

	for hepatitis C may lead to improvement in glucose metabolism in patients with diabetes, potentially resulting in symptomatic hypoglycemia if antidiabetic agents are continued at the same dose. Monitor for changes in glucose tolerance and inform patients of the risk of hypoglycemia during DAA therapy, particularly within the first 3 months. Modification of antidiabetic therapy may be necessary. • ***Hepatic effects:*** Hepatic decompensation and hepatic failure (including fatal cases) have been reported; cases occurred in patients with baseline cirrhosis with and without moderate or severe liver impairment (Child-Pugh class B or C). Assess hepatic function as clinically indicated; monitor patients with compensated cirrhosis or with evidence of advanced liver disease (eg, portal hypertension) for signs/symptoms of hepatic decompensation (eg, ascites, hepatic encephalopathy, variceal hemorrhage). Discontinue treatment in patients who develop signs/symptoms of hepatic decompensation/failure. • ***Hepatic impairment:*** Use is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh class B or C) or patients with history of prior hepatic decompensation. ***Concurrent drug therapy issues:*** • ***Amiodarone:*** Coadministration of amiodarone and sofosbuvir/velpatasvir/voxilaprevir is not recommended due to bradycardia risk. However, if patients have no treatment alternatives, patients should have inpatient cardiac monitoring for the first 48 hours, followed by daily outpatient or self-monitoring of heart rate for at least the first 2 weeks of treatment. Due to the long half-life of amiodarone, cardiac monitoring (as described) is also recommended if amiodarone was discontinued just prior to beginning treatment with sofosbuvir/velpatasvir/voxilaprevir. Patients should seek medical attention immediately if they experience fainting or near-fainting, dizziness, light-headedness, malaise, weakness, excessive tiredness, shortness of breath, chest pains, confusion, or memory problems.
Storage	Store below 30°C; dispense in original container. Refer to manufacturer PIL if there are specific considerations.

17. Tenofovir Alafenamide

Generic Name	Tenofovir Alafenamide
Dosage form/strengths	Tablets: 25 mg
Route of administration	Oral
Pharmacologic category	Antihepadnaviral, Reverse Transcriptase Inhibitor, Nucleotide (Anti-HBV) ATC: J05AF13
Indications	**Chronic hepatitis B**: Treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease
Dosage Regimen	**Dosing: Adult** **Chronic hepatitis B:** Oral: 25 mg once daily.
Dosage adjustment	**Dosing: Renal Impairment: Adult** CrCl ≥15 mL/minute: No dosage adjustment necessary. CrCl <15 mL/minute: Use is not recommended. ESRD requiring hemodialysis: No dosage adjustment necessary; administer postdialysis on hemodialysis days. **Dosing: Hepatic Impairment: Adult** Mild impairment (Child-Pugh class A): No dosage adjustment necessary. Decompensated cirrhosis (Child-Pugh class B or C): Use is not recommended.
Contra-indications	Hypersensitivity to tenofovir alafenamide or any component of the formulation
Adverse Drug Reactions	**>10%:** Nervous system: Headache (12%) Neuromuscular & skeletal: Decreased bone mineral density (≥5% at lumbar spine: 11%; ≥7% at femoral neck: 5%) **1% to 10%:** Cardiovascular: Increased serum creatine kinase (grades 3/4: 3%) Dermatologic: Skin rash (<5%) Endocrine & metabolic: Glycosuria (grades 3/4: 5%), increased amylase (grades 3/4: 3%), increased LDL cholesterol (grades 3/4: 6%) Gastrointestinal: Abdominal pain (9%), diarrhea (5%), dyspepsia (5%), flatulence (<5%), nausea (6%), vomiting (<5%) Hepatic: Increased serum alanine aminotransferase (grades 3/4: 8%), increased serum aspartate aminotransferase (grades 3/4: 3%) Nervous system: Fatigue (6%) Neuromuscular & skeletal: Arthralgia (5%), back pain (6%) Respiratory: Cough (8%)
Monitoring Parameters	Serum creatinine, estimated CrCl, serum phosphorus (in patients with chronic kidney disease), urine glucose, urine protein (prior to initiation and as clinically indicated during therapy); HIV testing (prior to initiation); hepatic function tests; monitor clinical and laboratory data closely for several months following therapy discontinuation.
Drug Interactions	***Risk X: Avoid combination*** Adefovir Carbamazepine Cladribine Fosphenytoin-Phenytoin Oxcarbazepine Phenobarbital Primidone Rifabutin Rifampin Rifapentine St John's Wort Tipranavir ***Risk D: Consider therapy modification*** Nonsteroidal Anti-Inflammatory Agents

Pregnancy and Lactation	Pregnancy Category B drug It is not known if tenofovir alafenamide is present in breast milk. In lactation Benefit should outweigh risk. According to some authorities: Use is not recommended.
Administration	**Administration: Oral:** Administer with food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Lactic acidosis/hepatomegaly: Lactic acidosis and severe hepatomegaly with steatosis, sometimes fatal, have been reported with the use of nucleoside analogs, alone or in combination with other antiretrovirals. Suspend treatment in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (marked transaminase elevation may/may not accompany hepatomegaly and steatosis). • Renal toxicity: Renal toxicity (acute renal failure, Fanconi syndrome, and/or proximal renal tubulopathy) has been reported with use of tenofovir prodrugs; patients with impaired renal function and those with concurrent or recent nephrotoxic therapy (including nonsteroidal anti-inflammatory drug use) are at an increased risk. Discontinue use in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. ***Disease-related concerns:*** • Hepatic impairment: Use is not recommended in patients with Child-Pugh class B or C hepatic impairment. • Hepatitis B acute exacerbation: **[US Boxed Warning]:** Discontinuation of anti-hepatitis B therapy may result in severe acute exacerbations of hepatitis B. Monitor clinical and laboratory data closely for several months after treatment discontinuation. If clinically indicated, anti-hepatitis B therapy may be resumed. • HIV-1 and HBV coinfection: Should not be used as a single agent for the treatment of HIV-1 due to resistance development risk. • Renal impairment: Use is not recommended in patients with CrCl <15 mL/minute who are not receiving hemodialysis. ***Other warnings/precautions:*** • HIV testing: HIV antibody testing should be offered to all HBV infected patients prior to treatment initiation. If HIV testing is positive, institute an appropriate antiretroviral (HIV-1) combination regimen.
Storage	Store below 30°C. Dispense in original container. Refer to manufacturer PIL if there are specific considerations.

18. Valacyclovir

Generic Name	Valacyclovir
Dosage form/strengths	Tablets 500mg, 1gm
Route of administration	Oral
Pharmacologic category	Antiviral Agent, Oral ATC: J05AB11
Indications	Treatment of herpes zoster (shingles) in immunocompetent patients; treatment of first-episode and recurrent genital herpes in immunocompetent patients; suppression of recurrent genital herpes and reduction of transmission of genital herpes in immunocompetent patients; suppression of genital herpes in patients with HIV; treatment of herpes labialis (cold sores); treatment of chickenpox in immunocompetent children
Dosage Regimen	**Adults** **Genital: Herpes simplex virus, mucocutaneous infection:** **Treatment of First Episodes** Oral Immunocompetent adults: 1 g twice daily for 7–10 days. extent duration of treatment if healing is incomplete after 10 days. Immunocompromised or HIV-infected adults: 1 g twice daily for 5–14 days. Initiate therapy within 48 hours of onset of signs and symptoms; efficacy not established if initiated >72 hours after onset of signs or symptoms. **Episodic Treatment of Recurrent Episodes** Oral Immunocompetent adults: 500 mg twice daily for 3 days or 1 g once daily for 5 days. Immunocompromised or HIV-infected adults: 1 g twice daily for 5–10 days; may be continued for 7–14 days. Initiate therapy at first sign or symptom of an episode; efficacy not established if initiated >24 hours after onset of signs or symptoms. **Suppressive Therapy of Recurrent Episodes** Oral Immunocompetent adults: 1 g once daily. Alternatively, 500 mg once daily for those with a history of ≤9 recurrences per year. Immunocompromised or HIV-infected adults: 500 mg twice daily. **Note:** Reassess need periodically (eg, annually) **Reduction of Transmission** Oral 500 mg once daily in source partner with a history of ≤9 recurrences per year. Efficacy for reducing transmission not established beyond a duration of 8 months in discordant couples. **Herpes Labialis** **Oral** Immunocompetent adults: *Treatment, recurrent infection (eg, cold sores)*: 2 g every 12 hours for 1 day only Initiate treatment at earliest symptom of cold sore (e.g., tingling, itching, burning). *Treatment, initial infection (eg, gingivostomatitis):* **Oral:** 1 g twice daily for 7 to 10 days Immunocompromised patients (including patients with HIV): *Treatment, initial or recurrent infection*: **Oral:** 1 g twice daily for 5 to 10 days and until complete lesion resolution

Mucocutaneous Herpes Simplex Virus (HSV) Infections
Chronic Suppression of Recurrent Episodes
Oral
HIV-infected adults: 500 mg twice daily for chronic suppressive or maintenance therapy (secondary prophylaxis) of HSV infections in those who have frequent or severe recurrences.
Herpes Zoster
Oral
Immunocompetent adults: 1 g 3 times daily for 7 days.
Immunocompromised patients (including patients with HIV):
Local dermatomal herpes zoster in HIV-infected adults or adolescents: 1 g 3 times daily for 7–10 days recommended by CDC and others.
Initiate therapy at earliest sign or symptom (preferably within 48 hours of rash onset); efficacy not established if initiated >72 hours after rash onset
Extensive cutaneous lesions or visceral involvement: **Oral:** 1 g 3 times daily to complete a 10- to 14-day course.
Pediatric Patients
Herpes labialis (cold sores), treatment:
Immunocompetent: Children ≥12 years and Adolescents: Oral: 2,000 mg every 12 hours for 1 day (2 doses); initiate at earliest symptom onset
HIV-exposed/-positive: Adolescents: Oral: 1,000 mg twice daily for 5 to 10 days.
Herpes simplex virus (HSV), genital infection; *immunocompetent* patients: Limited data available**:**
First episode; treatment: Children and Adolescents: Oral: 20 mg/kg/dose twice daily, maximum dose: 1,000 mg/dose; for 7 to 10 days.
Recurrent episodes; treatment: Begin with onset of symptoms or lesion appearance: Children and Adolescents:
Patient weight <50 kg: Oral: 20 mg/kg/dose twice daily; maximum dose: 1,000 mg/dose; for 5 days.
Patient weight ≥50 kg: Oral: 1,000 mg once daily for 5 days.
Suppressive therapy: Children and Adolescents: Oral: 20 mg/kg/dose once daily; maximum dose: 1,000 mg/dose.

Dosage adjustment

Dosing: Renal Impairment: Adult
Herpes zoster (shingles), treatment:
CrCl 30 to 49 mL/minute: Oral: 1 g every 12 hours
CrCl 10 to 29 mL/minute: Oral: 1 g every 24 hours
CrCl <10 mL/minute: Oral: 500 mg every 24 hours
Herpes simplex virus, genital:
Initial episode:
CrCl 10 to 29 mL/minute: Oral: 1 g every 24 hours
CrCl <10 mL/minute: Oral: 500 mg every 24 hours
Recurrent episode: CrCl <29 mL/minute: Oral: 500 mg every 24 hours
Suppressive therapy: CrCl <29 mL/minute: Oral:
For usual dose of 1 g every 24 hours or 500 mg every 12 hours, decrease dose to 500 mg every 24 hours
For usual dose of 500 mg every 24 hours, decrease dose to 500 mg every 48 hours
Herpes simplex virus, orolabial (immunocompetent patients):
CrCl 30 to 49 mL/minute: Oral: 1 g every 12 hours for 2 doses
CrCl 10 to 29 mL/minute: Oral: 500 mg every 12 hours for 2 doses
CrCl <10 mL/minute: Oral: 500 mg as a single dose

	Hemodialysis: Dialyzable (~33% removed during 4-hour session); administer dose postdialysis Chronic ambulatory peritoneal dialysis/continuous arteriovenous hemofiltration dialysis: Pharmacokinetic parameters are similar to those in patients with ESRD; supplemental dose not needed following dialysis **Dosing: Hepatic Impairment: Adult** No dosage adjustment necessary. **Dosing: Renal Impairment: Pediatric** **Herpes labialis:** Adolescents: CrCl 30 to 49 mL/minute: 1,000 mg every 12 hours for 2 doses CrCl 10 to 29 mL/minute: 500 mg every 12 hours for 2 doses CrCl <10 mL/minute: 500 mg as a single dose **Genital herpes:** Adolescents: Initial episode: CrCl 10 to 29 mL/minute: 1,000 mg every 24 hours CrCl <10 mL/minute: 500 mg every 24 hours Recurrent episode: CrCl ≤29 mL/minute: 500 mg every 24 hours Suppressive therapy: CrCl ≤29 mL/minute: For usual dose of 1,000 mg every 24 hours, decrease dose to 500 mg every 24 hours For usual dose of 500 mg every 24 hours, decrease dose to 500 mg every 48 hours HIV-infected patients: 500 mg every 24 hours Hemodialysis: Dialyzable (~33% removed during 4-hour session); administer dose postdialysis **Dosing: Hepatic Impairment: Pediatric** Children ≥2 years and Adolescents: No dosage adjustment necessary.
Contra-indications	Hypersensitivity to valacyclovir, acyclovir, or any component of the formulation
Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** Acute kidney injury Neurotoxicity Thrombotic microangiopathy **>10%:** Gastrointestinal: Abdominal pain (3% to 11%), nausea (8% to 15%) Hematologic & oncologic: Neutropenia (HIV-1-infected patients: 18% [placebo: 10%]) Hepatic: Increased serum alanine aminotransferase (2%; HIV-1-infected patients: 14%), increased serum aspartate aminotransferase (≤4%; HIV-1-infected patients: 16%) Nervous system: Headache (13% to 38%) Respiratory: Nasopharyngitis (16%) **1% to 10%:** Central nervous system: Fatigue, depression, dizziness Dermatologic: Skin rash Endocrine & metabolic: Dehydration Gastrointestinal: Vomiting, diarrhea Genitourinary: Dysmenorrhea Hematologic & oncologic: Thrombocytopenia, leukopenia Hepatic: Increased serum alkaline phosphatase Infection: Herpes simplex infection Neuromuscular & skeletal: Arthralgia Respiratory: Rhinorrhea Miscellaneous: Fever

Monitoring Parameters	Urinalysis, BUN, serum creatinine, liver enzymes, and CBC
Drug Interactions	***Risk X: Avoid combination*** Cladribine Foscarnet Varicella Virus Vaccine Zoster Vaccine (Live/Attenuated) ***Risk D: Consider therapy modification*** Tizanidine ***Risk C: Monitor therapy*** Clozapine Mycophenolate Tenofovir Products Theophylline Derivatives Zidovudine
Pregnancy and Lactation	Pregnancy Category B- No proven risk in humans. Valacyclovir is rapidly metabolized to acyclovir. Following administration of valacyclovir, acyclovir is present in breast milk; unchanged valacyclovir has not been detected in breast milk. valacyclovir is considered compatible with breastfeeding.
Administration	**Administration: Oral** If GI upset occurs, administer with meals. **Administration: Pediatric** Oral: May administer with or without food Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • CNS effects: CNS adverse effects (including agitation, hallucinations, confusion, delirium, seizures, and encephalopathy) have been reported in both adult and pediatric patients with or without renal dysfunction. Elderly patients are more likely to experience CNS adverse effects. • Thrombotic microangiopathy: Has occurred in immunocompromised patients (at doses of 8 g/day). ***Disease-related concerns:*** • Renal impairment: Use caution in patients with renal impairment, the elderly, and/or those receiving nephrotoxic agents. Acute renal failure and CNS effects have been observed in patients with renal dysfunction; dose adjustment may be required. Precipitation in renal tubules may occur; maintain adequate hydration. ***Special populations:*** • Elderly: Use with caution in the elderly; CNS effects have been reported. • Immunocompromised patients: Advanced HIV (CD4 <100 cells/mm^3): Safety and efficacy have not been established for treatment/suppression of recurrent genital herpes or disseminated herpes in patients with profound immunosuppression. ***Other warnings/precautions:*** • Appropriate use: For cold sores, treatment should begin at the earliest symptom (tingling, itching, burning). For genital herpes, treatment should begin as soon as possible after the first signs and symptoms (within 72 hours of onset of first diagnosis or within 24 hours of onset of recurrent episodes). For herpes zoster, treatment should begin within 72 hours of onset of rash. For chickenpox, treatment should begin with earliest sign or symptom.
Storage	Store at 15°C to 25°C Refer to manufacturer PIL if there are specific considerations.

19. Valganciclovir

Generic Name	Valganciclovir
Dosage form/strengths	Tablets 450mg
Route of administration	Oral
Pharmacologic category	Antiviral Agent ATC: J05AB14
Indications	**Cytomegalovirus, prophylaxis (solid organ transplant recipients):** Prevention of cytomegalovirus (CMV) in high-risk adult patients (donor CMV seropositive/recipient CMV seronegative) undergoing kidney, heart, or kidney/pancreas transplantation Prevention of CMV in high risk pediatric patients undergoing kidney transplant (age 4 months to 16 years) or heart transplant (age 1 month to 16 years) **CMV retinitis, treatment (AIDS-related):** Treatment of cytomegalovirus (CMV) retinitis in patients with acquired immunodeficiency syndrome (AIDS)
Dosage Regimen	**Dosing: Adult** **Cytomegalovirus (CMV) retinitis, treatment (AIDS-related): Oral:** Induction: 900 mg twice daily for 14 to 21 days followed by maintenance therapy. Maintenance: 900 mg once daily **CMV, prophylaxis (solid organ transplant recipients): Oral:** 900 mg once daily; duration of prophylaxis is dependent on type of transplant, as well as donor and recipient CMV serostatus **Dosing: Pediatric** **Note:** In pediatric patients, valganciclovir oral solution is the preferred oral dosage form in pediatric patients for accuracy in dosing; valganciclovir tablets can be considered if the calculated dose is within 10% of the available tablet strength (450 mg). In pediatric patients, dosing may be based on either BSA (mg/m^2) or weight (mg/kg); use extra precaution to verify dosing parameters during calculations. **Prevention of CMV disease:** Oral: Following solid organ transplantation: *Heart, kidney or liver transplantation:* Oral: Dosing based on BSA and CrCl calculation using modified Schwartz formula which bases k constant on age*: Dose (mg) = 7 x BSA x CrCl* administered once daily Maximum daily dose: 900 mg/day. ***CrCl calculation (based on the modified Schwartz formula):** CrCl (mL/minute/1.73 m^2) = [k x height (cm)] ÷ SCr (mg/dL) Calculated using a modified Schwartz formula where k = • 0.33 in infants <1 year of age with low birthweight for GA • 0.45 in infants <1 year of age with birthweight appropriate for GA • 0.45 in children 1 to <2 years • 0.55 in boys age 2 to <13 years • 0.55 in girls age 2 to <16 years • 0.7 in boys age 13 to 16 years Limit the CrCl used to calculate dosage to a value of 150 mL/minute/1.73 m^2, regardless of value calculated with the Schwartz equation, to avoid overexposure. Initiate therapy within 10 days after transplant; duration of prophylaxis varies depending on organ(s) transplanted, donor and recipient CMV serostatus, and immunosuppressive regimen;

typically continued for 3 to 6 months; may be continued up to 12 months in certain cases

CMV retinitis; treatment: Adolescents: Oral:

Induction (active retinitis): 900 mg twice daily for 14 to 21 days

Maintenance: Following induction treatment or for patients with inactive CMV retinitis who require maintenance therapy: 900 mg once daily for at least 3 to 6 months

Dosage adjustment

Dosing: Renal Impairment: Adult

Clcr (mL/minute)	Initial Treatment (Induction) Dosage	Maintenance Dosage
40–59	450 mg twice daily	450 mg once daily
25–39	450 mg once daily	450 mg once every 2 days
10–24	450 mg once every 2 days	450 mg twice weekly
<10 (hemodialysis patients)	Not recommended	Not recommended

Dosing: Renal Impairment: Pediatric

Infants, Children, and Adolescents 1 month to 16 years: No additional dosage adjustments required; use of equation adjusts for renal function.

Adolescents >16 years: refer to adult dosing

Dosing: Hepatic Impairment: Adult

There are no dosage adjustments data.

Hazardous Drugs Handling Considerations

Hazardous agent.

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

Contra-indications

Hypersensitivity (eg, anaphylaxis) to valganciclovir, ganciclovir, or any component of the formulation

Canadian labeling: Additional contraindications (not in US labeling): Hypersensitivity to acyclovir or valacyclovir

Adverse Drug Reactions

Significant considerations:

Hematologic toxicity

Impairment of fertility

Fetal toxicity

Mutagenesis and carcinogenesis

>10%:

Cardiovascular: Hypertension (12% to 18%)

Central nervous system: Headache (6% to 22%), insomnia (6% to 20%)

Gastrointestinal: Diarrhea (16% to 41%), nausea (8% to 30%), vomiting (3% to 21%), abdominal pain (15%)

Hematologic & oncologic: Anemia (≤31%), thrombocytopenia (≤22%), neutropenia (3% to 19%)

Immunologic: Graft rejection (24%)

Neuromuscular & skeletal: Tremor (12% to 28%)

Ophthalmic: Retinal detachment (15%)

Renal: Increased serum creatinine (S_{cr} >1.5 to 2.5 mg/dL: 12% to 50%; S_{cr} >2.5: 3% to 17%)

	Miscellaneous: Fever (9% to 31%) **1% to 10%:** Cardiovascular: Hypotension (≥5%), peripheral edema (≥5%), cardiac arrhythmia (<5%) Central nervous system: Peripheral neuropathy (9%), paresthesia (≤8%), anxiety (≥5%), chills (≥5%), depression (≥5%), dizziness (≥5%), fatigue (≥5%), malaise (≥5%), pain (≥5%), agitation (<5%), confusion (<5%), hallucination (<5%), psychosis (<5%), seizure (<5%) Dermatologic: Dermatitis (≥5%), increased wound secretion (≥5%), night sweats (≥5%), pruritus (≥5%), cellulitis (<5%) Endocrine & metabolic: Hyperkalemia (≥5%), hypophosphatemia (≥5%), weight loss (≥5%) Gastrointestinal: Abdominal distention (≥5%), constipation (≥5%), decreased appetite (≥5%), dyspepsia (≥5%), oral mucosa ulcer (≥5%), dysgeusia (<5%), pancreatitis (<5%) Genitourinary: Hematuria (≥5%), urinary tract infection (≥5%) Hematologic & oncologic: Bone marrow depression (<5%; including aplastic anemia), febrile neutropenia (<5%), hemorrhage (<5%; associated with thrombocytopenia), pancytopenia (<5%) Hepatic: Hepatic insufficiency (≥5%), increased serum ALT (<5%), increased serum AST (<5%) Hypersensitivity: Hypersensitivity reaction (<5%) Immunologic: Organ transplant rejection (6% to 9%) Infection: Candidiasis (≥5%; including oral candidiasis), influenza (≥5%), wound infection (≥5%), sepsis (<5%) Neuromuscular & skeletal: Arthralgia (≥5%), back pain (≥5%), muscle spasm (≥5%), myalgia (≥5%), weakness (≥5%), limb pain (<5%) Ophthalmic: Eye pain (≥5%), macular edema (<5%) Otic: Deafness (<5%) Renal: Decreased creatinine clearance (≥5%), renal impairment (≥5%), renal failure (<5%) Respiratory: Cough (≥5%), dyspnea (≥5%), pharyngitis (≥5%; including nasopharyngitis), upper respiratory tract infection (≥5%) Miscellaneous: Postoperative complication (≥5%), postoperative pain (<5%), wound dehiscence (<5%)
Monitoring Parameters	CBC, platelet count, serum creatinine at baseline and periodically during therapy; monitor CBC and platelet count more frequently during therapy in infants and in patients with renal impairment, those with previous drug-induced leukopenia, and those with neutrophil counts <1,000 cells/mm^3 at treatment initiation; pregnancy test prior to initiation in females of reproductive potentia
Drug Interactions	***Risk X: Avoid combination*** Cladribine ***Risk D: Consider therapy modification*** Imipenem ***Risk C: Monitor therapy*** Amphotericin B Cyclosporine Didanosine Mycophenolate Probenecid Tenofovir Products Zidovudine
Pregnancy and Lactation	Based on animal data, valganciclovir has the potential to cause birth defects in humans. Based on animal data and limited human data, valganciclovir may cause temporary or permanent inhibition of spermatogenesis in males and suppression of fertility in females. It is not known if ganciclovir or valganciclovir are present in breast milk. Due to the potential for serious adverse reactions in the breastfed infant, breastfeeding is not recommended
Administration	Valganciclovir should be administered with meals. Do not break or crush tablets. **Administration: Pediatric** Due to the carcinogenic and mutagenic potential, avoid direct contact with broken or crushed tablets, powder for oral solution, and oral solution. Consideration should be given to handling and

	disposal according to guidelines issued for antineoplastic drugs; however, there is no consensus on the need for these precautions. Oral: Administer with meals. The preferred dosage form for pediatric patients is the oral solution; however, valganciclovir tablets may be used as long as the calculated dose is within 10% of the available tablet strength (450 mg) Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Acute renal failure: Acute renal failure may occur; ensure adequate hydration and use with caution in patients receiving concomitant nephrotoxic agents. • Blood dyscrasias: [US Boxed Warning]: Severe leukopenia, neutropenia, anemia, thrombocytopenia, pancytopenia, and bone marrow failure, including aplastic anemia have been reported. May occur at any time during treatment and worsen with continued use; cell counts usually begin to recover within 3 to 7 days of treatment discontinuation. Do not use in patients with an absolute neutrophil count <500 cells/mm^3, platelet count <25,000/mm^3, or hemoglobin <8 g/dL; use with caution in patients with preexisting bone marrow suppression, cytopenias, or in those receiving myelosuppressive drugs/irradiation. Monitor CBC and platelet count at baseline and frequently during therapy, especially in infants and in patients with renal impairment, those with previous drug-induced leukopenia, and those with neutrophil counts <1,000 cells/mm^3 at treatment initiation. • Carcinogenic/teratogenic: [US Boxed Warning]: May cause temporary or permanent inhibition of spermatogenesis and suppression of fertility; has the potential to cause birth defects and cancers in humans. ***Disease-related concerns:*** • Renal impairment: Use with caution in patients with impaired renal function; dosage adjustment required. ***Special populations:*** • Elderly: Acute renal failure may occur in elderly patients with or without preexisting renal impairment; use with caution and adjust dose as needed based on renal function. • Liver transplant recipients: Not indicated for use in liver transplant patients (higher incidence of tissue-invasive cytomegalovirus [CMV] relative to oral ganciclovir was observed in trials). • Pediatric: The preferred dosage form for pediatric patients is the oral solution; however, valganciclovir tablets may be used so long as the calculated dose is within 10% of the available tablet strength (450 mg). Use of valganciclovir for the treatment of congenital CMV disease has not been evaluated.
Storage	Tablet: Store at 20°C to 25°C; excursions permitted to 15°C to 30°C Refer to manufacturer PIL if there are specific considerations.

Carbapenenems

1. Ertapenem

Watch Group

Generic Name	Ertapenem
Dosage form/strengths	**Powder for injection**: 1g
Route of administration	IV, IM
Pharmacologic category	Antibiotic, Carbapenem ATC: J01DH03
Indications	**Intra-abdominal infection, complicated:** For the treatment of complicated intra-abdominal infections **Pelvic infection:** For the treatment of acute pelvic infections, including postpartum endomyometritis, septic abortion, and postsurgical gynecologic infections **Pneumonia, community acquired:** For the treatment of community-acquired pneumonia (CAP) **Skin and skin structure infection, complicated:** For the treatment of complicated skin and skin structure infections, including diabetic foot infections without osteomyelitis. Ertapenem has not been studied in diabetic foot infections with concomitant osteomyelitis. **Surgical prophylaxis:** For the prophylaxis of surgical site infection in adults following elective colorectal surgery. **Urinary tract infection, complicated:** For the treatment of complicated urinary tract infections (UTIs),
Dosage Regimen	**Adults** **Gynecologic Infections** **IV or IM** 1 g once daily for 3–10 days. **Intra-abdominal Infections** **IV or IM** 1 g once daily for 5–14 days. **Respiratory Tract Infections** **Community-acquired Pneumonia** IV or IM 1 g once daily. Usual duration is 10–14 days; treatment may be switched to an appropriate oral anti-infective after ≥3 days. **Skin and Skin Structure Infections** **IV or IM** 1 g once daily for 7–14 days. In adults with diabetic foot infections, anti-infective therapy (parenteral or parenteral followed by oral) has been given for up to 28 days. **Urinary Tract Infections (UTIs)** **IV or IM** 1 g once daily. Usual duration is 10–14 days; treatment may be switched to an appropriate oral anti-infective after ≥3 days **Pediatric Patients**

	Gynecologic Infections **IV or IM** Children 3 months to 12 years of age: 15 mg/kg twice daily (up to 1 g daily) for 3–10 days. Adolescents ≥13 years of age: 1 g once daily for 3–10 days. **Intra-abdominal Infections** **IV or IM** Children 3 months to 12 years of age: 15 mg/kg twice daily (up to 1 g daily) for 5–14 days. Adolescents ≥13 years of age: 1 g once daily for 5–14 days. **Respiratory Tract Infections** **Community-acquired Pneumonia** IV or IM Children 3 months to 12 years of age: 15 mg/kg twice daily (up to 1 g daily). Usual duration is 10–14 days; treatment may be switched to an appropriate oral anti-infective after ≥3 days. Adolescents ≥13 years of age: 1 g once daily. Usual duration is 10–14 days; treatment may be switched to an appropriate oral anti-infective after ≥3 days. **Skin and Skin Structure Infections** **IV or IM** Children 3 months to 12 years of age: 15 mg/kg twice daily (up to 1 g daily) for 7–14 days. Adolescents ≥13 years of age: 1 g once daily for 7–14 days. **Urinary Tract Infections (UTIs)** **IV or IM** Children 3 months to 12 years of age: 15 mg/kg twice daily (up to 1 g daily). Usual duration is 10–14 days; treatment may be switched to an appropriate oral anti-infective after ≥3 days. Adolescents ≥13 years of age: 1 g once daily. Usual duration is 10–14 days; treatment may be switched to an appropriate oral anti-infective after ≥3 days
Dosage adjustment	**Dosing: renal impairment: Adult** Adults with Clcr ≤30 mL/minute, including those with end-stage renal disease (Clcr ≤10 mL/minute) and those undergoing hemodialysis, should receive 500 mg once daily **Dosing: Renal Impairment: Pediatric** There are no pediatric specific recommendations; based on experience in adult patients, dosage adjustment suggested **Dosing: Hepatic Impairment:** Adjustments cannot be recommended (lack of experience and research in this patient population
Contra-indications	Known hypersensitivity to any component of this product or to other drugs in the same class or in patients who have demonstrated anaphylactic reactions to beta-lactams; known hypersensitivity to local anesthetics of the amide type due to the use of lidocaine as a diluent (IM use only).
Adverse Drug Reactions	Gastrointestinal: Diarrhea (6% to 12%) **1% to 10%:** **Cardiovascular**: Asystole (<2%), atrial fibrillation (<2%), bradycardia (<2%), cardiac arrhythmia (<2%), cardiac failure (<2%), chest pain (infants, children, adolescents, adults: <2%), edema (≤3%), facial edema (<2%), flushing (<2%), heart murmur (<2%), hypertension (<2%), hypotension (1% to 2%), phlebitis (infants, children, adolescents, adults: <2%), septic shock (<2%), subdural hematoma (<2%), syncope (<2%), tachycardia (<2%), thrombophlebitis (<2%), ventricular tachycardia (<2%) **Dermatologic**: Dermatitis (infants, children, adolescents, adults: <2%), desquamation (<2%), diaphoresis (<2%), erythema of skin (<2%), erythematous rash (infants, children, and adolescents: <2%), genital rash (infants, children, and adolescents: <2%), injection site pruritus (infants, children, and adolescents: <2%), pruritus (infants, children, adolescents, adults: 1% to 2%), skin lesion (infants, children, and adolescents: <2%), skin rash (infants, children, adolescents, adults:

2% to 3%), urticaria (<2%)
Endocrine & metabolic: Decreased serum albumin (<2%), decreased serum potassium (<2%), dehydration (<2%), gout (<2%), increased serum glucose (<2%), increased serum potassium (<2%), increased serum sodium (<2%), weight loss (<2%)
Gastrointestinal: Abdominal distention (<2%), abdominal pain (infants, children, adolescents, adults: 4% to 5%), acid regurgitation (<2%), anorexia (<2%), cholelithiasis (<2%), *Clostridioides difficile*-associated diarrhea (<2%), constipation (infants, children, adolescents, adults: 2% to 4%), decreased appetite (infants, children, and adolescents: <2%), duodenitis (<2%), dysgeusia (<2%), dyspepsia (<2%), dysphagia (<2%), esophagitis (<2%), flatulence (<2%), gastritis (<2%), gastrointestinal hemorrhage (<2%), hemorrhoids (<2%), hiccups (<2%), intestinal obstruction (<2%), nausea (infants, children, adolescents: <2%; adults: 6% to 9%), oral candidiasis (infants, children, adolescents, adults: <2%), oral mucosa ulcer (<2%), pancreatitis (<2%), pyloric stenosis (<2%), sore throat (<2%), stomatitis (<2%), upper abdominal pain (infants, children, and adolescents: <2%), vomiting (infants, children, adolescents, adults: 4% to 10%)
Genitourinary: Anuria (<2%), bladder dysfunction (<2%), finding of blood in urine (1% to 3%), hematuria (<2%), oliguria (<2%), proteinuria (infants, children, and adolescents: <2%), urinary retention (<2%), vaginitis (1% to 3%), vulvovaginal candidiasis (<2%), vulvovaginal pruritus (<2%), vulvovaginitis (<2%)
Hematologic & oncologic: Decreased hematocrit (3%), decreased hemoglobin (5%), decreased neutrophils (infants, children, adolescents: 6%; adults: <2%), decreased platelet count (<2%), decreased white blood cell count (infants, children, adolescents, adults: <2%), eosinophilia (infants, children, adolescents, adults: 1% to 2%), hematoma (<2%), leukocyturia (2% to 3%), prolonged partial thromboplastin time (<2%), prolonged prothrombin time (<2%), thrombocythemia (infants, children, adolescents: <2%; adults: 4% to 7%)
Hepatic: Increased serum alanine aminotransferase (infants, children, adolescents, adults: 4% to 9%), increased serum alkaline phosphatase (infants, children, adolescents: <2%; adults: 4% to 7%), increased serum aspartate transaminase (infants, children, adolescents, adults: 4% to 8%), increased serum bilirubin (<2%; including increased direct serum bilirubin or increased indirect serum bilirubin), jaundice (<2%)
Infection: Abscess (abdominal: infants, children, and adolescents: <2%), candidiasis (infants, children, adolescents, adults: <2%), herpes simplex infection (infants, children, and adolescents: <2%), septicemia (<2%)
Local: Erythema at injection site (infants, children, and adolescents: 4%), induration at injection site (infants, children, adolescents, adults: <2%), infused vein complication (5% to 7%), infusion-site pain (infants, children, adolescents: 7%), injection site phlebitis (infants, children, adolescents: <2%), pain at injection site (<2%), swelling at injection site (infants, children, and adolescents: <2%), warm sensation at injection site (infants, children, and adolescents: <2%)
Nervous system: Aggressive behavior (<2%), altered mental status (infants, children, adolescents, adults: 3% to 5%; including agitation, confusion, decreased mental acuity, disorientation, drowsiness, stupor), anxiety (<2%), chills (<2%), depression (<2%), dizziness (infants, children, adolescents, adults: 2%), fatigue (<2%), flank pain (<2%), headache (infants, children, adolescents, adults: 4% to 7%), hypoesthesia (<2%), hypothermia (infants, children, and adolescents: <2%), insomnia (infants, children, adolescents, adults: ≤3%), malaise (<2%), nervousness (<2%), pain (<2%), paresthesia (<2%), vertigo (<2%), voice disorder (<2%)
Neuromuscular & skeletal: Arthralgia (infants, children, and adolescents: <2%), asthenia (<2%), lower extremity pain (<2%), muscle spasm (<2%), tremor (<2%)
Renal: Increased blood urea nitrogen (<2%), increased serum creatinine (<2%), renal insufficiency (<2%)
Respiratory: Asthma (<2%), bronchoconstriction (<2%), cough (≤4%), dyspnea (1% to 3%),

	epistaxis (<2%), hemoptysis (<2%), hypoxemia (<2%), nasopharyngitis (<2%), pharyngitis (<2%; including viral), pleural effusion (<2%), pleuritic chest pain (<2%), rales (<2%), respiratory distress (<2%), rhinitis (<2%), rhinorrhea (<2%), rhonchi (<2%), upper respiratory tract infection (2%), wheezing (<2%) Miscellaneous: Fever (infants, children, adolescents, adults: 2% to 5%), swelling (infants, children, adolescents, adults: ≤3%), tissue necrosis (<2%)
Monitoring Parameters	Periodic renal, hepatic, and hematopoietic assessment during prolonged therapy; neurological assessment.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Valproate Products, Typhoid Vaccine, Sodium Picosulfate ***Risk C: Monitor therapy*** BCG Vaccine (Immunization) Lactobacillus and Estriol: Probenecid: Tacrolimus (Systemic)
Pregnancy and Lactation	pregnancy category: Not assigned. Risk summary: Insufficient data available on use of this drug in pregnant women Animal studies have revealed evidence of slightly decreased fetal weight and effects on vertebral ossification Ertapenem is present in breast milk. The relative infant dose (RID) of ertapenem is <1% The decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother. In general, antibiotics that are present in breast milk may cause non-dose-related modification of bowel flora. Monitor infants for GI disturbances, such as thrush or diarrhea
Administration	**Administration: IM** Avoid injection into a blood vessel. Make sure patient does not have an allergy to lidocaine or another anesthetic of the amide type. Administer by deep IM injection into a large muscle mass (eg, gluteal muscle or lateral part of the thigh). **Administration: IV** Administer as an IV infusion over 30 minutes. Do not infuse with dextrose-containing solutions. **Reconstitution and Dilution** **IV Infusion** Reconstitute 1-g vial with 10 mL of sterile water for injection, 0.9% sodium chloride injection, or bacteriostatic water for injection. shake well; Further dilute dose with NS; for adolescents and adults, transfer dose to 50 mL NS; for children, dilute dose to a final concentration ≤20 mg/mL. **IM** Reconstitute 1,000 mg vial with 3.2 mL of 1% lidocaine HCl injection (without epinephrine); shake well. Administer within 1 hour of reconstitution. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Anaphylaxis/hypersensitivity reactions: Serious hypersensitivity reactions, including anaphylaxis, have been reported (some without a history of previous allergic reactions to beta-lactams). • CNS effects: Carbapenems have been associated with CNS adverse effects, including confusional states and seizures (myoclonic); use caution with CNS disorders (eg, brain lesions and

	history of seizures) and adjust dose in renal impairment to avoid drug accumulation, which may increase seizure risk. • Superinfection: Use may result in fungal or bacterial superinfection, including *Clostridioides* (formerly *Clostridium*) *difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Renal impairment: Use with caution in patients with renal impairment; dosage adjustment required in patients with moderate to severe renal dysfunction. Increased seizure risk has been reported in patients with renal dysfunction. ***Concurrent drug therapy issues:*** • Valproic acid and derivatives: Carbapenems, including ertapenem, may decrease the serum concentration of divalproex sodium/valproic acid increasing the risk of breakthrough seizures. Concurrent use of carbapenem antibiotics with divalproex sodium/valproic acid is generally not recommended. Alternative antimicrobial agents should be considered, but if a concurrent carbapenem is necessary, consider additional antiseizure medication. ***Special populations:*** • Elderly: Lower doses (based upon renal function) are often required in the elderly. ***Other warnings/precautions:*** • IM administration: Doses for IM administration are mixed with lidocaine; consult Lidocaine (Systemic) information for associated Warnings/Precautions.
Storage	Prior to reconstitution, store vials at ≤25°C. The reconstituted IM solution should be used within 1 hour after preparation. The reconstituted IV solution may be stored at room temperature 25°C and used within 6 hours, or stored for 24 hours under refrigeration 5°C and used within 4 hours after removal from refrigeration. Do not freeze. Refer to manufacturer PIL if there are specific considerations.

Watch Group

2. Imipenem and Cilastatin

Generic Name	Imipenem and Cilastatin
Dosage form/strengths	**Powder for injection:** 500/500mg
Route of administration	*IV*
Pharmacologic category	Antibiotic, Carbapenem ATC: J01DH51
Indications	For treatment of: Bacterial septicemia Bone and joint infections Endocarditis Gynecologic infections Intra-abdominal infections Lower respiratory tract infections Skin and skin structure infections Urinary tract infections (complicated and uncomplicated)
Dosage Regimen	**Dosing: Adult** Doses based on imipenem content. Recommended IV adult dosages are for adults weighing ≥70 kg. Modification of dosage is recommended for patients weighing <70 kg **Usual dosage range: IV:** **Susceptible bacterial species:** 500 mg every 6 hours or 1,000 mg every 8 hours (maximum dose: 4,000 mg/day) **Intermediate susceptibility bacterial species:** 1,000 mg every 6 hours (maximum dose: 4,000 mg/day) **Dosing: Pediatric** **Note:** Dosage recommendations are based on imipenem component**.** **General Dosage for Neonates** **IV** **Neonates <1 week of age weighing ≥1.5 kg:** 25 mg/kg every 12 hours. **Neonates 1–4 weeks of age weighing ≥1.5 kg:** 25 mg/kg every 8 hours. **General Dosage for Infants and Children** **IV** **Children 1–3 months of age weighing ≥1.5 kg: 15–**25 mg every 6 hours**,** maximum daily dose: 4,000 mg/day
Dosage adjustment	**Dosing: Renal Impairment: Adult** **Note:** Estimation of renal function for the purpose of dosing adjustment should be done using the Cockcroft-Gault formula: • Usual dosing regimen of 500 mg every 6 hours: CrCl ≥90 mL/minute: No dosage adjustment necessary. CrCl ≥60 to <90 mL/minute: 400 mg every 6 hours CrCl ≥30 to <60 mL/minute: 300 mg every 6 hours CrCl ≥15 to <30 mL/minute: 200 mg every 6 hours CrCl <15 mL/minute: Do not administer imipenem and cilastatin unless hemodialysis is instituted within 48 hours. • Usual dosing regimen of 1,000 mg every 8 hours: CrCl ≥90 mL/minute: No dosage adjustment necessary. CrCl ≥60 to <90 mL/minute: 500 mg every 6 hours

	CrCl ≥30 to <60 mL/minute: 500 mg every 8 hours CrCl ≥15 to <30 mL/minute: 500 mg every 12 hours CrCl <15 mL/minute: Do not administer imipenem and cilastatin unless hemodialysis is instituted within 48 hours. • Usual dosing regimen of 1,000 mg every 6 hours: CrCl ≥90 mL/minute: No dosage adjustment necessary. CrCl ≥60 to <90 mL/minute: 750 mg every 8 hours CrCl ≥30 to <60 mL/minute: 500 mg every 6 hours CrCl ≥15 to <30 mL/minute: 500 mg every 12 hours CrCl <15 mL/minute: Do not administer imipenem and cilastatin unless hemodialysis is instituted within 48 hours. **Dosing: Renal Impairment: Pediatric** Infants, Children, and Adolescents: IV: Patient weight <30 kg and impaired renal function: Use not recommended The following adjustments have been recommended: **Note:** Renally adjusted dose recommendations are based on doses of 60 to 100 mg/kg/day divided every 6 hours. GFR 30 to 50 mL/minute/1.73 m^2: Administer 7 to 13 mg/kg/dose every 8 hours GFR 10 to 29 mL/minute/1.73 m^2: Administer 7.5 to 12.5 mg/kg/dose every 12 hours GFR <10 mL/minute/1.73 m^2: Administer 7.5 to 12.5 mg/kg/dose every 24 hours Intermittent hemodialysis (IHD): Dialysis: Moderately dialyzable (20% to 50%): 7.5 to 12.5 mg/kg/dose every 24 hours (administer after hemodialysis on dialysis days) Peritoneal dialysis (PD): 7.5 to 12.5 mg/kg/dose every 24 hours Continuous renal replacement therapy (CRRT): 7 to 13 mg/kg/dose every 8 hours **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to imipenem/cilastatin or any component of the formulation
Adverse Drug Reactions	**>10%** **Hematologic & oncologic:** Decreased hematocrit (infants and children 3 months to 12 years: 18%; neonates and infants <3 months: 2%), decreased hemoglobin (infants and children 3 months to 12 years: 15%), eosinophilia (neonates, infants, and children to 12 years: 9% to 13%), thrombocythemia (infants and children 3 months to 12 years: 13%; neonates and infants <3 months: 4%) **Hepatic:** Increased serum AST (infants and children 3 months to 12 years: 18%; neonates and infants <3 months: 6%), increased serum ALT (infants and children 3 months to 12 years: 11%; neonates and infants <3 months: 3%) **1% to 10%**: **Cardiovascular**: Phlebitis (2% to 3%), tachycardia (neonates and infants ≤3 months: 2%; adults <1%) **Central nervous system:** Seizure (neonates and infants ≤3 months: 6%; adults <1%) **Dermatologic**: Skin rash (≤2%) **Gastrointestinal**: Diarrhea (neonates, infants, and children to 12 years: 3% to 4%; adults 2%), nausea (2%), oral candidiasis (neonates and infants ≤3 months: 2%), vomiting (≤1% to 2%), gastroenteritis (≤1%) **Genitourinary**: Proteinuria (infants and children 3 months to 12 years: 8%), urine discoloration (≤1%), oliguria (neonates and infants ≤3 months: 2%; adults <1%) **Hematologic & oncologic**: Neutropenia (infants and children 3 months to 12 years: 3%; adults <1%), decreased platelet count (neonates and infants <3 months: 2%), increased hematocrit (neonates and infants <3 months: 1%)

	Hepatic: Increased serum alkaline phosphatase (neonates and infants <3 months: 3%), increased serum bilirubin (neonates and infants <3 months: 3%), decreased serum bilirubin (neonates and infants <3 months: 1%) **Local**: Irritation at injection site (infants, children, and adolescents 3 months to 16 years: 1%) **Renal**: Increased serum creatinine (neonates and infants <3 months: 5%)
Monitoring Parameters	Periodic renal, hepatic, and hematologic function tests; monitor for signs of anaphylaxis during first dose
Drug Interactions	***Risk X: Avoid combination*** *BCG (Intravesical), Cholera Vaccine* ***Risk D: Consider therapy modification*** *Ganciclovir-Valganciclovir Sodium Picosulfate Typhoid Vaccine Valproate Products* ***Risk C: Monitor therapy*** *BCG Vaccine Cyclosporine Lactobacillus and Estriol Probenecid*
Pregnancy and Lactation	**pregnancy category C** Imipenem is not one of the preferred antibiotics used for the management of cystic fibrosis in lactating females; however, when a safer alternative is not available, imipenem is the preferred carbapenem antibiotic. Due to poor oral bioavailability, exposure to a breastfed infant is expected to be limited
Administration	**Administration: IV** For IV infusion only; do not administer IV push. Infuse doses ≤500 mg over 20 to 30 minutes; infuse doses >500 mg over 40 to 60 minutes. If nausea and/or vomiting occur during administration, decrease the rate of IV infusion. **Preparation for Administration: Adult** Reconstitute vials with approximately 10 mL of NS, D5W, D5NS. Shake well and transfer to 100 mL of an appropriate infusion solution; repeat transfer with an additional 10 mL of infusion solution to ensure complete transfer of vial contents to the infusion solution. Agitate resulting mixture until clear. Solutions range from colorless to yellow. concentrations >5 mg/mL may have shortened stability; Imipenem is inactivated at acidic or alkaline pH. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • CNS effects: including confusion states and seizures (myoclonic); use caution with CNS disorders and adjust dose in renal impairment to avoid drug accumulation, which may increase seizure risk. • Hypersensitivity reactions: Serious hypersensitivity/anaphylactic reactions have been reported, including fatalities • Superinfection: Prolonged use ***Disease-related concerns:*** • Renal impairment. ***Concurrent drug therapy issues:*** • Valproic acid and derivatives: Concurrent use of carbapenem antibiotics with divalproex sodium/valproic acid is generally not recommended as increasing the risk of breakthrough seizures. ***Special populations:*** • Pediatric: Not recommended in pediatric CNS infections due to seizure potential. Not recommended in pediatric patients <30 kg with impaired renal function (no data available).

Storage	Store intact vials at <25°C. Reconstituted solution is stable for 4 hours at room temperature or 24 hours when refrigerated at 5°C. Do not freeze. Refer to manufacturer PIL if there are specific considerations.

3. Meropenem

Watch Group

Generic Name	Meropenem
Dosage form/strengths	**Powder for injection**: 500mg, 1gm
Route of administration	*IV*
Pharmacologic category	Antibiotic, Carbapenem ATC: J01DH02
Indications	**Intra-abdominal infections:** Treatment of complicated appendicitis and peritonitis in adult and pediatric patients **Meningitis, bacterial:** Treatment of bacterial meningitis in pediatric patients 3 months and older **Skin and skin structure infection, complicated:** Treatment of complicated skin and skin structure infections in adults and pediatric patients 3 months and older
Dosage Regimen	**Dosing: Adult** **Note:** Infusion method: Dosing is presented based on the traditional infusion method over 30 minutes, unless otherwise specified. **Usual dosage range:** *Traditional intermittent infusion method (over 30 minutes)*: IV: 500 mg every 6 hours or 1 g every 8 hours 500 mg every 6 hours achieves comparable pharmacokinetic and pharmacodynamic parameters to 1 g every 8 hours **Meningitis** **IV:** 2 g every 8 hours. Treatment duration is 7 to 21 days depending on causative pathogen(s) and clinical response. **Note:** Consider use of an extended or continuous infusion for more resistant pathogens **Dosing: Pediatric** **General dosing, susceptible infection (non-CNS)**: Infants, Children, and Adolescents: IV: Children≥3 months weighing≤50 kg:10-20 mg/kg/dose every 8 hours Children ≥3 months weighing >50 kg: 500-1000mg every 8 hours **Meningitis**: Children ≥3 months of age weighing ≤50 kg: 40 mg/kg (up to 2 g) every 8 hours. Children ≥3 months weighing >50 kg: 2 g every 8 hours. extended infusions may be needed for infections due to isolates with elevated MICs **Prescribing Limits** **Pediatric Patients** **IV:** 2 g every 8 hours - Safety and efficacy not established in children <3 months of age
Dosage adjustment	**Dosing: Renal Impairment: Adult**

CrCl (mL/minute)	If the usual recommended dose is 1 g every 8 hours[c]	If the usual recommended dose is 2 g every 8 hours[c]
>50 to <130	No dosage adjustment necessary	No dosage adjustment necessary
>25 to ≤50	1 g every 12 hours	2 g every 12 hours
10 to ≤25	500 mg every 12	1 g every 12 hours

	hours	
<10	500 mg every 24 hours	1 g every 24 hours

Dosing: Renal Impairment: Pediatric
Data insufficient to make dosage recommendations for pediatric patients with renal impairment
Dosing: Hepatic Impairment:
No dosage adjustment necessary.

Contra-indications

Hypersensitivity to meropenem, other drugs in the same class, or any component of the formulation; patients who have experienced anaphylactic reactions to beta-lactams

Adverse Drug Reactions

1% to 10%:
CNS: Headache, pain
Dermatologic: Skin rash
Endocrine & metabolic: Hypoglycemia, hypervolemia
Gastrointestinal: Nausea, diarrhea, constipation, vomiting, oral candidiasis
Infection: Sepsis
Local: Inflammation at injection site

Monitoring Parameters

Perform culture and sensitivity testing prior to initiating therapy. Monitor for signs of anaphylaxis during first dose. During prolonged therapy, monitor renal function, liver function, CBC

Drug Interactions

Risk X: Avoid combination
BCG (Intravesical) Cholera Vaccine Probenecid
Risk D: Consider therapy modification
Sodium Picosulfate Typhoid Vaccine Valproate Products
Risk C: Monitor therapy
BCG Vaccine Lactobacillus and Estriol

Pregnancy and Lactation

Pregnancy Category C
Meropenem is present in breast milk.
Information related to the use of meropenem in breastfeeding women is limited.

Administration

Administration: IV
Administer IV infusion over 15 to 30 minutes; IV bolus injection (5 to 20 mL) over 3 to 5 minutes
IV push: Infants ≥3 months, Children, and Adolescents: Administer reconstituted solution (up to 1,000 mg) over 3 to 5 minutes; safety data is limited with 40 mg/kg doses up to a maximum of 2,000 mg
Preparation for Administration:
Parenteral: Reconstitute meropenem 500 mg and 1,000 mg vials with 10 mL and 20 mL SWFI respectively to yield a concentration of 50 mg/mL. For IV infusion, may further dilute with D5W or NS to a final concentration ranging from 1 to 20 mg/mL.
N.B. Hypersensitivity test must be done before using injection form of this medicine.
Refer to manufacturer PIL if there are specific considerations.

Warnings/ Precautions

Concerns related to adverse effects:
• Anaphylaxis/hypersensitivity reactions
• CNS effects: Carbapenems have been associated with CNS adverse effects, including confusional states and seizures (myoclonic); use caution with CNS disorders (eg, brain lesions and history of seizures).
• Dermatological effects: Severe cutaneous adverse reactions, including Stevens-Johnson syndrome. discontinue immediately for severe reactions.

	• Superinfection: Prolonged use ***Disease-related concerns:*** • Renal impairment: Use with caution in patients with renal impairment; dosage adjustment required in patients with creatinine clearance ≤50 mL/minute. Increased seizure risk and thrombocytopenia have been reported in patients with renal impairment. ***Special populations:*** • Elderly: Lower doses (based upon renal function) are often required in the elderly.
Storage	• Vials: stored at controlled room temperature 20°C to 25°C. • Stability of vial after reconstitution (up to 50 mg/mL) with SWFI: Stable for up to 3 hours at up to 25°C or for up to 13 hours at up to 5°C. • Infusion admixture (1 to 20 mg/mL): Solution is stable when diluted in NS for 1 hour at up to 25°C or 15 hours at up to 5°C. Solutions constituted with dextrose injection 5% should be used immediately Refer to manufacturer PIL if there are specific considerations.

Cephalosporins

Access Group

a) First Generation Cephalosporins

1. Cefadroxil

Generic Name	Cefadroxil
Dosage form/strengths	Tablets 1g, Capsule 250mg, 500mg Oral suspension 125mg/5ml, 250mg/5ml, 500mg/5ml Oral drops 100mg/ml
Route of administration	*Oral*
Pharmacologic category	Antibiotic, Cephalosporin (First Generation) ATC: J01DB05
Indications	**Pharyngitis and/or tonsillitis:** Treatment of pharyngitis and/or tonsillitis caused by *Streptococcus pyogenes* (group A beta-hemolytic streptococci). **Skin and skin structure infections:** Treatment of skin and skin structure infections caused by staphylococci and/or streptococci. **Urinary tract infection:** Treatment of urinary tract infections caused by *Escherichia coli*, *Proteus mirabilis*, and *Klebsiella* species.
Dosage Regimen	**Dosing: Adult** **Skin and skin structure infections:** Oral: 1 g daily in a single or 2 divided doses **Streptococcal pharyngitis (group A) (alternative agent for mild [non-anaphylactic] penicillin allergy):** Oral: 1 g once daily for 10 days **Urinary tract infection (UTI) (alternative agent):** **Note:** Use with caution and only when recommended agents cannot be used (due to decreased efficacy of oral beta-lactams compared to other agents) **Cystitis, acute uncomplicated:** Oral: 500 mg twice daily for 5 to 7 days **UTI, complicated (including pyelonephritis):** Oral: 1 g twice daily for 10 to 14 days. **Dosing: Pediatric** **General dosing, susceptible infection:** Mild to moderate infection: Infants, Children, and Adolescents: Oral: 15 mg/kg/dose twice daily; maximum daily dose: 2,000 mg/**day** **Impetigo:** Children and Adolescents: Oral: 30 mg/kg/day in a single dose or divided every 12 hours; maximum daily dose: 1,000 mg/**day** **Pharyngitis/tonsillitis:** Children and Adolescents: Oral: 30 mg/kg/day in a single dose or divided every 12 hours for 10 days; maximum daily dose: 1,000 mg/**day** **Skin and skin structure infections:** Children and Adolescents: Oral: 15 mg/kg/dose every 12 hours; maximum daily dose: 1,000 mg/**day** **Urinary tract infections:** Children and Adolescents: Oral: 15 mg/kg/dose every 12 hours; maximum daily dose: 2,000 mg/**day**
Dosage adjustment	**Dosing: Renal Impairment: Adult** Initial: 1 g as a single dose. Maintenance: CrCl >50 mL/minute: No dosage adjustment necessary. CrCl 25 to 50 mL/minute: 500 mg every 12 hours. CrCl 10 to 25 mL/minute: 500 mg every 24 hours. CrCl <10 mL/minute: 500 mg every 36 hours

	Dosing: Renal Impairment: Pediatric Infants, Children, and Adolescents: Dosing based on a usual dose of 30 mg/kg/day in divided doses every 12 hours: CrCl ≥30 mL/minute/1.73 m^2: No dosage adjustment necessary CrCl 10 to 29 mL/minute/1.73 m^2: 15 mg/kg/dose every 24 hours CrCl <10 mL/minute/1.73 m^2: 15 mg/kg/dose every 36 hours Hemodialysis, intermittent: 15 mg/kg/dose every 24 hours Peritoneal dialysis: 15 mg/kg/dose every 36 hours **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to cefadroxil, any component of the formulation, or other cephalosporins
Adverse Drug Reactions	**1% to 10%:** Gastrointestinal: Diarrhea
Monitoring Parameters	Monitor renal function. Observe for signs and symptoms of anaphylaxis during first dose.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine, ***Risk D: Consider therapy modification*** Tolvaptan, Typhoid Vaccine, Sodium Picosulfate: ***Risk C: Monitor therapy*** Acemetacin, Aminoglycosides, BCG Vaccine (Immunization), Dichlorphenamide, Lactobacillus and Estriol, Methotrexate, Mycophenolate, Probenecid, Teriflunomide, Tetracyclines, Vitamin K Antagonists
Pregnancy and Lactation	**Pregnancy Risk Factor** B Cefadroxil is present in breast milk. Caution should be exercised when administering cefadroxil to breastfeeding women. Monitor infants for GI disturbances.
Administration	**Administration: Oral** Administer around-the-clock to promote less variation in peak and trough serum levels. Administer without regards to meals; administration with food diminishes GI complaints. **Administration: Pediatric** Oral: May be administered without regard to food; administration with food may decrease nausea or vomiting; shake suspension well before use. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity reactions: Hypersensitivity reactions, including anaphylaxis, may occur. If an allergic reaction occurs, discontinue treatment and institute supportive measures. • Penicillin allergy: Use with caution in patients with a history of penicillin allergy. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment.
Storage	Store capsules, tablets and unreconstituted oral suspension at 15°C to 30°C. After reconstitution, oral suspension may be stored for 14 days under refrigeration (4°C). Refer to manufacturer PIL if there are specific considerations.

2. Cefazolin

Generic Name	Cefazolin
Dosage form/strengths	Vial 500mg, 1g
Route of administration	*IV, IM*
Pharmacologic category	First-generation cephalosporin antibacterial ATC: J01DB04
Indications	**Treatment of** Biliary tract infection Bloodstream infection Bone and joint infection Endocarditis, treatment Genital infection: (ie, prostatitis, epididymitis) Respiratory tract infection Skin and soft tissue infection. Urinary tract infection **Surgical prophylaxis:** To reduce the incidence of certain postoperative infections in adults and pediatric patients 10 to 17 years of age undergoing surgical procedures.
Dosage Regimen	**Adult:** **Bloodstream infection:** **P**athogen-directed therapy for methicillin-susceptible staphylococci: IV: 2 g every 8 hours treat uncomplicated Staphylococcus aureus bacteremia for ≥14 days starting from day of first negative blood culture, with longer courses warranted for endocarditis or metastatic sites of infection Pathogen-directed therapy for susceptible Enterobacteriaceae: IV: 2 g every 8 hours. Usual duration is 7 to 14 days; individualize depending on source and extent of infection as well as clinical response. A 7-day duration is recommended for patients with uncomplicated Enterobacteriaceae infection who respond appropriately to antibiotic therapy **Endocarditis, treatment:** Pathogen-directed therapy for methicillin-susceptible staphylococci (alternative agent for patients with nonsevere, non-IgE-mediated penicillin allergy): Native valve: IV: 2 g every 8 hours for 6 weeks Prosthetic valve: IV: 2 g every 8 hours for ≥6 weeks (combine with rifampin for entire duration of therapy and gentamicin for the first 2 weeks) **Intra-abdominal infection, community-acquired (mild to moderate infection in low-risk patients):** Note: Reserve for patients with low risk for resistant pathogens (eg, local Enterobacteriaceae resistance rate to cefazolin <10% and no recent antibiotic exposure)

	Cholecystitis, acute: IV: 1 to 2 g every 8 hours; continue for 1 day after gallbladder removal or until clinical resolution in patients managed nonoperatively. Note: The addition of anaerobic therapy is recommended if biliary-enteric anastomosis is present. **Osteomyelitis and/or discitis:** Treatment, pathogen-directed therapy for methicillin-susceptible S. aureus: IV: 2 g every 8 hours for ≥6 weeks depending on extent of infection, debridement, and clinical response. Prevention, following open fractures: IV: 2 g for patients <120 kg or 3 g for patients ≥120 kg every 8 hours; ideally administer within 6 hours of injury. **Pneumonia**: Pathogen-directed therapy for methicillin-susceptible S. aureus: IV: 2 g every 8 hours. Minimum duration is 5 to 7 days **Urinary tract infection, complicated (including pyelonephritis):** Pathogen-directed therapy for susceptible organisms: IV: 1 g every 8 hours **Pediatric:** General dosing, susceptible infection: Infants, Children, and Adolescents: IM, IV: Mild to moderate infections: 25 to 100 mg/kg/day divided every 8 hours; maximum daily dose: 6 g/day Severe infections (eg, bone/joint infections): 100 to 150 mg/kg/day divided every 6 to 8 hours; maximum daily dose: 12 g/day
Dosage adjustment	**Dosing in renal impairment: Adult** CrCl ≥50 mL/minute: 1 to 2 g every 8 hours. CrCl 30 to <50 mL/minute: 1 to 2 g every 8 to 12 hours. CrCl >10 to <30 mL/minute: 500 mg to 1 g every 12 hours (some experts give 2 g every 12 hours for severe infections in patients with CrCl 10 to <30 mL/minute). CrCl ≤10 mL/minute or haemodialysis: 500 mg to 1 g every 24 hours. **Dosing: Renal Impairment: Pediatric** Infants >1 month, Children, and Adolescents: After initial loading dose is administered, modify dose based on the degree of renal impairment: CrCl >70 mL/minute: No dosage adjustment required CrCl 40 to 70 mL/minute: Administer 60% of the usual daily dose divided every 12 hours CrCl 20 to 40 mL/minute: Administer 25% of the usual daily dose divided every 12 hours CrCl 5 to 20 mL/minute: Administer 10% of the usual daily dose given every 24 hours Hemodialysis: 25 mg/kg/dose every 24 hours Peritoneal dialysis: 25 mg/kg/dose every 24 hours Continuous renal replacement therapy: 25 mg/kg/dose every 8 hours **Dosing in hepatic impairment adults & pediatrics:** There are no dosage adjustments data.
Contra-indications	hypersensitivity reactions to the drug
Adverse Drug Reactions	**Frequency not defined:** Cardiovascular: Localized phlebitis Central nervous system: Seizure Dermatologic: Pruritus, skin rash, Stevens-Johnson syndrome Gastrointestinal: Abdominal cramps, anorexia, diarrhea, nausea, oral candidiasis,

	pseudomembranous colitis, vomiting Genitourinary: Vaginitis Hepatic: Hepatitis, increased serum transaminases Hematologic: Eosinophilia, leukopenia, neutropenia, thrombocythemia, thrombocytopenia Hypersensitivity: Anaphylaxis Local: Pain at injection site Renal: Increased blood urea nitrogen, increased serum creatinine, renal failure Miscellaneous: Fever
Monitoring Parameters	Renal function periodically, hepatic function tests, CBC; monitor for signs of anaphylaxis during first dose
Drug Interactions	***Risk X: Avoid combination:*** BCG (Intravesical), Cholera Vaccine, ***Risk D: Consider therapy modification:*** Rifampin, Typhoid Vaccine ***Risk C: Monitor therapy*** Aminoglycosides BCG Vaccine (Immunization) Fosphenytoin Immune Checkpoint Inhibitors Lactobacillus and Estriol Phenytoin Probenecid Vitamin K Antagonists (eg, warfarin)
Pregnancy	Adverse events have not been reported in the fetus following administration of cefazolin prior to cesarean delivery. Cefazolin is present in breast milk. Caution should be exercised when administering cefazolin to breastfeeding women.
Administration	**Administration: IM** Inject deep IM into large muscle mass. **Administration: IV** Inject direct IV over 3 to 5 minutes or may infuse as an intermittent infusion over 30 to 60 minutes. **Preparation for Administration:** Dilute 500 mg vial with 2 mL SWFI and 1 g vial with 2.5 mL SWFI; reconstituted solution may be directly injected after further dilution with 5 mL SWFI or further diluted for IV administration in 50 to 100 mL compatible solution (eg, D5W, NS); 10 g vial may be diluted with 45 mL to yield 1 g/5 mL or 96 mL to yield 1 g/10 mL. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Elevated INR: May be associated with increased INR, especially in nutritionally-deficient patients, prolonged treatment, hepatic or renal disease. • Hypersensitivity reactions • Penicillin allergy • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including Clostridioides (formerly Clostridium) difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment.
Storage	• Store intact vials at room temperature and protect from temperatures exceeding 40°C. • Reconstituted solutions of cefazolin are light yellow to yellow. Protection from light

	is recommended for the powder and for the reconstituted solutions. Reconstituted solutions are stable for 24 hours at room temperature and for 10 days under refrigeration. • Stability of parenteral admixture in D5W, D5LR, D51/4NS, D51/2NS, D5NS, D10W, LR, or NS at room temperature (25°C) is 48 hours. • Stability of parenteral admixture at refrigeration temperature (4°C) is 14 days. Refer to manufacturer PIL if there are specific considerations.

3. Cephalexin

Generic Name	Cephalexin
Dosage form/ strengths	Oral suspension: 125mg/5ml, 250mg/5ml Tablets 250mg, 500mg, 1000mg Capsule 250mg, 500mg, Vial 500mg, 1g
Route of administration	*Oral , parentral*
Pharmacologic action	Antibiotic, Cephalosporin (First Generation) ATC: J01DB01
Indications	**Bone infections:** Treatment of bone infections caused by *Staphylococcus aureus* and/or *Proteus mirabilis*. **Genitourinary tract infections:** Treatment of genitourinary tract infections, including acute prostatitis, caused by *Escherichia coli*, *P. mirabilis*, and *Klebsiella pneumoniae*. **Otitis media:** Treatment of otitis media caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, *S. aureus*, *Streptococcus pyogenes*, and *Moraxella catarrhalis*. **Respiratory tract infections:** Treatment of respiratory tract infections (including pharyngitis) caused by *S. pneumoniae* and *S. pyogenes*. **Skin and skin structure infections:** Treatment of skin and skin structure infections caused by *S. aureus* and/or *S. pyogenes*.
Dosage Regimen	**Usual adult dosage range:** Oral: 250 to 1,000 mg every 6 hours or 500 mg every 12 hours (maximum: 4 g/day). **Dosing: Pediatric** **General dosing, susceptible infection**: Infants, Children, and Adolescents: Mild to moderate infection: Oral: 25 to 50 mg/kg/day divided every 6 or 12 hours; maximum daily dose: 2,000 mg/**day**. Severe infection (eg, bone and joint infections): Oral: 75 to 100 mg/kg/day divided every 6 to 8 hours; maximum daily dose: 4,000 mg/**day**. • Suspension/tablet bioequivalence: Tablets and oral suspension are not bioequivalent; do not substitute on a mg-per-mg basis.
Dosage adjustment	**Dosing: Renal Impairment: Adult** CrCl 30 to 59 mL/minute: Maximum recommended daily dose: 1,000 mg/day. CrCl 15 to 29 mL/minute: 250 mg every 8 to 12 hours CrCl 5 to 14 mL/minute: 250 every 24 hours CrCl 1 to 4 mL/minute: 250 mg every 48 to 60 hours End-stage renal disease (on intermittent hemodialysis): The following guidelines have been used by some clinicians: Oral: 250 to 500 mg every 12 to 24 hours; moderately dialyzable (20% to 50%); give dose after dialysis session. Peritoneal dialysis: The following guidelines have been used by some clinicians: Oral: 250 to 500 mg every 12 to 24 hours. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.

Contra-indications	Hypersensitivity to cephalexin, other cephalosporins, or any component of the formulation
Adverse Drug Reactions	**Frequency not defined:** **Central nervous system:** Agitation, confusion, dizziness, fatigue, hallucination, headache **Dermatologic**: Erythema multiforme (rare), genital pruritus, skin rash, Stevens-Johnson syndrome (rare), toxic epidermal necrolysis (rare), urticaria **Gastrointestinal**: Abdominal pain, diarrhea, dyspepsia, gastritis, nausea (rare), pseudomembranous colitis, vomiting (rare) **Genitourinary:** Genital candidiasis, vaginal discharge, vaginitis **Hematologic & oncologic**: Eosinophilia, hemolytic anemia, neutropenia, thrombocytopenia **Hepatic:** Cholestatic jaundice (rare), hepatitis (transient, rare), increased serum ALT, increased serum AST **Hypersensitivity**: Anaphylaxis, angioedema, hypersensitivity reaction **Neuromuscular & skeletal:** Arthralgia, arthritis, arthropathy **Renal:** Interstitial nephritis (rare)
Monitoring Parameters	With prolonged therapy monitor renal, hepatic, and hematologic function periodically; monitor for signs of anaphylaxis during first dose
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine, ***Risk D: Consider therapy modification*** Multivitamins/Minerals (with ADEK, Folate, Iron), Sodium Picosulfate, Sucroferric Oxyhydroxide, Typhoid Vaccine, Zinc Salts ***Risk C: Monitor therapy*** Aminoglycosides, BCG Vaccine (Immunization), Lactobacillus and Estriol, Metformin, Probenecid, Vitamin K Antagonists
Pregnancy and Lactation	Pregnancy Category B Cephalexin is present in breast milk. When an antibiotic is needed, cephalexin may be used to treat mastitis in breastfeeding patients allergic to preferred agents. The decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother.Monitor infants for GI disturbances
Administration	**Administration: Oral adult, Pediatric** Administer without regard to food. If GI distress, take with food. Give around-the-clock to promote less variation in peak and trough serum levels. Oral suspension: Shake suspension well before use. Administer with an accurate measuring device; do not use a household teaspoon (overdosage may occur). **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Hypersensitivity: Allergic reactions (eg, rash, urticaria, angioedema, anaphylaxis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis [TEN]) have been reported. If an allergic reaction occurs, discontinue immediately and institute appropriate treatment. • Elevated INR: May be associated with increased INR, especially in nutritionally-deficient patients, prolonged treatment, hepatic or renal disease. • Penicillin allergy: Use with caution in patients with a history of penicillin allergy, especially IgE-mediated reactions (eg, anaphylaxis, angioedema, urticaria). • Seizure disorder: Use with caution in patients with a history of seizure disorder; high levels, particularly in the presence of renal impairment, may increase risk of seizures.

	• Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months post antibiotic treatment • A false-positive reaction may occur when testing for the presence of glucose in the urine using Benedict's solution or Fehling's solution
Storage	- Capsule: Store at 25°C; excursions permitted to 15ºC to 30ºC. - Powder for oral suspension: Store at 20°C to 25°C. - Refrigerate after reconstitution; discard after 14 days. - Tablet: Store at 20°C to 25°C. Refer to manufacturer PIL if there are specific considerations.

4. Cephradine

Generic Name	Cephradine
Dosage form/strengths	Capsule 250mg, 500mg, 1g Tablets 1g Oral suspension 125mg/5ml, 250mg/5ml, Vial 250 mg, 500mg, 1g
Route of administration	*Oral, IV, IM*
Pharmacologic action	a first-generation cephalosporin antibacterial ATC: J01DB09
Indications	Treatment of infections caused by susceptible Gram-positive and Gram-negative bacteria (including infections of the respiratory and urinary tracts, bones and joints, and of the skin and skin structure)
Dosage Regimen	**Adult:** **Oral**: 1 to 2 g daily in 2 to 4 divided doses; up to 4 g daily **IV, IM**: 2 to 4 g daily in 4 divided doses; up to 8 g daily may be given parenterally. For surgical infection prophylaxis, 1 to 2 g may be given pre-operatively by intramuscular or intravenous injection; subsequent parenteral or oral doses are given as appropriate **Pediatric:** The usual oral dose is 25 to 50 mg/kg daily in 2 or 4 divided doses; for otitis media 75 to 100 mg/kg daily in divided doses every 6 to 12 hours (to a maximum of 4 g daily) may be given. Cefradine is given parenterally in a dose of 50 to 100 mg/kg daily in 4 divided doses, increasing to 200 to 300 mg/kg daily in severe infections.
Dosage adjustment	**Dosing in renal impairment:** Cl_{cr} more than 20 mL/minute: 500 mg every 6 hours Cl_{cr} 5 to 20 mL/minute: 250 mg every 6 hours Cl_{cr} less than 5 mL/minute: 250 mg every 12 hours Patients undergoing chronic, intermittent haemodialysis may be given a 250-mg dose at the start of the session, repeated after 6 to 12 hours, then again 36 to 48 hours after the initial dose, and again at the start of the next haemodialysis if more than 30 hours have elapsed since the previous dose. Further dosage modification may be required in children with renal impairment.
Contra-indications	hypersensitivity reactions to the drug
Adverse Drug Reactions	Gastrointestinal disturbances and hypersensitivity reactions. Pseudomembranous colitis has been reported.
Monitoring Parameters	Renal functions
Drug Interactions	• The renal excretion of cefalexin, and many other cephalosporins, is delayed by probenecid. • There have been isolated reports of cefalexin decreasing the efficacy of oestrogen-containing oral contraceptives.1However, evidence does not generally support an interaction between broad-spectrum antibacterials and hormonal contraceptives • Warfarin: The concomitant use of cephradine with warfarin may result in

	increased INR and thereby increase the risk for bleeding. If concomitant use is deemed necessary, more frequent monitoring of INR is recommended especially during initiation and discontinuation of the antibiotic.
Pregnancy and Lactation	Pregnancy factor B Cephradine is excreted into human milk in small amounts. Adverse effects in the nursing infant are unlikely
Administration	IM,IV: deep intramuscular injection or intravenously by slow injection over 3 to 5 minutes or by intermittent or continuous infusion **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	Use of **Cephradine** in patients with renal dysfunction should be monitored intensively. A modified dosage schedule in patients with decreased renal function is necessary
Storage	Store at room temperature. Refer to manufacturer PIL if there are specific considerations.

b) Second Generation Cephalosporins

Watch Group

1. Cefaclor

Generic Name	Cefaclor
Dosage form/strengths	Oral suspension 125mg/5ml, 250mg/5ml, 375mg/5ml Modified Release Tablet: 375mg, 500mg, 750mg Capsule 250mg, 500mg
Route of administration	*Oral*
Pharmacologic action	Antibiotic, Cephalosporin (Second Generation) ATC: J01DC04
Indications	**Treatment of** Acute bacterial exacerbations of chronic bronchitis (extended-release tablets only) Lower respiratory tract infections (capsules and oral suspension only) including pneumonia Otitis media (capsules and oral suspension only) Pharyngitis and tonsillitis Secondary bacterial infections of acute bronchitis (extended-release tablets only) Skin and skin structure infections, uncomplicated Urinary tract infections (capsules and oral suspension only)
Dosage Regimen	**Dosing Adult:** **Note:** An ER tablet dose of 500 mg twice daily is clinically equivalent to an IR capsule dose of 250 mg 3 times daily; an ER tablet dose of 500 mg twice daily is NOT clinically equivalent to 500 mg 3 times daily of other cefaclor formulations. **Treatment of susceptible infections:** Oral: Immediate-release: 250 to 500 mg every 8 hours Extended-release: 500 mg every 12 hours **Indication-specific dosing:** **Acute bacterial exacerbations of chronic bronchitis:** Oral: Extended-release: 500 mg every 12 hours for 7 days **Secondary bacterial infection of acute bronchitis:** Oral: Extended-release: 500 mg every 12 hours for 7 days **Pneumonia, community-acquired, outpatient empiric therapy (patients with comorbidities): Oral:** Immediate release: 500 mg every 8 hours as part of an appropriate combination regimen **Streptococcal pharyngitis, group A (alternative agent for mild, nonanaphylactic penicillin allergy):** **Oral:** Immediate release: 250 mg every 8 hours for 10 days **Urinary tract infection (alternative agent):** **Note:** Use only when first-line agents cannot be used; limited evidence suggests inferior efficacy of oral beta-lactams. *Cystitis, acute uncomplicated or acute simple cystitis (infection limited to the bladder without signs/symptoms of upper tract, prostate, or systemic infection), treatment:* **Oral:** Immediate release: 250 mg every 8 hours for 5 to 7 days *Urinary tract infection, complicated (including pyelonephritis):* **Oral:** Immediate release: 500 mg 3 times daily for 10 to 14 days

	Dosing: Pediatric **General dosing, susceptible infection:** Mild to moderate infection: Infants, Children, and Adolescents: Oral, immediate release: 20 to 40 mg/kg/day divided every 8 to 12 hours. Maximum daily dose: 1,500 mg/**day**
Dosage adjustment	**Dosing: Renal Impairment: Adult** **Alternative recommendations:** Oral, immediate-release: Mild to severe impairment: No dosage adjustment necessary. use with caution. End-stage renal disease (ESRD) on intermittent hemodialysis (IHD) (administer after hemodialysis on dialysis days): Supplement with 250 to 500 mg after dialysis. Peritoneal dialysis: Administer 250 to 500 mg every 8 hours. **Dosing: Renal Impairment: Pediatric** Dosing based on usual dose of 20 to 40 mg/kg/day in divided doses every 8 to 12 hours Infants, Children, and Adolescents: Oral, immediate release: GFR ≥10 mL/minute/1.73 m^2: No dosage adjustment necessary. GFR <10 mL/minute/1.73 m^2: Administer 50% of the recommended dose. End-stage renal disease (ERD) on intermittent hemodialysis (IHD) (supplemental dose posthemodialysis needed): Administer 50% of the recommended dose. Peritoneal dialysis: Administer 50% of the recommended dose. Hemodialysis: Hemodialysis shortens half-life by 25% to 35% Moderately dialyzable (20% to 50%) **Dosing: Hepatic Impairment:** There are no dosage adjustments needed
Contra-indications	Hypersensitivity to cefaclor, any component of the formulation, or other cephalosporins
Adverse Drug Reactions	**1% to 10%:** **Dermatologic**: Rash (1% to 2%; includes erythematous rash, maculopapular rash, or morbilliform rash) **Gastrointestinal**: Diarrhea (3%) **Genitourinary**: Vaginitis (2%), vulvovaginal candidiasis (2%) **Hematologic & oncologic**: Eosinophilia (2%) **Hepatic**: Increased serum transaminases (3%)
Monitoring Parameters	Monitor renal function. Observe for signs of anaphylaxis during first dose.
Drug Interactions	***Risk X: Avoid combination*:** BCG (Intravesical), Cholera Vaccine, ***Risk D: Consider therapy modification*:** Tolvaptan, Typhoid Vaccine, Sodium Picosulfate: ***Risk C: Monitor therapy*:** Acemetacin, Aminoglycosides, BCG Vaccine (Immunization), Dichlorphenamide, Lactobacillus and Estriol, Methotrexate, Mycophenolate, Probenecid, Teriflunomide, Tetracyclines, Vitamin K Antagonists
Pregnancy and Lactation	**Pregnancy Risk Factor** B Small amounts of cefaclor are excreted in breast milk. Caution should be exercised when administering cefaclor to nursing women. Nondose-related effects could include

	modification of bowel flora.
Administration	**Administration: Oral** Administer around-the-clock to promote less variation in peak and trough serum levels. Capsules and oral suspension: Administer without regard to meals; shake oral suspension well before using. ER tablets: Do not chew, crush, or split; administer with or within 1 hour of food. Bariatric surgery: Some institutions may have specific protocols that conflict with these recommendations; refer to institutional protocols as appropriate. Switch to IR formulation. Capsule may be opened and contents sprinkled onto soft food of choice. Patient should be instructed to swallow the mixture without biting down or chewing. **Administration: Pediatric** Oral: Administer around-the-clock to promote less variation in peak and trough serum levels. Capsules and oral suspension: Administer without regard to meals; shake oral suspension well before using. Extended release tablets: Do not chew, crush, or split; administer with or within 1 hour of food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity: Anaphylactic reactions have occurred. If a serious hypersensitivity reaction occurs, discontinue and institute emergency supportive measures, including airway management and treatment (eg, epinephrine, antihistamines, and/or corticosteroids). • Penicillin allergy: Use with caution in patients with a history of penicillin allergy. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. **Geriatric Considerations** Has not been studied in the elderly. Adjust dose for renal function in elderly. Considered to be one of the drugs of choice in the outpatient treatment of community-acquired pneumonia in elderly. **Warnings: Additional Pediatric Considerations** May cause serum sickness-like reaction (estimated incidence ranges from 0.024% to 0.2% per drug course); majority of reactions have occurred in children <5 years of age with symptoms of fever, rash, erythema multiforme, and arthralgia, often occurring during the second or third exposure.
Storage	Store at 20°C to 25°C. Refrigerate suspension after reconstitution and discard after 14 days. Refer to manufacturer PIL if there are specific considerations.

2. Cefoxitin

Watch Group

Generic Name	Cefoxitin
Dosage form/strengths	Powder for Solution for Injection: 1gm, 2gm
Route of administration	IV, IM
Pharmacologic category	Antibiotic, Cephalosporin (Second Generation) ATC: J01DC01
Indications	**Bacteremia/sepsis** **Bone and joint infections** **Gynecological infections** **Lower respiratory tract infections:** pneumonia and lung abscess. **Septicemia** **Skin and skin structure infections** **Urinary tract infections**.
Dosage Regimen	**Dosing: Adult, Geriatric** Usual dosage range: IV: 1 to 2 g every 6 to 8 hours. **Pelvic inflammatory disease:** *Inpatients:* IV: 2 g every 6 hours plus doxycycline for at least 24 to 48 hours after clinical improvement, followed by oral doxycycline to complete 14 days. *Outpatients:* IM: 2 g as a single dose plus oral probenecid, followed by oral doxycycline (with or without concomitant metronidazole) for 14 days. **Surgical (perioperative) prophylaxis:** IV: 2 g within 60 minutes prior to surgical incision. Doses may be repeated in 2 hours if procedure is lengthy or if there is excessive blood loss. **Dosing: Pediatric** General dosing: Infants, Children, and Adolescents: IM, IV: Mild to moderate infection: 80 mg/kg/day divided every 6 to 8 hours; maximum daily dose: 4,000 mg/day Severe infection: 160 mg/kg/day divided every 6 hours; maximum daily dose: 12 g/day **Intra-abdominal infections, complicated: Infants, Children, and** Adolescents: IV: 160 mg/kg/day divided every 4 to 6 hours; maximum daily dose: 8 g/day. **Peritonitis, prophylaxis for patients receiving peritoneal dialysis undergoing gastrointestinal or genitourinary procedures**: Limited data available: Infants, Children, and Adolescents: IV: 30 to 40 mg/kg administered 30 to 60 minutes before procedure; maximum dose: 2,000 mg/dose. **Surgical prophylaxis: IV:** Infants ≥3 months, Children, and Adolescents: 30 to 40 mg/kg 30 to 60 minutes prior to initial incision, followed by 30 to 40 mg/kg every 6 hours for up to 24 hours; maximum single dose: 2,000 mg
Dosage adjustment	**Dosing: Renal Impairment: Adult** Loading dose: 1 to 2 g, followed by maintenance dosing according to CrCl. Maintenance dosage: CrCl 30 to 50 mL/minute: 1 to 2 g every 8 to 12 hours CrCl 10 to 29 mL/minute: 1 to 2 g every 12 to 24 hours

	CrCl 5 to 9 mL/minute: 0.5 to 1 g every 12 to 24 hours CrCl <5 mL/minute: 0.5 to 1 g every 24 to 48 hours Hemodialysis: Loading dose: 1 to 2 g after each hemodialysis; maintenance dose as noted above based on creatinine clearance **Dosing: Renal Impairment: Pediatric** adjusted dose recommendations are based on doses of 20 to 40 mg/kg/dose every 6 hours. GFR >50 mL/minute/1.73 m^2: No adjustment required. GFR 30 to 50 mL/minute/1.73 m^2: 20 to 40 mg/kg/dose every 8 hours GFR 10 to 29 mL/minute/1.73 m^2: 20 to 40 mg/kg/dose every 12 hours GFR <10 mL/minute/1.73 m^2: 20 to 40 mg/kg/dose every 24 hours Intermittent hemodialysis: Moderately dialyzable (20% to 50%): 20 to 40 mg/kg/dose every 24 hours Peritoneal dialysis (PD): 20 to 40 mg/kg/dose every 24 hours Continuous renal replacement therapy (CRRT): 20 to 40 mg/kg/dose every 8 hours **Dosing: Hepatic Impairment: Adult, Pediatric** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to cefoxitin, any component of the formulation, or other cephalosporins
Adverse Drug Reactions	**1% to 10%:** Gastrointestinal: Diarrhea
Monitoring Parameters	Monitor renal function periodically when used in combination with other nephrotoxic drugs; prothrombin time. Observe for signs and symptoms of anaphylaxis during first dose. CBC with prolonged use.
Drug Interactions	**Risk X: Avoid combination** BCG (Intravesical), Cholera Vaccine. **Risk D: *Consider therapy modification*** Sodium Picosulfate, Typhoid Vaccine **Risk C: Monitor therapy** Aminoglycosides BCG Vaccine (Immunization) Immune Checkpoint Inhibitors Lactobacillus and Estriol Probenecid Vitamin K Antagonists (eg, warfarin)
Pregnancy and Lactation	Pregnancy Category B. There are no adequate and well-controlled trials in pregnant women Cefoxitin is present in breast milk. Cephalosporins are generally considered acceptable for use in breastfeeding women. In general, antibiotics that are present in breast milk may cause nondose-related modification of bowel flora. Monitor infants for GI disturbances, such as thrush or diarrhea.
Administration	**Adult, Pediatric** **IM:** Inject deep IM into large muscle mass. **IV:** Can be administered IV push over 3 to 5 minutes or by IV intermittent infusion over 10 to 60 minutes **Preparation for Administration: Adult** IV Push: reconstitute 1 g vial with at least 10 mL, and 2 g vial with 10 or 20 mL of SWFI, bacteriostatic water for injection, NS, or D_5W. For IV infusion, solutions may be further diluted in in 50 to 1000 mL of NS, D_5NS, D_5W, LR,

	mannitol 5% or 10%, or sodium bicarbonate 5%. **Preparation for Administration: Pediatric** IV Push: Reconstitute vials with SWFI, bacteriostatic water for injection, NS, or D5W to a final concentration of 95 to180 mg/mL. Intermittent IV infusion: Further dilute to a final concentration not to exceed 40 mg/mL in NS, D5NS, D5W, LR, mannitol 5% or 10%, or sodium bicarbonate 5%. In fluid restricted patients, a concentration of 125 mg/mL using SWFI results in a maximum recommended osmolality for peripheral infusion. IM: Reconstitute vial with 1 to 2 mL of 0.5% or 1% lidocaine. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	**Concerns related to adverse effects:** • Hypersensitivity: Use with caution in patients with a history of penicillin allergy, especially IgE-mediated hypersensitivity reactions (eg, anaphylaxis, angioedema, urticaria). • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. **Disease-related concerns:** • GI disease: Use with caution in patients with a history of gastrointestinal disease, particularly colitis. • Renal impairment: Use with caution in patients with renal impairment; modify dosage in severe impairment. • Seizure disorders: Use with caution in patients with a history of seizure disorder; high levels, particularly in the presence of renal impairment, may increase risk of seizures. **Special populations:** • Children: In pediatric patients ≥3 months of age, higher doses have been associated with an increased incidence of eosinophilia and elevated AST. • Elderly: This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Elderly patients are more likely to have decreased renal function; use care in dose selection and monitor renal function. Other: • Discontinuation of therapy: For group A beta-hemolytic streptococcal infection, antimicrobial therapy should be given for at least 10 days to guard against the risk of rheumatic fever or glomerulonephritis. • Drug/Laboratory Test Interactions: High concentrations of cefoxitin (>100 micrograms/mL) may interfere with measurement of serum and urine creatinine levels. Serum samples from patients treated with cefoxitin should not be analyzed for creatinine if withdrawn within 2 hours of drug administration. A false-positive reaction for glucose in the urine may occur.
Storage	**Storage/Stability** Vials at 2°C and 25°C Avoid exposure to high temperatures. Cefoxitin tends to darken depending on storage conditions. Reconstituted solutions of 1 g per 10 mL in SWFI, bacteriostatic water for injection, N.S 0.9% injection, or D5W injection are stable for 6 hours at room temperature or for 7 days under refrigeration (<5°C). Do not freeze. Refer to manufacturer PIL if there are specific considerations.

3. Cefprozil

Watch Group

Generic Name	Cefprozil
Dosage form/strengths	Tablets 250mg, 500mg Powder for Oral Suspension 125 mg/5ml 250 mg/5ml
Route of administration	*Oral*
Pharmacologic action	Second Generation Cephalosporin Antibiotic ATC: J01DC10
Indications	**Acute bacterial exacerbation of chronic bronchitis:** Treatment of mild to moderate acute bacterial exacerbations of chronic bronchitis. **Otitis media:** Treatment of mild to moderate otitis media. **Pharyngitis/tonsillitis:** Treatment of mild to moderate pharyngitis/tonsillitis. **Skin and skin-structure infections, uncomplicated:** Treatment of mild to moderate uncomplicated skin and skin-structure infections.
Dosage Regimen	**Dosing: Adult** **Acute bacterial exacerbation of chronic bronchitis: Oral:** 500 mg every 12 hours for 10 days. **Pharyngitis/tonsillitis: Oral:** 500 mg every 24 hours for 10 days (administer for ≥10 days if due to *S. pyogenes*). **Skin and skin-structure infections, uncomplicated: Oral:** 250 or 500 mg every 12 hours, or 500 mg every 24 hours for 10 days. **Dosing: Pediatric** **General dosing, susceptible infection** Infants, Children, and Adolescents: Oral: Mild to moderate infection: 7.5 to 15 mg/kg/dose twice daily; maximum single dose: 500 mg/dose. **Bronchitis, acute bacterial exacerbation of chronic bronchitis:** Adolescents: Oral: 500 mg every 12 hours for 10 days. **Otitis media, acute:** Infants ≥6 months and Children: Oral: 15 mg/kg/dose every 12 hours for 10 days; maximum single dose: 500 mg/dose. **Note:** Cefprozil is not routinely recommended as a treatment option in the acute otitis media guidelines. **Pharyngitis/tonsillitis:** Children ≥2 years: Oral: 7.5 mg/kg/dose every 12 hours for 10 days; maximum single dose: 500 mg/dose. Adolescents: Oral: 500 mg every 24 hours for 10 days. **Rhinosinusitis: Note:** Not recommended for the empiric monotherapy of acute sinusitis due to risk of resistance Infants ≥6 months and Children: Oral: 7.5 to 15 mg/kg/dose every 12 hours for 10 days; maximum single dose: 500 mg/dose. Adolescents: Oral: 250 to 500 mg every 12 hours for 10 days. **Skin and skin structure infection, uncomplicated:** Oral: Children ≥2 years: 20 mg/kg/dose once daily for 10 days; maximum single dose: 500 mg/dose. Adolescents: 250 mg every 12 hours **or** 500 mg every 12 to 24 hours for 10 days. **Urinary tract infection:** Oral: Infants ≥2 months and Children ≤2 years: 15 mg/kg/dose twice daily for 7 to 14 days.
Dosage adjustment	**Dosing: Renal Impairment:** CrCl ≥30 mL/minute: No dosage adjustment necessary. CrCl <30 mL/minute: Reduce usual recommended dose by 50%. End-stage renal disease on hemodialysis: Give dose after dialysis on dialysis days. **Dosing: Hepatic Impairment:**

	No dosage adjustment necessary.
Contra-indications	Hypersensitivity to cefprozil, any component of the formulation, or other cephalosporins.
Adverse Drug Reactions	**1% to 10%:** Central nervous system: Dizziness (1%) Dermatologic: Diaper rash (2%), genital pruritus (2%) Gastrointestinal: Nausea (4%), diarrhea (3%), abdominal pain (1%), vomiting (1%) Genitourinary: Vaginitis Hepatic: Increased serum transaminases (2%) Infection: Superinfection
Monitoring Parameters	Monitor renal functions specially in elderly patients.
Drug Interactions	• Aminoglycoside antibiotics: Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporin antibiotics. • Probenecid: Concomitant administration of probenecid doubled the AUC for cefprozil.
Pregnancy and Lactation	**Pregnancy category B.** Small amounts of cefprozil are excreted in breast milk. Caution should be exercised when administering cefprozil to nursing women. Nondose-related effects could include modification of bowel flora.
Administration	Oral: Take with or without food. Take with food if it causes an upset stomach. Shake suspension well before use. Measure liquid doses carefully. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity: If a serious hypersensitivity reaction occurs, discontinue and institute emergency supportive measures, including airway management and treatment (eg, epinephrine, antihistamines and/or corticosteroids). • Penicillin allergy: Use with caution in patients with a history of penicillin allergy. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Gastrointestinal disease: Use with caution in patients with a history of gastrointestinal disease, particularly colitis. • Renal impairment: Use with caution in patients with renal impairment; modify dosage in severe impairment. ***Dosage form specific issues:*** • Benzyl alcohol and derivatives: Some dosage forms may contain sodium benzoate/benzoic acid; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; avoid or use dosage forms containing benzyl alcohol derivative with caution in neonates. • Phenylalanine: Some products may contain phenylalanine. • Polysorbate 80: Some dosage forms may contain polysorbate 80 (also known as Tweens). Hypersensitivity reactions, usually a delayed reaction, have been reported following exposure to pharmaceutical products containing polysorbate 80 in certain individuals.
Storage	Store tablets at room temperature in a dry place. Store suspension in a refrigerator. Throw away any part not used after 2 weeks. Refer to manufacturer PIL if there are specific considerations.

4. Cefuroxime

Watch Group

Generic Name	Cefuroxime
Dosage form/strengths	**Oral suspension** 125mg/5ml, 250mg/5ml **Tablets** 125mg, 250mg, 500mg, 1g, **Powder for injection** 250mg, 750mg, 1500mg,
Route of administration	*Oral, IV, IM*
Pharmacologic action	Antibiotic, Cephalosporin (Second Generation) ATC: J01DC02
Indications	**Bone and joint infections (injection only)** **Chronic obstructive pulmonary disease, acute exacerbation (tablets only):** Treatment of mild to moderate acute bacterial exacerbations of chronic bronchitis in adults and adolescents ≥13 years of age **Lower respiratory tract infections (injection only)** **Lyme disease (early) (tablets only):** Treatment of adults and adolescents ≥13 years of age **Otitis media, acute (tablets and oral suspension only):** Treatment of pediatric patients ≥3 months of age with acute bacterial otitis media **Pharyngitis/tonsillitis (tablets and oral suspension only):** Treatment of mild to moderate pharyngitis/tonsillitis **Septicemia (injection only)** **Sinusitis, acute bacterial (tablets and oral suspension only):** Treatment of mild to moderate acute bacterial maxillary sinusitis **Skin and skin-structure infections (impetigo) (oral suspension only):** Treatment of pediatric patients 3 months to 12 years of age. **Skin and skin-structure infections (injection; tablets [uncomplicated infections only]):** Treatment of adults and pediatric patients >3 months of age with skin and skin-structure infections **Surgical prophylaxis (injection only):** Prophylaxis of infection in patients undergoing surgical procedures that are classified as clean-contaminated or potentially contaminated procedures. **Urinary tract infections (tablets and injection only):** Treatment of adults and pediatric patients >3 months of age with urinary tract
Dosage Regimen	**Adults** **General Adult Dosage** **Oral** Tablets: 250 or 500 mg twice daily for 10 days **IV or IM:** 750–1.5 g every 8 hours for 5–10 days. **Life-threatening Infections or Those Caused by Less Susceptible Organisms** IV or IM: 1.5 g every 6 hours **Pediatric Patients** **General dosing, susceptible infection** Infants, Children, and Adolescents: **Mild to moderate infection:** Oral: 20 to 30 mg/kg/day divided twice daily; maximum dose: 500 mg/dose IM, IV: 75 to 100 mg/kg/day divided in 3 doses; maximum dose: 1,500 mg/dose **Severe infection**: IM, IV: 100 to 200 mg/kg/day divided in 3 to 4 doses; maximum dose: 1,500 mg/dose
Dosage adjustment	**Dosing: Renal Impairment: Adult** Adults with impaired renal function: 750 mg IM or IV every 12 hours in those with Cl_{cr} 10–20

	mL/minute or 750 mg IM or IV every 24 hours in those with Cl_{cr} <10 mL/minute. **Children with impaired renal function**: Adjust dosing frequency for IM or IV cefuroxime similar to those recommended for adults with renal impairment. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to cefuroxime, any component of the formulation, or other beta-lactam antibacterial drugs (eg, penicillins and cephalosporins)
Adverse Drug Reactions	**>10%:** Gastrointestinal: Diarrhea (4% to 11%, duration dependent) **Hematologic & oncologic**: Decreased hematocrit (≤10%), decreased hemoglobin (≤10%
Monitoring Parameters	Monitor renal, hepatic, and hematologic function periodically with prolonged therapy. Monitor prothrombin time in patients at risk of prolongation during cephalosporin therapy (nutritionally-deficient, prolonged treatment, renal or hepatic disease). Observe for signs and symptoms of anaphylaxis during first dose
Drug Interactions	• ***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine, Histamine H2 Receptor Antagonists, Proton Pump Inhibitors • ***Risk D: Consider therapy modification*** Antacids, Sodium Picosulfate, Typhoid Vaccine • ***Risk C: Monitor therapy*** Aminoglycosides, BCG Vaccine (Immunization), Lactobacillus and Estriol, Probenecid, Vitamin K Antagonists
Pregnancy and Lactation	**Pregnancy** Category B Beta-lactam antibiotics are generally considered compatible with breastfeeding when used in usual recommended doses; cefuroxime was not specifically included within this report. the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother.
Administration	**Administration: IM** • Prepare IM injections by reconstituting vial containing 750 mg of cefuroxime with 3 mL of sterile water for injection to provide a suspension containing approximately 220 mg/mL. • Inject deep IM into large muscle mass. **Administration: IV** • Reconstitute vials containing 750 mg or 1.5 g of cefuroxime with 8 or 16 mL of sterile water for injection, respectively, to provide solutions containing approximately 90 mg/mL. • Inject direct IV over 3 to 5 minutes. Infuse intermittent infusion over 15 to 30 minutes. **Administration: Oral** Suspension: Administer with food. Shake well before use. Tablet: May administer with or without food. administer with food to decrease GI upset; avoid crushing the tablet due to its bitter taste **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Elevated INR: May be associated with increased INR, especially in nutritionally-deficient patients, prolonged treatment, hepatic or renal disease. Hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactam drugs. Before initiating therapy, carefully investigate previous penicillin, cephalosporin, or other allergen hypersensitivity. Use caution if given to a patient with a penicillin or other beta-lactam allergy because cross sensitivity among beta-lactam antibacterial drugs has been established. If an allergic reaction occurs, discontinue and institute appropriate therapy.

	• Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment
Storage	• Injection: Store intact vials at 15°C to 30°C; protect from light. Reconstituted solution is stable for 24 hours at room temperature and 48 hours when refrigerated. IV infusion in NS or D5W solution is stable for 24 hours at room temperature, 7 days when refrigerated, or 26 weeks when frozen. After freezing, thawed solution is stable for 24 hours at room temperature or 21 days when refrigerated. • Oral suspension: Prior to reconstitution, store at 2°C to 30°C. Reconstituted suspension is stable for 10 days at 2°C to 8°C. • Tablet: Store at 15°C to 30°C • Refer to manufacturer PIL if there are specific considerations.

c) Third Generation Cephalosporins

Watch Group

1. Cefdinir

Generic Name	Cefdinir
Dosage form/strengths	Oral suspension: 125mg/5ml, 250mg/5ml Capsule 300mg,
Route of administration	*Oral*
Pharmacologic action	Antibiotic, Cephalosporin (Third Generation) ATC: J01DD15
Indications	**Chronic obstructive pulmonary disease, acute exacerbation**: Treatment of acute exacerbations of chronic bronchitis in adults and adolescents **Otitis media, acute**: Treatment of acute bacterial otitis media in pediatrics **Pneumonia, community-acquired**: Treatment of community-acquired pneumonia in adults and adolescents **Sinusitis, acute**: Treatment of acute maxillary sinusitis in adults and adolescents Skin and skin structure infections, uncomplicated: Treatment of uncomplicated skin and skin structure infections in adults, adolescents, and pediatric patients Streptococcal pharyngitis (group A): Treatment of pharyngitis/tonsillitis in adults, adolescents, and pediatric patients
Dosage Regimen	**Dosing: Adult**: The total daily dose for all infections is 600 mg. Once-daily dosing for 10 days is as effective as twice dosing. Once-daily dosing has not been studied in *pneumonia or skin infections*; therefore, should be administered twice daily in these infections. **Dosing: Pediatric** **General dosing, susceptible infection**: Mild to moderate infections: Infants, Children, and Adolescents: Oral: 14 mg/kg/day in divided doses 1 to 2 times daily; maximum daily dose: 600 mg/day
Dosage adjustment	**Dosing: Renal Impairment: Adult** CrCl ≥30 mL/minute: No dosage adjustment necessary. CrCl <30 mL/minute: Oral: 300 mg once daily ESRD requiring intermittent hemodialysis (IHD): Dialyzable: (63%): Oral: Initial dose: 300 mg (or 7 mg/kg/dose) every other day. Postdialysis, 300 mg (or 7 mg/kg/dose) should be given. Subsequent doses (300 mg or 7 mg/kg/dose) should be administered every other day. **Dosing: Renal Impairment: Pediatric** Infants ≥6 months and Children: CrCl ≥30 mL/minute/1.73 m^2: No adjustment required CrCl <30 mL/minute/1.73 m^2: 7 mg/kg/dose once daily; maximum daily dose: 300 mg/day Adolescents: CrCl ≥30 mL/minute: No adjustment required CrCl <30 mL/minute: 300 mg once daily Hemodialysis: Dialyzable (63%): Infants ≥6 months, Children, and Adolescents: Initial dose: 7 mg/kg/dose (maximum dose: 300 mg) every other day. At the conclusion of each hemodialysis session, an additional dose (7 mg/kg/dose up to 300 mg) should be given.

	Subsequent doses should be administered every other day. **Dosing: Hepatic Impairment:** No dosage adjustment necessary.
Contra-indications	Hypersensitivity to cefdinir, any component of the formulation, or other cephalosporins.
Adverse Drug Reactions	**Gastrointestinal**: Diarrhea (8% to 15%) **Central nervous system:** Headache (2%) **Dermatologic**: Skin rash (≤3%) **Genitourinary**: Vulvovaginal candidiasis (≤4%)
Monitoring Parameters	Monitor renal function. Observe for signs and symptoms of anaphylaxis during first dose.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine, ***Risk D: Consider therapy modification*** Iron Preparations, Multivitamins/Minerals (with ADEK, Folate, Iron), Sodium Picosulfate, Typhoid Vaccine ***Risk C: Monitor therapy*** Aminoglycosides, BCG Vaccine (Immunization), Lactobacillus and Estriol, Metformin, Probenecid, Vitamin K Antagonists
Pregnancy and Lactation	**Pregnancy Risk Factor:** B Cefdinir was not detectable in breast milk following a single cefdinir 600 mg dose.
Administration	**Administration: Oral** May be administered with or without food. Administer at least 2 hours before or after antacids or iron supplements. Shake suspension well before use. **Administration: Pediatric** Oral: May administer with or without food; administer with food if stomach upset occurs; administer cefdinir at least 2 hours before or after antacids or iron supplements; shake suspension well before use. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Penicillin allergy: Use with caution in patients with a history of penicillin allergy, especially IgE-mediated reactions (eg, anaphylaxis, angioedema, urticaria). • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. **Geriatric Considerations** Cefdinir has not been studied exclusively in the elderly. Patients ≥65 years of age have been included in clinical trials. No information is available on the elderly's response or tolerance. • coadministered Iron-containing products do not affect the pharmacokinetics of cefdinir but may result in the development of red-appearing, nonbloody stools
Storage	Store at 20°C to 25°C. Store reconstituted suspension at room temperature 20°C to 25°C for 10 days. Refer to manufacturer PIL if there are specific considerations.

Watch Group

2. Cefixime

Generic Name	Cefixime
Dosage form/strengths	**Oral suspension** 100mg/5ml, 200mg/5ml **Tablets** 200mg **Capsules** 200mg, 400mg
Route of administration	*Oral*
Pharmacologic category	Antibiotic, Cephalosporin (Third Generation) ATC: J01DD08
Indications	**Acute Otitis Media (AOM)** **Pharyngitis and tonsillitis** **Acute exacerbations of chronic bronchitis** **Uncomplicated cervical/urethral gonorrhea** **Uncomplicated urinary tract infections**
Dosage Regimen	**Dosing: Adult: Usual dosage range:** Oral: 400 mg daily divided every 12 to 24 hours. **Pediatric dosing; susceptible infection (mild to moderate):** Infants, Children, and Adolescents: Oral: 8 mg/kg/day divided every 12 to 24 hours; maximum daily dose: 400 mg/day • Do *not* use capsules or conventional tablets for treatment of Acute otitis media.
Dosage adjustment	**Dosing: Renal Impairment: Adult** oral suspension is recommended CrCl ≥60 mL/minute: No dosage adjustment necessary. CrCl 21 to 59 mL/minute: 260 mg once daily CrCl ≤20 mL/minute: 170-180 mg once daily Intermittent hemodialysis (not significantly removed by hemodialysis): Suspension: 260 mg once daily Adults undergoing peritoneal dialysis: tablet: 200 mg once daily oral suspension: 170-180 mg once daily **Dosing: Renal Impairment: Pediatric** Infants ≥6 months, Children, and Adolescents: Very limited data available **Dosing: Hepatic Impairment:** No dosage adjustment needed.
Contra-indications	Hypersensitivity to cefixime, any component of the formulation, or other cephalosporins or penicillins
Adverse Drug Reactions	**>10%:** Gastrointestinal: Diarrhea (16%) **2% to 10%:** Gastrointestinal: Abdominal pain, nausea, dyspepsia, flatulence, loose stools <2%: Acute renal failure, hepatitis
Monitoring Parameters	Renal function; with prolonged therapy, monitor renal and hepatic function periodically. Observe for signs and symptoms of anaphylaxis during first dose. When used as part of alternative treatment for gonococcal infection, test-of-cure 7 days after dose
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine, ***Risk D: Consider therapy modification*** Sodium Picosulfate, Typhoid Vaccine

	Risk C: Monitor therapy Aminoglycosides, BCG Vaccine (Immunization), Lactobacillus and Estriol, Probenecid, Vitamin K Antagonists
Pregnancy and Lactation	Pregnancy Category B It is not known whether cefixime is present in breast milk.
Administration	Administer without regard to meals. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Dermatologic reactions**: Severe cutaneous reactions (eg, toxic epidermal necrolysis, Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms [DRESS]) have been reported. If a reaction occurs, discontinue and institute supportive therapy. • **Hemolytic anemia**: Immune-mediated hemolytic anemia (including fatalities) have been reported. Monitor patient (including hematologic parameters and drug-induced antibody testing when clinically appropriate) during and for 2 to 3 weeks after therapy. If hemolytic anemia occurs during therapy, discontinue use. • **Hypersensitivity**: Hypersensitivity and anaphylaxis have been reported in patients receiving beta-lactam drugs. Use caution in patients with a history of hypersensitivity to cephalosporins, penicillins, or other beta-lactams. If administered to penicillin-sensitive patients, use with caution and discontinue use if allergic reaction occurs. • **Renal failure**: May cause acute renal failure including tubulointerstitial nephritis. If renal failure occurs, discontinue and initiate appropriate supportive therapy. • **Superinfection**: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. • Gastrointestinal disease: Use with caution in patients with a history of gastrointestinal disease. • **Hemolytic anemia:** Should not be administered to patients with a history of cephalosporin-associated hemolytic anemia; recurrence of hemolysis is more severe
Storage	• Capsule, chewable tablet: Store at 20°C to 25°C. • Powder for suspension: Prior to reconstitution, store at 20°C to 25°C. After reconstitution, suspension may be stored for 14 days at room temperature or under refrigeration. • Refer to manufacturer PIL if there are specific considerations.

Watch Group

3. Cefpodoxime

Generic Name	Cefpodoxime
Dosage form/strengths	Oral Suspension: 50,100 mg/5 mL Oral tablets 100, 200 mg
Route of administration	Oral
Pharmacologic category	Antibiotic, Cephalosporin (Third Generation) ATC: J01DD13
Indications	– Chronic obstructive pulmonary disease, acute exacerbation – Cystitis, acute uncomplicated – Otitis media, acute – Pneumonia, community-acquired – Rhinosinusitis, acute bacterial – Skin and soft tissue infection – Streptococcal pharyngitis, group A
Dosage Regimen	**Dosing: Adult, Geriatric** **Chronic obstructive pulmonary disease, acute exacerbation: Note:** Avoid use in patients with risk factors for *Pseudomonas* infection or poor outcomes (eg, ≥65 years of age with major comorbidities, FEV_1 <50% predicted, frequent exacerbations). Oral: 200 mg twice daily for 3 to 7 days **Otitis media, acute (alternative agent for patients with penicillin allergy that does not preclude cephalosporin use):** Oral: 200 mg twice daily. Duration is 5 to 7 days for mild to moderate infection and 10 days for severe infection. **Pneumonia, community-acquired, outpatient empiric therapy (alternative agent):** Oral: 200 mg twice daily as part of an appropriate combination regimen. Duration of therapy is for a minimum of 5 days; patients should be clinically stable with normal vital signs before therapy is discontinued. **Rhino sinusitis, acute bacterial (alternative agent for patients with penicillin allergy who are able to tolerate cephalosporins):** Oral: 200 mg twice daily with clindamycin for 5 to 7 days; some experts use as monotherapy when the risk of drug-resistant *S. pneumoniae* is low (eg, <65 years of age, low endemic resistance, few comorbidities, no recent hospitalization or antibiotic use). **Skin and soft tissue infection (alternative agent**): Oral: 400 mg every 12 hours for 7 to 14 days. **Streptococcal pharyngitis, group A (alternative agent for mild, non-anaphylactic penicillin allergy):** Oral: 100 mg twice daily for 5 to 10 days. **Urinary tract infection (alternative agent):** Note: Use only when first-line agents cannot be used; *Cystitis, acute uncomplicated or acute simple cystitis (infection limited to the bladder without signs/symptoms of upper tract, prostate, or systemic infection):* Oral: 100 mg twice daily for 5 to 7 days. **Dosing: Pediatric** **General dosing, susceptible infection: Mild to moderate infections: Infants, Children, and Adolescents:** Oral: 5 mg/kg/dose every 12 hours; usual maximum dose: 200 mg/dose; however, in patients ≥12 years, higher doses (ie, 400 mg/dose) may be required for some types of infection. **Bronchitis, bacterial exacerbation of chronic: Children ≥12 years and Adolescents:** Oral: 200 mg

	every 12 hours for 10 days **Otitis media, acute: Infants and Children 2 months to 12 years:** Oral: 5 mg/kg/dose every 12 hours; maximum dose: 200 mg/dose. AAP guidelines recommend duration based on patient age: If <2 years of age or severe symptoms (any age): 10-day course; if 2 to 5 years of age with mild to moderate symptoms: 7-day course; if ≥6 years of age with mild to moderate symptoms: 5- to 7-day course. **Pharyngitis/tonsillitis:** **Infants ≥2 months and Children <12 years:** Oral: 5 mg/kg/dose every 12 hours for 5 to 10 days; maximum dose: 100 mg/dose **Children ≥12 years and Adolescents:** Oral: 100 mg every 12 hours for 5 to 10 days **Pneumonia, acute community-acquired:** **Infants >3 months and Children <12 years:** Limited data available: Oral: 5 mg/kg/dose every 12 hours; maximum dose: 200 mg/dose **Children ≥12 years and Adolescents:** Oral: 200 mg every 12 hours for 14 days **Rhino sinusitis, acute maxillary:** **Infants ≥2 months and Children <12 years:** Oral: 5 mg/kg/dose every 12 hours for 10 days; maximum dose: 200 mg/dose; Note: IDSA recommends use in combination with clindamycin for 10 to 14 days in patients with non-type 1 penicillin allergy, after failure of initial therapy or in patients at risk for antibiotic resistance (eg, daycare attendance, age <2 years, recent hospitalization, antibiotic use within the past month). **Children ≥12 years and Adolescents:** Oral: 200 mg every 12 hours for 10 days. **Skin and skin structure: Children ≥12 years and Adolescents:** Oral: 400 mg every 12 hours for 7 to 14 days **Urinary tract infection, uncomplicated: Children ≥12 years and Adolescents:** Oral: 100 mg every 12 hours for 7 days
Dosage adjustment	**Dosing: Renal Impairment: Adult** CrCl ≥30 mL/minute: No dosage adjustment necessary. CrCl <30 mL/minute: Administer usual recommended dose every 24 hours. **Hemodialysis, intermittent (thrice weekly):** Dialyzable (~50%): 100 to 200 mg every 24 hours; when scheduled dose falls on a dialysis day, administer after hemodialysis. **Peritoneal dialysis:** Negligible clearance: 100 to 200 mg every 24 hours. **CRRT:** Recommendations are based on high-flux dialyzers and effluent flow rates of 20 to 25 mL/kg/hour (or ~1,500 to 3,000 mL/hour), unless otherwise noted. Close monitoring of response and adverse reactions due to drug accumulation is important. Dose as for CrCl ≥30 mL/minute. **PIRRT (eg, sustained, low-efficiency diafiltration):** Appropriate dosing requires consideration of adequate drug concentrations (eg, site of infection) and consideration of initial loading doses. Close monitoring of response and adverse reactions due to drug accumulation is important. Dose as for CrCl ≥30 mL/minute. **Dosing: Renal Impairment: Pediatric** Infants ≥2 months, Children, and Adolescents: CrCl ≥30 mL/minute: No dosage adjustment necessary. CrCl <30 mL/minute: Administer every 24 hours. Hemodialysis: Approximately 23% removed during a 3-hour dialysis session. Administer dose 3 times weekly after hemodialysis. **Dosing: Hepatic Impairment: Adult** Cirrhosis (with or without ascites): no dosage adjustments. **Dosing: Hepatic Impairment: Pediatric** Infants ≥ 2 months, Children, and Adolescents: No dosage adjustment necessary in patients with

	cirrhosis.
Contra-indications	Hypersensitivity to cefpodoxime, any component of the formulation, or other cephalosporins.
Adverse Drug Reactions	**>10%:** Dermatologic: Diaper rash (12%) Gastrointestinal: Diarrhea (infants and toddlers 15%) **1% to 10%:** Central nervous system: Headache (1%) Dermatologic: Skin rash (1%) Gastrointestinal: Diarrhea (7%), nausea (4%), abdominal pain (2%), vomiting (1% to 2%) Genitourinary: Vaginal infection (3%)
Monitoring Parameters	Monitor renal function. Observe for signs and symptoms of anaphylaxis during first dose.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine. **Risk D: *Consider therapy modification*** Sodium Picosulfate, LIVE Typhoid Vaccine
Pregnancy and Lactation	Pregnancy Category B. There are no adequate and well-controlled trials in pregnant women Cefpodoxime is present in breast milk. Due to the potential for serious adverse reactions in the breastfed infant, a decision be made to discontinue breastfeeding or to discontinue the drug, taking into account the importance of treatment to the mother.
Administration	**Preparation: Oral suspension:** Reconstitute powder for oral suspension with appropriate amount of water as specified on the bottle. Shake vigorously until suspended. **Administration: Oral** Administer around-the-clock to promote less variation in peak and trough serum levels. Administer tablets with food; suspension may be administered without regard to food. Shake suspension well before using. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Beta-lactam allergy: Use with caution in patients with a history of beta-lactam allergy, especially IgE-mediated reactions (e.g., anaphylaxis, angioedema, urticaria). • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months post antibiotic treatment. ***Disease-related concerns:*** • Renal impairment: Use with caution in patients with renal impairment; modify dosage in severe impairment. ***Dosage form specific issues:*** • Benzyl alcohol and derivatives: Some dosage forms may contain sodium benzoate/benzoic acid; benzoic acid (benzoate),large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates; the “gasping syndrome” consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension, and cardiovascular collapse; avoid or use dosage forms containing benzyl alcohol derivative with caution in neonates.

Storage	**Storage/Stability** Suspension: Store at 20°C to 25°C; after reconstitution, suspension may be stored in refrigerator for 14 days. Tablet: Store at 20°C to 25°C; protect from light. Refer to manufacturer PIL if there are specific considerations.

4. Cefoperazone

Watch Group

Generic Name	Cefoperazone
Dosage form/strengths	500 mg vial, 1 gm vial, 2gm
Route of administration	Parenteral IV, IM
Pharmacologic category	Third-generation cephalosporin antibacterial ATC: J01DD12
Indications	Respiratory Tract Infections Peritonitis and Other Intra-Abdominal Infections Bacterial Septicemia Infections of the Skin and Skin Structures Pelvic Inflammatory Disease, Endometritis, and Other Infections of the Female Genital Tract Urinary Tract Infections Some Enterococcal Infections
Dosage Regimen	**Adult Dosing** • The usual adult daily dose: 2 - 4 grams daily divided every 12 hours. • In severe infections: up to 6–12 grams daily divided into 2, 3 or 4 times from 1.5 to 4 grams per dose. • In case of Streptococcus pyogenes, therapy should be continued for at least 10 days.
Dosage adjustment	There are no dosage adjustments for hepatic or renal impairment. Dose of cefoperazone should not exceed 4 g daily in patients with liver disease or biliary obstruction or 1 to 2 g daily in those with both hepatic and renal impairment; if higher doses are used plasma concentrations of cefoperazone should be monitored
Contra-indications	contraindicated in patients with known hypersensitivity to the cephalosporin-class of antibacterial drugs.
Adverse Drug Reactions	**Hypersensitivity:** skin reactions, drug fever, or a change in Coombs' test has been reported. These reactions are more likely to occur in patients with a history of allergies, particularly to penicillin. **Hematology:** reversible neutropenia may occur with prolonged administration. Decreased hemoglobins or hematocrits have been reported. Transient eosinophilia has occurred. **Hepatic**: mild transient elevations of liver function enzymes have been observed in 5–10% of the patients. **Gastrointestinal** Diarrhea or loose stools has been reported in 1 in 30 patients. Most of these experiences have been mild or moderate in severity and self-limiting in nature. Nausea and vomiting have been reported rarely. Symptoms of pseudomembranous colitis can appear during or for several weeks subsequent to antibiotic therapy **Renal Function Tests:** Transient elevations of the BUN and serum creatinine have been noted. **Local Reactions** well tolerated following intramuscular administration. Occasionally, transient pain (1 in

	140) may follow intramuscular administration. In case of intravenous infusion some patients may develop phlebitis at the infusion site.
Monitoring Parameters	CBC, hepatic functions. Prothrombin time should be monitored in patients at risk of hypoprothrombinaemia and vitamin K used if necessary.
Drug Interactions	• Admixture of cefoperazone sodium with aminoglycosides is not recommended because of the potential for inactivation of either drug. • Incompatibility with other drugs including diltiazem, doxorubicin, pentamidine, perphenazine, pethidine, promethazine, and remifentanil. • A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution.
Pregnancy and Lactation	Pregnancy Category B Cefoperazone is excreted into human milk in small amounts. Adverse effects in the nursing infant are unlikely. Other cephalosporins have been classified as compatible with breast-feeding by the American Academy of Pediatrics.
Administration	**Preparation for IV** General Cefoperazone concentrations between 2 mg/mL and 50 mg/mL are recommended for intravenous administration. Compatible solutions: 0.9% Sodium Chloride, Dextrose 5% ,10% or Dextrose and Sodium Chloride Injection Preparation of Vials initially reconstitute with a minimum of 2.8 mL per gram of cefoperazone of any compatible reconstituting solution. For ease of reconstitution the use of 5 mL of compatible solution per gram vial is recommended. Intermittent Infusion should be administered over a 15–30 minutes time period. **Continuous Infusion** can be used for continuous infusion after dilution to a final concentration of between 2 and 25 mg cefoperazone per mL. **Preparation for Intramuscular Injection** Any suitable solution listed above may be used to prepare cefoperazone for intramuscular injection. When concentrations of 250 mg/mL or more are to be administered, a lidocaine solution should be used. These solutions should be prepared using a combination of Sterile Water for Injection and 2% Lidocaine Hydrochloride Injection (USP) that approximates a 0.5% Lidocaine Hydrochloride Solution. A two-step dilution process as follows is recommended: First, add the required amount of Sterile Water for Injection and agitate until powder is completely dissolved. Second, add the required amount of 2% lidocaine and mix. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Cefoperazone has the potential for promoting colonisation and superinfection with resistant organisms. Changes in bowel flora may be more marked than with cefotaxime because of the greater biliary excretion of cefoperazone; diarrhoea may occur more often. • Hypoprothrombinaemia has been reported in patients treated with cefoperazone and has rarely been associated with bleeding episodes. Prothrombin time should be monitored in patients at risk of hypoprothrombinaemia and vitamin K used if necessary. When administered by intravenous infusion some patients may develop phlebitis (1

	in 120) at the infusion site
Storage	Stored at or below 25°C and protected from light prior to reconstitution. After reconstitution, protection from light is not necessary. Refer to manufacturer PIL if there are specific considerations.

5. Cefoperazone and Sulbactam

Generic Name	Cefoperazone and Sulbactam
Dosage form/strengths	Injection, powder for reconstitution: Cefoperazone 1000 mg ; Sulbactam 500 mg
Route of administration	IV, IM
Pharmacologic category	Antibiotic, Cephalosporin ATC: J01DD62
Indications	Upper and lower respiratory tract infections Urinary tract infections Skin, soft tissue, bone and joint infections Bacterial septicemia, meningitis Intra-abdominal and soft tissue infections: peritonitis, cholecystitis, cholangitis. Gynecology infections: pelvic inflammatory disease, endometritis, gonorrhea.
Dosage Regimen	**Dosage:** **Adult** Usual dose: IM, IV: Adults: 1-2 g (cefoperazone) every 12 hours; maximum daily dose: 4 g (sulbactam). Additional administration of cefoperazone (without sulbactam) may be required in Severe Cases **Pediatric** Recommended doses: 60-120 mg/kg/day, given in equally divided doses every 6-12 hours. For serious infections: Up to 160 mg/kg/day, Max dose of sulbactam: 80 mg/kg/day
Dosage adjustment	**CrCl (mL/min)** 15-30 mL/min should receive a maximum of 1 g of sulbactam every 12 hours (maximum daily dosage of 2 g sulbactam), **CrCl (mL/min): <15** should receive a maximum of 500 mg of sulbactam every 12 hours (maximum daily dosage of 1 g sulbactam). In severe infections it may be necessary to administer additional cefoperazone Hemodialysis: dosing must be scheduled to follow a dialysis period.
Contra-indications	Hypersensitivity to cefoperazone, sulbactam, or other β-lactam antibacterial (e.g. cephalosporin, penicillin).
Adverse Drug Reactions	***Significant:*** **Vitamin K deficiency** resulting to coagulopathy, overgrowth of non-susceptible organisms (prolonged use). ***Blood and lymphatic system disorders:*** Neutropenia, leucopenia, eosinophilia, thrombocytopenia, hypo prothrombinaemia. ***Gastrointestinal disorders:*** Nausea, vomiting, diarrhea. ***General disorders and administration site conditions:*** Pyrexia, chills, infusion site phlebitis, injection site pain. ***Hepatobiliary disorders:*** Jaundice ***Investigations:*** Decreased Hb conc, hematocrit; increased AST, ALT, blood alkaline phosphatase, blood bilirubin. ***Nervous system disorders:*** Headache. ***Renal and urinary disorders:*** Hematuria, Transient elevations in BUN and serum creatinine concentrations

	Skin and subcutaneous tissue disorders: Pruritus, urticaria, Rash, skin reactions, fever ***Vascular disorders:*** Hypotension, vasculitis. **Potentially Fatal:** *Clostridium-difficile*-associated diarrhea, hypersensitivity reactions including anaphylactic and severe cutaneous adverse reactions (e.g. toxic epidermal necrolysis, Stevens-Johnson syndrome); serious hemorrhage.
Monitoring Parameters	Symptoms of overdose include blood in the urine, diarrhea, nausea, upper abdominal pain, and vomiting. Hematologic status (e.g. prothrombin time), renal, and hepatic function. Perform culture and susceptibility tests; consult local institutional recommendations before treatment initiation due to antibiotic resistance risks.
Drug Interactions	***Category: X, Avoid combination*** live cholera vaccine & typhoid vaccine, rifampin, BCG ***Category: D, consider therapy modification*** alcohol, aminoglycosides, heparin, warfarin
Pregnancy and Lactation	category B There are no adequate and well-controlled studies in pregnant women Only small quantities of cefoperazone and sulbactam are excreted in human milk. Although both drugs pass poorly into breast milk of nursing mothers, caution should be exercised when cefoperazone/sulbactam is administered to a nursing mother
Administration	**IV:** For IV infusion, each vial should be reconstituted with 5-10 ml SWFI, 0.9%NACL, 5% dextrose in water, and then diluted to 20 ml using the same diluent followed by admin over 15-60 minutes. For IV injection, each vial should be reconstituted as above and given over at least 3 minutes. **IM:** Vial should be reconstituted with 5 ml SWFI then Lidocaine HCl 2% **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	Patient with severe biliary obstruction, poor diet, malabsorption states (e.g. cystic fibrosis). Patient on prolonged IV alimentation regimens or receiving anticoagulant therapy. In patients with hepatic dysfunction and concomitant renal impairment, cefoperazone serum concentrations should be monitored and dosage adjusted as necessary and not exceed 2 g/day of cefoperazone. Sulbactam/cefoperazone has been effectively used in infants. It has not been extensively studied in premature infants or neonates.
Storage	Before reconstitution: Store below 25°C. Protect from light Reconstituted solutions are stable for 7 days at 2-8°C and for 24 hours at 8-25°C. All unused portions after the above stated time periods should be discarded. Refer to manufacturer PIL if there are specific considerations.

Watch Group

6. Cefotaxime

Generic Name	Cefotaxime
Dosage form/strengths	Vial 250 mg, 500 mg, 1 gm, 2gm
Route of administration	*IV, IM*
Pharmacological category	Antibiotic, Cephalosporin (Third Generation) ATC: J01DD01
Indications	**Treatment of:** **Bacteremia/Septicemia.** **Bone or joint infections.** **CNS infections:** (eg, meningitis, ventriculitis) **Genitourinary infections:** including urinary tract infections **Gynecologic infections:** including pelvic inflammatory disease, endometritis, and pelvic cellulitis **Intraabdominal infection** mild to moderates community-acquired infection in patients without risk factors for resistance: including peritonitis **Lower respiratory tract infections:** including pneumonia **Skin and skin structure infections** **Surgical prophylaxis**: Reduce the incidence of certain infections in patients undergoing surgical procedures (eg, abdominal or vaginal hysterectomy, GI and GU tract surgery) that may be classified as contaminated or potentially contaminated; reduce the incidence of certain postoperative infections in patients undergoing cesarean section.
Dosage Regimen	**Adults** **General Adult Dosage** **Uncomplicated Infections** **IV or IM:** 1 g every 12 hours. **Moderate to Severe Infections** **IV or IM:** 1–2 g every 8 hours. **Infections needing higher-doses:** 2 g IV every 6 to 8 hours **Life-threatening infections:** 2 g IV every 4 hours **Cesarean section: IM, IV:** 1 g IV as soon as the umbilical cord is clamped, then 1 g IV or IM at 6 and 12 hours after the first dose. **Pediatric Patients** **General Dosage** **IV or IM** 0-1 week: 50 mg/kg IV every 12 hours 1-4 weeks: 50 mg/kg IV every 8 hours 1 month-12 years: 50-180 mg/kg/day IV divided every 4-6 hours >12 years: refere to adult dose **Prescribing Limits** **Adults** Maximum 12 g daily

	Pediatric Patients Maximum 12 g daily for children weighing >50 kg. Weighing less than 50 kg: 180 mg/kg/day IV/IM is FDA-approved maximum; however, doses up to 300 mg/kg/day (Max: 12 g/day) have been used off-label for meningitis. **Neonates** 8 days and older: 150 mg/kg/day IV/IM is maximum; however, doses up to 200 mg/kg/day have been used off-label for meningitis. 0 to 7 days: 100 mg/kg/day IV/IM is maximum; however, doses up to 150 mg/kg/day have been used off-label for meningitis.
Dosage adjustment	• **Renal impairment:** **Adults:** CrCl <20 mL/minute/1.73 m2: Dose should be decreased by 50%. **Intermittent Hemodialysis Dialysis**: approximately 50% of the serum concentration of cefotaxime is removed during a standard hemodialysis session. Some clinicians recommend that 0.5 to 2 g be given as single daily doses and that a supplemental dose of cefotaxime be given after each hemodialysis session. **Peritoneal dialysis:** give 1 g IV/IM every 24 hours **Pediatrics:** CrCl 30 to 50 mL/min/1.73 m2: 35 to 70 mg/kg/dose IV/IM every 8 to 12 hours. CrCl 10 to 29 mL/min/1.73 m2: 35 to 70 mg/kg/dose IV/IM every 12 hours. CrCl less than 10 mL/min/1.73 m2: 35 to 70 mg/kg/dose IV/IM every 24 hours. **Intermittent Hemodialysis Dialysis/ Peritoneal dialysis**: the recommended dose is 35 to 70 mg/kg/dose IV/IM every 24 hours, given after hemodialysis on dialysis days. • **hepatic impairment.** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to cefotaxime, any component of the formulation, or other cephalosporins
Adverse Drug Reactions	**1% to 10%:** Dermatologic: Pruritus, skin rash Gastrointestinal: Colitis, diarrhea, nausea, vomiting Hematologic & oncologic: Eosinophilia Local (IM): Induration at injection site, inflammation at injection site, pain at injection site, tenderness at injection site Miscellaneous: Fever
Monitoring Parameters	Observe for signs and symptoms of anaphylaxis during first dose; CBC with differential (especially with long courses [>10 days]); renal function
Drug Interactions	***Risk X: Avoid combination*** BCG, Cholera Vaccine ***Risk D: Consider therapy modification*** Probenecid, Sodium Picosulfate, Typhoid Vaccine
Pregnancy and Lactation	**Pregnancy risk factor B.** Cefotaxime is present in breast milk. cephalosporins are generally considered acceptable for use in breastfeeding women. Monitor infants for GI disturbances, such as thrush or diarrhea
Administration	**Administration: IM** Inject deep IM into large muscle mass. Individual doses of 2 g may be given if the dose

	is divided and administered in different IM sites. **Administration: IV** Inject directly IV as a bolus over at least 3 to 5 minutes. Infuse intermittent infusion over 15 to 30 minutes. Rapid administration (i.e., less than 60 seconds) of cefotaxime through a central venous catheter can result in infusion-related reactions that include potentially life-threatening arrhythmias. Avoid rapid bolus intravenous administration of cefotaxime. **Preparation for Administration:** Parenteral: IM: Reconstitute powder for injection with SWFI to a final concentration between 230 to 330 mg/mL (2ml for 500mg vial, 3ml for 1 gm vial and 5ml for 2 gm vial). Shake to dissolve. IV: IV Push: Reconstitute vials with at least 10 mL SWFI to a maximum concentration of 200 mg/mL. Intermittent infusion: Reconstitute powder for injection with SWFI, resultant concentration dependent upon product. Dilute dose to a final concentration of 10 to 40 mg/mL with NS, D5W, D5NS, or LR; some centers have used concentrations up to 60 mg/mL. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Arrhythmia: in rapid (<1 minute) bolus injection via central venous catheter. • Granulocytopenia: Granulocytopenia and more rarely agranulocytosis may develop during prolonged treatment (>10 days). • Penicillin allergy: Use with caution in patients with a history of penicillin allergy, especially IgE-mediated reactions (eg, anaphylaxis, angioedema, urticaria). • Superinfection: Prolonged use • Tissue inflammation: Minimize tissue inflammation by changing infusion sites when needed. ***Disease-related concerns:*** • Colitis: Use with caution in patients with a history of colitis. • Renal impairment: Use with caution in patients with renal impairment; dosage adjustment may be required.
Storage	Store intact vials below 30°C. Protect from light. Reconstituted solution is stable for 12 to 24 hours at room temperature, 7 to 10 days when refrigerated, for 13 weeks when frozen. For IV infusion in NS or D_5W, solution is stable for 1 day at room temperature, 5 days when refrigerated. Refer to manufacturer PIL if there are specific considerations.

Watch Group

7. Ceftazidime

Generic Name	Ceftazidime
Dosage form/strengths	Vial 250 mg , 500 mg, 1 gm, 2gm
Route of administration	*IV, IM*
Pharmacologic category	Antibiotic, Cephalosporin (Third Generation) ATC: J01DD02
Indications	**Treatment of:** Bloodstream infection (gram-negative bacteremia Bone and joint infections CNS infections Empiric therapy in immunocompromised patients Gynecologic infections Intra-abdominal infections Lower respiratory tract infections Skin and soft tissue infections Urinary tract infections
Dosage Regimen	**Adults** **General Adult Dosage** Traditional intermittent infusion method: IV: 1 to 2 g every 8 hours infused over 30 minutes. For treatment of very severe life-threatening infections, especially in immunocompromised hosts: 2 g every 8 hours. Extended infusion method (off-label method): IV: 2 g every 8 hours infused over 3 to 4 hours; may give first dose over 30 minutes, especially when rapid attainment of therapeutic drug concentrations is desired (eg, sepsis). Continuous infusion method (off-label method): IV: 6 g infused over 24 hours; may give first dose of 2 g over 30 minutes, especially when rapid attainment of therapeutic drug concentrations is desired (eg, sepsis). **Pediatric Patients** **General dosing**, susceptible infection IM, IV: Infants, Children, and Adolescents: Non-Pseudomonas spp. infections: 90 to 150 mg/kg/day divided every 8 hours; maximum daily dose: 6 g/day. Pseudomonas spp. infections: Mild to moderate infections: 90 to 150 mg/kg/day divided every 8 hours; maximum daily dose: 6 g/day. Severe infections: 200 to 300 mg/kg/day divided every 8 hours; maximum daily dose: 12 g/day.
Dosage adjustment	• **Renal impairment: adults dosing** **If the usual recommended dose is 1 g every 8 hours** CrCl 31- 50 mL/minute : 1 gm /12 hr.

	Crcl 16-30 ml/min: 1gm/24hr. Crcl <= 15 ml/min: 500mg/24 hr. **If the usual recommended dose is 2 g every 8 hours** CrCl 31- 50 mL/minute : 2 gm /12 hr. Crcl 16-30 ml/min: 2gm/24hr. Crcl <= 15 ml/min: 1gm/24 hr. Hemodialysis, intermittent (thrice weekly): Dialyzable IV: 500 mg to 1 g every 24 hours; administer after hemodialysis on dialysis days. Peritoneal dialysis: IV: 1 g every 24 hours **Renal Impairment: Pediatric dosing** Infants, Children, and Adolescents: Renally adjusted dose recommendations are based on a usual dose of 25 to 50 mg/kg/dose every 8 hours: GFR 30 to 50 mL/minute/1.73 m2: 50 mg/kg/dose every 12 hours. GFR 10 to 29 mL/minute/1.73 m2: 50 mg/kg/dose every 24 hours. GFR <10 mL/minute/1.73 m2: 50 mg/kg/dose every 48 hours. Hemodialysis: Dialyzable (50% to 100%): 50 mg/kg/dose every 48 hours, give after dialysis on dialysis days. Peritoneal dialysis: 50 mg/kg/dose every 48 hours. • **Hepatic impairment adults & pediatrics.** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to ceftazidime, other cephalosporins, penicillins, other beta-lactam antibiotics, or any component of the formulation
Adverse Drug Reactions	**1% to 10%:** Dermatologic: Pruritus (<2%), skin rash (<2%) Endocrine & metabolic: Increased lactate dehydrogenase (6%), increased gamma-glutamyl transferase (5%) Gastrointestinal: Diarrhea (1%) Hematologic & oncologic: Eosinophilia (8%), positive direct Coombs test (4%; without hemolysis), thrombocythemia (2%) Hepatic: Increased serum ALT (7%), increased serum AST (6%), increased serum alkaline phosphatase (4%) Hypersensitivity: Hypersensitivity reactions (2%) Local: Inflammation at injection site (1%), injection site phlebitis (1%) Miscellaneous: Fever (<2%)
Monitoring Parameters	Monitor renal function. Observe for signs and symptoms of anaphylaxis during first dose.
Drug Interactions	**Risk X Avoid combination:** BCG, Cholera Vaccine **Risk D: Consider therapy modification** Chloramphenicol (systemic), typhoid vaccine
Pregnancy and Lactation	**Pregnancy risk factor B.** Ceftazidime is considered compatible with breastfeeding when used in usual recommended doses. Monitor infants for GI disturbances, such as thrush or diarrhea
Administration	**Administration: IM** Inject deep IM into large mass muscle. **Administration: IV** Ceftazidime can be administered IV push over 3 to 5 minutes or IV intermittent infusion over 15 to 30 minutes.

	Preparation for Administration: for adults **Parenteral:** **IM:** Using SWFI, bacteriostatic water for injection, lidocaine 0.5%, or lidocaine 1%, reconstitute the 500 mg vials with 1.5 mL or the 1 g vials with 3 mL; final concentration of ~280 mg/mL. **IV:** 500 mg vial: Reconstitute with 5.3 mL SWFI (final concentration ~100 mg/mL). 1 g or 2 g vial: Reconstitute with 10 mL SWFI. Note: After reconstitution, may dilute further with a compatible solution [eg, D_5W, NS] to administer via IV infusion **Preparation for Administration: Pediatric** **IM:** as adults **IV:** IV push: Reconstitute vial using SWFI to a concentration of 100 to 170 mg/mL. Intermittent IV infusion: Further dilute with a compatible solution (eg, D5W, NS) to a final concentration ≤40 mg/mL. In fluid-restricted patients, a concentration of 125 mg/mL using SWFI results in a maximum recommended osmolality for peripheral infusion. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Elevated INR: May be associated with increased INR, especially in nutritionally deficient patients, prolonged treatment, hepatic or renal disease. Monitor INR during treatment if patient is at risk; administer vitamin K as clinically indicated. • Hemolytic anemia: Immune-mediated hemolytic anemia, sometimes fatal, has been observed in patients receiving cephalosporins, including ceftazidime. If a patient develops anemia while on ceftazidime, discontinue treatment until the etiology is determined. • Hypersensitivity: Hypersensitivity and anaphylaxis have been reported in patients receiving beta-lactam drugs. Use caution in patients with a history of hypersensitivity to penicillins or other beta-lactams; use is contraindicated in patients with cephalosporin allergy. If severe hypersensitivity occurs, discontinue immediately and institute supportive emergency measures. • Neurotoxicity: High ceftazidime levels in patients with renal insufficiency can lead to seizures, nonconvulsive status epilepticus, encephalopathy, coma, asterixis, myoclonia, and neuromuscular excitability. Adjust dosage based on renal function. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *Clostridioides* (formerly *Clostridium*) *difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • GI disease: Use with caution in patients with a history of GI disease, especially colitis. • Renal impairment: Use with caution in patients with renal impairment; dosage adjustment recommended. • Seizure disorders: Use with caution in patients with a history of seizure disorder; high levels, particularly in the presence of renal impairment, may increase risk of seizures.
Storage	Vials: Store intact vials at 20°C to 25°C. Protect from light. Refer to manufacturer PIL if there are specific considerations.

8. Ceftazidime and Avibactam

Reserve Group

Generic Name	Ceftazidime and Avibactam
Dosage form/strengths	**Powder for injection: 2 g/0.5 g**
Route of administration	IV
Pharmacologic action	Cephalosporin Combination, Third Generation Cephalosporins ATC: J01DD52
Indications	**Intra-abdominal infections, complicated:** Treatment of complicated intra-abdominal infections (cIAI) in adult and pediatric patients ≥3 months of age, in combination with metronidazole **Pneumonia, hospital-acquired and ventilator-associated:** in adult patients **Urinary tract infections, complicated (including pyelonephritis):** Treatment of complicated urinary tract infections (cUTI) (including pyelonephritis) in adult and pediatric patients ≥3 months of age
Dosage Regimen	**Dosing: Adult** **Note:** Dosage recommendations are expressed as total grams of the ceftazidime/avibactam combination. **Intra-abdominal infections, complicated: IV:** 2.5 g every 8 hours in combination with metronidazole for 5 to 14 days **Pneumonia, hospital-acquired and ventilator-associated (HAP/VAP):** IV: 2.5 g every 8 hours for 7 to 14 days **Urinary tract infections, complicated (including pyelonephritis):** IV: 2.5 g every 8 hours for 7 to 14 days **Dosing pediatric:** **Note**: Dosage recommendations are based on the ceftazidime component. Dosing presented is based on traditional infusion method (IV infusion over 2 hours). **Intra-abdominal infections, complicated (cIAI): Note:** Use in combination with metronidazole; treat for 5 to 14 days depending upon severity and clinical response: Infants ≥3 months to <6 months: IV: 40 mg ceftazidime/kg/dose every 8 hours. Infants ≥6 months, Children, and Adolescents <18 years: IV: 50 mg ceftazidime/kg/dose every 8 hours; maximum dose: 2,000 mg ceftazidime/dose. Adolescents ≥18 years: 2,000 mg ceftazidime every 8 hours. **Urinary tract infections, complicated (cUTI) (including pyelonephritis): Note:** Treat for 7 to 14 days depending upon severity and clinical response: Infant ≥3 months to <6 months: IV: 40 mg ceftazidime/kg/dose every 8 hours. Infants ≥6 months, Children, and Adolescents <18 years: IV: 50 mg ceftazidime/kg/dose every 8 hours; maximum dose: 2,000 mg ceftazidime/dose. Adolescents ≥18 years: 2,000 mg ceftazidime every 8 hours. **Pneumonia, hospital-acquired and ventilator-associated (HAP/VAP):** Adolescents ≥18 years: IV: 2,000 mg ceftazidime every 8 hours for 7 to 14 days.
Dosage adjustment	**Dosing: Renal Impairment: Adult** Dosage recommendations are expressed as total grams of the ceftazidime/avibactam combination:

	CrCl >50 mL/minute: No dosage adjustment necessary. CrCl 31 to 50 mL/minute: 1.25 g (1 g/0.25 g) every 8 hours CrCl 16 to 30 mL/minute: 0.94 g (0.75 g/0.1875 g) every 12 hours CrCl 6 to 15 mL/minute: 0.94 g (0.75 g/0.1875 g) every 24 hours CrCl ≤5 mL/minute: 0.94 g (0.75 g/0.1875 g) every 48 hours **Hemodialysis, intermittent (thrice weekly):** Dialyzable (~55%): 0.94 g every 24 to 48 hours depending on patient's residual kidney function; when scheduled dose falls on a dialysis day, administer after hemodialysis**.** **Dosing: Hepatic Impairment: Adult:** No dosage adjustment necessary. **Dosing: Renal Impairment: Pediatric** **Infants ≥3 months and Children <2 years**: insufficient data to provide any recommendations for use in patients with eGFR <50 mL/minute/1.73 m^2; use with caution. **Children ≥2 years and Adolescents <18 years:** IV: ○ eGFR >50 mL/minute/1.73 m^2: No dosage adjustment necessary. ○ eGFR 31 to 50 mL/minute/1.73 m^2: 25 mg ceftazidime/kg/dose every 8 hours; maximum dose: 1,000 mg ceftazidime/dose. ○ eGFR 16 to 30 mL/minute/1.73 m^2: 19 mg ceftazidime/kg/dose every 12 hours; maximum dose: 750 mg ceftazidime/dose. ○ eGFR 6 to 15 mL/minute/1.73 m^2: 19 mg ceftazidime/kg/dose every 24 hours; maximum dose: 750 mg ceftazidime/dose. ○ eGFR ≤5 mL/minute/1.73 m^2: 19 mg ceftazidime/kg/dose every 48 hours; maximum dose: 750 mg ceftazidime/dose. End-stage renal disease (ESRD) on intermittent hemodialysis (IHD): Administer after hemodialysis on dialysis days; base dose upon patient's estimated renal function **Adolescents ≥18 years**: IV: CrCl >50 mL/minute: No dosage adjustment necessary. CrCl 31 to 50 mL/minute: 1,000 mg ceftazidime every 8 hours. CrCl 16 to 30 mL/minute: 750 mg ceftazidime every 12 hours. CrCl 6 to 15 mL/minute: 750 mg ceftazidime every 24 hours. CrCl ≤5 mL/minute: 750 mg ceftazidime every 48 hours. End-stage renal disease (ESRD) on intermittent hemodialysis (IHD): Administer after hemodialysis on dialysis days; base dose upon patient's estimated renal function **Dosing: Hepatic Impairment: Pediatric** Infants ≥3 months, Children, and Adolescents: No dosage adjustment necessary.
Contra-indications	Known serious hypersensitivity to ceftazidime, avibactam, other cephalosporins, or any component of the formulation
Adverse Drug Reactions	**>10%:** Hematologic & oncologic: Positive direct coombs test (3% to 21%) **1% to 10%:** Dermatologic: Injection site phlebitis (children and adolescents: >3%; adults: <1%), skin rash (children and adolescents: >3%; adults: <1%), pruritus (2%) Gastrointestinal: Vomiting (>3%), diarrhea (≥3%), nausea (3%), constipation (2%), upper abdominal pain (1%)
Monitoring Parameters	Monitor for signs of anaphylaxis during first dose. Monitor renal function at baseline in all patients, and at least daily in patients with changing

	renal function. Observe for seizures or other neurologic activity, especially in patients with renal impairment.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine Probenecid ***Risk D: Consider therapy modification*** Chloramphenicol (Systemic) Sodium Picosulfate Tolvaptan Typhoid Vaccine
Pregnancy and Lactation	**Pregnancy Category** B. Ceftazidime is excreted in breast milk. It is not known if avibactam is excreted in breast milk. The decision to continue or discontinue breast-feeding during therapy should take into account the risk of infant exposure, the benefits of breast-feeding to the infant, and benefits of treatment to the mother.
Administration	**Administration: IV** Administer by intermittent IV infusion over 2 hours. **Preparation for Administration:** Reconstitute 2.5 g vial with 10 mL of NS, D5W, SWFI, LR, or other compatible solution; mix gently; resultant concentration: Ceftazidime ~167 mg/mL and avibactam ~42 mg/mL. Withdraw volume for desired dose and further dilute in a compatible IV solution to achieve a final ceftazidime concentration of 8 to 40 mg/mL and an avibactam concentration of 2 to 10 mg/mL; mix gently. Solution ranges in color from clear to light yellow. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	**Concerns related to adverse effects:** • Hypersensitivity reactions • Neurotoxicity: Severe neurological reactions have been reported with ceftazidime, including asterixis, coma, encephalopathy, myoclonus, neuromuscular excitability, seizures, and nonconvulsive status epilepticus. Risk may be increased in the presence of renal impairment; ensure dose adjusted for renal function. Discontinue therapy if patient develops neurotoxicity. • Superinfection: Prolonged use ***Disease-related concerns:*** • Renal impairment: Monitor renal function at baseline and at least daily in adult and pediatric patients with changing renal function. Adjust the dose accordingly.
Storage	• Vials: Store intact vials at 25°C (15-30°C). Protect from light. • After reconstitution, contents of the vial should be transferred within 30 minutes to an infusion bag for further dilution. • Admixed solutions in NS, D5W, LR, are stable up to 12 hours at room temperature and 24 hours at 2°C to 8°C. Use solutions previously stored at 2°C to 8°C within 12 hours of subsequent storage at room temperature. • Refer to manufacturer PIL if there are specific considerations.

9. Ceftriaxone

Watch Group

Generic Name	Ceftriaxone
Dosage form/strengths	Vial 250mg, 500 mg, 1 gm, 2gm
Route of administration	*IM, IV*
Pharmacologic category	Antibiotic, Cephalosporin (Third Generation) ATC: J01DD04
Indications	**Blood stream infection** **Bone and joint infections (osteomyelitis and/or discitis, prosthetic joint infection, septic arthritis)** **Gonococcal infection, uncomplicated (cervical/urethral, rectal, and pharyngeal)** **Intra-abdominal infection, community-acquired (mild to moderate infection in low-risk patients)** **Lower respiratory tract infections (pneumonia, community-acquired)** **Meningitis, bacterial** **Otitis media, acute** **Pelvic inflammatory disease (mild to moderate):** Caused by *N. gonorrhoeae*. Ceftriaxone, like other cephalosporins, has no activity against *Chlamydia trachomatis* **Skin and soft tissue infections** **Urinary tract infection, complicated (including pyelonephritis)** **Surgical prophylaxis, colorectal:** To reduce the incidence of postoperative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated.
Dosage Regimen	**Adults Dosing** **General Adult Dosage** **IV or IM** 1–2 g once or devided twice daily. **Meningitis and Other CNS Infections** IV 2 g every 12 hours. **Pediatric Dosing:** Infants, Children, and Adolescents: IM, IV: **Mild to moderate infection:** 50 to 75 mg/kg/dose once daily; maximum daily dose: 1,000 mg/day. Higher doses are recommended in certain infections (eg, endocarditis, meningitis) **Severe infection (eg, meningitis, penicillin-resistant pneumococcal pneumonia):** 100 mg/kg/day divided every 12 to 24 hours; maximum daily dose: 4,000 mg/day **Premature and Term Neonates:** 50 mg/kg/dose IV or IM every 24 hours **Prescribing Limits** **Adults** Maximum 4 g daily **Pediatric Patients** Endocarditis or meningitis: Maximum 4 g daily.

	Most other infections: Maximum 2 g daily.
Dosage adjustment	No dosage adjustments for renal or hepatic impairment. however, in patients with concurrent renal and hepatic impairment, maximum daily dose should not exceed 2 g.
Contra-indications	Hypersensitivity to ceftriaxone, any component of the formulation, or other cephalosporins; concomitant use with intravenous calcium-containing solutions/products in neonates (≤28 days); IV use of ceftriaxone solutions containing lidocaine do not use in hyperbilirubinemic neonates, particularly those who are premature since ceftriaxone is reported to displace bilirubin from albumin binding sites
Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** • Hypersensitivity: Serious and sometimes fatal hypersensitivity has been reported. Hypersensitivity reactions (immediate and delayed) range from maculopapular skin rash to rare cases of anaphylaxis and anaphylactic shock. Severe cutaneous adverse reactions (SCARs), including acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) have been reported. Urticaria and serum sickness-like reaction have also occurred. Mechanism: Non dose-related; immunologic. Immediate hypersensitivity reactions (eg, anaphylaxis, urticaria) are IgE-mediated. Delayed hypersensitivity reactions, including maculopapular rash and SCARs, are T-cell-mediated. Onset: Immediate hypersensitivity reactions: rapid; occur within 1 hour of administration but may occur up to 6 hours after exposure. Delayed hypersensitivity reactions: Maculopapular reactions: intermediate; occur 7 to 10 days after initiation. Other reactions (including SCARs): varied; occur after 7 to 14 days up to 3 months. Risk factors: Cross-reactivity between penicillins and cephalosporins and among cephalosporins is mostly related to side chain similarity. A meta-analysis showed negligible cross-reactivity between penicillins and third-generation cephalosporins, such as ceftriaxone Assessment of allergy: Unlike penicillin skin testing, cephalosporin skin testing has several limitations. Specific skin testing of cephalosporins has not been standardized, but some centers use this type of testing in the evaluation of cephalosporin allergy. If skin tests are negative, intradermal testing may be performed • Ceftriaxone-calcium precipitation Ceftriaxone may exhibit incompatibility with calcium, causing precipitation. Fatal lung and kidney damage associated with calcium-ceftriaxone precipitates has been observed in premature and term neonates. However, ceftriaxone and calcium-containing solutions may be administered sequentially of one another for use in patients **other than neonates** if infusion lines are thoroughly flushed (with a compatible fluid) between infusions • Clostridioides difficile infection • Immune hemolytic anemia • Kernicterus **>10%:** Dermatologic: Skin tightness Local: Induration at injection site, warm sensation at injection site **1% to 10%:** Dermatologic: Skin rash Gastrointestinal: Diarrhea

	Genitourinary: Casts in urine, vaginitis Hematologic & oncologic: Eosinophilia, leukopenia, thrombocythemia Hepatic: Increased serum transaminases Local: Pain at injection site, tenderness at injection site Renal: Increased blood urea nitrogen
Monitoring Parameters	Prothrombin time/INR. Observe for signs and symptoms of anaphylaxis
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Calcium Salts (Intravenous) Ringer's Injection (Lactated) Sodium Picosulfate, Typhoid Vaccine
Pregnancy and Lactation	Ceftriaxone is considered compatible with pregnancy and breastfeeding when used in usual recommended doses. Monitor infants for GI disturbances
Administration	**Administration: IM** Inject deep IM into large muscle mass; a concentration of 250 mg/mL or 350 mg/mL is recommended; can be diluted with D_5W, NS, SWFI or 1% lidocaine for IM administration only. **Administration: IV** Do not coadminister with calcium-containing solutions. Infuse as an intermittent infusion over 30 minutes. IV push administration over 1 to 4 minutes has been reported (concentration: 100 mg/mL), primarily in patients outside the hospital setting, although a 2 g dose administered IV push over 5 minutes resulted in tachycardia, restlessness, diaphoresis, and palpitations in one patient **Administration: Pediatric** **Parenteral:** Do not coadminister with calcium-containing solutions. **IM:** Administer IM injections deep into a large muscle mass **Intermittent IV infusion:** **Neonates:** Administer over 60 minutes to decrease risk of bilirubin encephalopathy **Infants, Children, and Adolescents:** Administer over 30 minutes; shorter infusion times (15 minutes) have been reported **IV Push:** Administration over 2 to 4 minutes has been reported in pediatric patients >11 years and adults primarily in the outpatient setting and over 5 minutes in pediatric patients ages newborn to 15 years with meningitis. Rapid IVP injection over 5 minutes of a 2,000 mg dose resulted in tachycardia, restlessness, diaphoresis, and palpitations in an adult patient. IV push administration in young infants may also have been a contributing factor in risk of cardiopulmonary events occurring from interactions between ceftriaxone and calcium. **Preparation of IV infusion:** Reconstitute powder with appropriate IV diluent (including SWFI, D_5W, $D_{10}W$, NS) to create an initial solution of ~100 mg/mL. Recommended volume to add: 250 mg vial: 2.4 mL 500 mg vial: 4.8 mL 1 g vial: 9.6 mL 2 g vial: 19.2 mL **Note:** After reconstitution of powder, further dilution into a volume of compatible

	solution (eg, 50-100 mL of D_5W or NS) is recommended or to a final concentration of 10 to 40 mg/mL for pediatrics **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Elevated INR: rarely occured especially in nutritionally-deficient patients, prolonged treatment, hepatic or renal disease. • Hemolytic anemia: Severe cases (including some fatalities) have been reported. • Pancreatitis • Superinfection: Prolonged use. ***Disease-related concerns:*** • Gallbladder pseudolithiasis: Abnormal gallbladder sonograms have been reported, possibly due to ceftriaxone-calcium precipitates; probability is greatest in pediatric patients. disontinue • Renal/hepatic impairment (concurrent): Use with caution; dosage should not exceed 2 g/day without close clinical monitoring ***Special populations:*** • Neonates: Use extreme caution in neonates due to risk of hyperbilirubinemia, particularly in premature infants (contraindicated in hyperbilirubinemic neonates and neonates <41 weeks postmenstrual age).
Storage	**Powder for injection:** store at ≤25°C. Protect from light. **Stability of reconstituted solutions:** ○ 10 to 100 mg/mL: Reconstituted in D_5W, NS, or SWFI: Stable for 2 days at room temperature of 25°C or for 10 days when refrigerated at 4°C. Do not refreeze. ○ Reconstituted in lidocaine 1% solution or bacteriostatic water: Stable for 1 day at room temperature of 25°C or for 10 days when refrigerated at 4°C. ○ 250 to 350 mg/mL: Reconstituted in D_5W, NS, lidocaine 1% solution, bacteriostatic water, or SWFI: Stable for 1 day at room temperature of 25°C or for 3 days when refrigerated at 4°C ○ Refer to manufacturer PIL if there are specific considerations.

Watch Group

d) Fourth Generation Cephalosporins

1. Cefepime

Generic Name	Cefepime
Dosage form/strengths	Vial 500mg, 1g, 2g
Route of administration	*Parentral (IM, IV)*
Pharmacologic action	Antibiotic, Cephalosporin (Fourth Generation) ATC: J01DE01
Indications	**Intra-abdominal infection:** Treatment, in combination with metronidazole, of complicated intra-abdominal infections **Neutropenic fever:** Empiric treatment of febrile neutropenic patients. **Pneumonia (moderate to severe):** Treatment of moderate to severe pneumonia **Skin and soft tissue infection:** Treatment of moderate to severe skin and soft tissue infections **Urinary tract infection, including pyelonephritis:** Treatment of urinary tract infections, including pyelonephritis including cases associated with concurrent bacteremia with these microorganisms.
Dosage Regimen	**Dosing: Adult** **Usual dosage range:** *Traditional intermittent infusion method (over 30 minutes):* IV: 1 to 2 g every 8 to 12 hours. For coverage of serious *Pseudomonas aeruginosa* infections: 2 g every 8 hours for 7 to 10 days or until resolution of neutropenia. **Dosing: Pediatric (2 months up to 16 years)** **General dosing, susceptible infection:** *Traditional intermittent-infusion method*: • Non-*Pseudomonas* spp. infections: IM, IV: 50 mg/kg/dose every 12 hours; maximum dose: 2,000 mg/dose (for uncomplicated and complicated urinary tract infections, uncomplicated skin and skin structure infections, and pneumonia) • *Pseudomonas* spp. infections (suspected or proven): IM, IV: 50 mg/kg/dose every 8 hours; maximum dose: 2,000 mg/dose (For moderate to severe pneumonia due to *P. aeruginosa* and for febrile neutropenic patients).
Dosage adjustment	**Dosing: Renal Impairment: Adult**

Creatinine Clearance (mL/min)	Recommended Maintenance Schedule		
Greater than 60	1 g /12 hours	2 g /12 hours	2 g /8 hours
30 to 60	1 g /24 hours	2 g /24 hours	2 g /12 hours
11 to 29	500 mg /24 hours	1 g /24 hours	2 g /24 hours

Less than 11	250 mg /24 hours	500 mg /24 hours	1 g /24 hours
Continuous Ambulatory Peritoneal Dialysis (CAPD)	1 g /48 hours	2 g /48 hours	2 g /48 hours
Hemodialysis*	1 g on day 1, then 500 mg / 24 hours thereafter		1 g /24 hours

Cefepime for injection should be administered at the same time each day and following the completion of hemodialysis on hemodialysis days

Dosing: Renal Impairment: pediatric

Changes in the dosing regimen proportional to those in adults are recommended for pediatric patients.

Dosing: Hepatic Impairment:

No dosage adjustment necessary.

Contra-indications

Hypersensitivity to cefepime, other cephalosporins, penicillins, other beta-lactam antibiotics, or any component of the formulation

Adverse Drug Reactions

Hematologic & oncologic: Positive direct Coombs test (without hemolysis; 16%)
Endocrine & metabolic: Hypophosphatemia (3%)

Monitoring Parameters

Monitor renal function. Observe for signs and symptoms of anaphylaxis during first dose.

Drug Interactions

Risk X: Avoid combination
BCG (Intravesical), Cholera Vaccine,
Risk D: Consider therapy modification
Sodium Picosulfate, Typhoid Vaccine
Risk C: Monitor therapy
Aminoglycosides, BCG Vaccine (Immunization), Lactobacillus and Estriol, Probenecid, Vitamin K Antagonists

Pregnancy and Lactation

Pregnancy Category B
Cefepime is present in breast milk
Breastfeeding may continue when otherwise appropriate, however discontinuing the antibiotic or changing to an alternate maternal therapy may be needed

Administration

Administration: IM
Inject deep IM into large muscle mass.
Administration: IV
Administer as an intermittent infusion over 30 minutes
Preparation for Administration: Adult
IV: Reconstitute 500 mg vial with 5 mL and 1 or 2 g vial with 10 mL of a compatible diluent (resulting concentration of 100 mg/mL for 500 mg and 1 g vial and 160 mg/mL for 2 g vial) and further dilute in a compatible IV infusion fluid.
IM: Reconstitute 500 mg or 1 g vial with 1.3 mL or 2.4 mL, respectively, of SWFI, NS, D5W, lidocaine 0.5% or 1%, or bacteriostatic water for injection; resulting concentration is 280 mg/mL.
Preparation for Administration: Pediatric

	Parenteral: IV: Reconstitute 500 mg vial with 5 mL and 1 or 2 g vial with 10 mL of a compatible diluent (resulting concentration of 100 mg/mL for 500 mg and 1 g vial and 160 mg/mL for 2 g vial); further dilute in D5W, NS, D10W, D5NS, or D5LR; final concentration should not exceed 40 mg/mL. IM: Reconstitute 500 mg or 1 g vial with 1.3 mL or 2.4 mL, respectively, of SWFI, NS, D5W, lidocaine 0.5% or 1%, or bacteriostatic water for injection to a final concentration of 280 mg/mL **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Elevated INR: May be associated with increased INR, especially in nutritionally-deficient patients, prolonged treatment, hepatic or renal disease. • Hypersensitivity: May occur; use caution in patients with a history of penicillin sensitivity; cross-hypersensitivity may occur. If a hypersensitivity reaction occurs, discontinue therapy and institute supportive measures. • Neurotoxicity: Severe neurological reactions (some fatal) have been reported, including encephalopathy, aphasia, myoclonus, seizures, and nonconvulsive status epilepticus. Risk may be increased in the presence of renal impairment; ensure dose adjusted for renal function and discontinue therapy if patient develops neurotoxicity; effects are often reversible upon discontinuation of cefepime. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. • Elderly: Serious adverse reactions have occurred in elderly patients with renal insufficiency given unadjusted doses of cefepime, including life-threatening or fatal occurrences of encephalopathy, myoclonus, and seizures. • The administration of Cefepime may result in a false-positive reaction for glucose in the urine with certain methods. It is recommended that glucose tests based on enzymatic glucose oxidase reactions be used.
Storage	• Vials: Store intact vials at 20°C to 25°C. Protect from light. • After reconstitution, stable in NS and D5W for 24 hours at 20°C to 25°C and 7 days at 2°C to 8°C. • Refer to manufacturer PIL if there are specific considerations.

e) Fifth Generation Cephalosporins

Reserve Group

1. Ceftaroline fosamil

Generic Name	Ceftaroline fosamil
Dosage form/strengths	Powder for Reconstitution for I.V. infusion: 400mg, 600mg
Route of administration	IV
Pharmacologic category	Antibiotic, Cephalosporin (Fifth Generation) ATC: JO1DI02
Indications	effective in treating complicated skin and soft tissue infections and community-acquired pneumonia and its side effects in both adults and children. It had shown activity against certain bacteria, such as MRSA, against which other beta-lactam antibiotics do not work
Dosage Regimen	**Dosing: Adult** **Note:** Reserve for patients with or at risk for methicillin-resistant *S. aureus* infection who cannot receive preferred agents **Pneumonia:** ***Community-acquired pneumonia (alternative agent):*** Inpatients without risk factors for *Pseudomonas aeruginosa*: **IV:** 600 mg every 12 hours as part of an appropriate combination regimen. Total duration (including oral step-down therapy) is a minimum of 7 days for methicillin-resistant *S. aureus* (MRSA) infection; patients should be clinically stable with normal vital signs before therapy is discontinued. **Note:** Switch to a narrower beta-lactam if MRSA is not isolated **Skin and soft tissue infection (alternative agent):** **IV:** 600 mg every 12 hours. Total duration of therapy is ≥5 days (including oral step-down therapy); may extend up to 14 days depending on severity and clinical response **Dosing: pediatric:** **Pneumonia, community acquired:** Treatment duration is dependent on severity of infection and clinical response. Infants ≥2 months and Children <2 years: IV: 8 mg/kg/dose every 8 hours for 5 to 7 days. Children ≥2 years and Adolescents <18 years: ≤33 kg: IV: 12 mg/kg/dose every 8 hours for 5 to 7 days. >33 kg: IV: 400 mg every 8 hours **or** 600 mg every 12 hours for 5 to 7 days. Adolescents ≥18 years: 600 mg every 12 hours for 5 to 7 days. **Skin and skin structure infection:** Treatment duration is variable (5 to 14 days); dependent on severity of infection and clinical response. Infants ≥2 months and Children <2 years: IV: 8 mg/kg/dose every 8 hours. Children ≥2 years and Adolescents <18 years: ≤33 kg: IV: 12 mg/kg/dose every 8 hours. >33 kg: IV: 400 mg every 8 hours **or** 600 mg every 12 hours. Adolescents ≥18 years: IV: 600 mg every 12 hours.
Dosage adjustment	**Dosing: Altered Kidney Function: Adult**

CrCl	Modification If the usual recommended dose is 600 mg IV every 12 hours
>50 mL/minute	No dosage adjustment necessary
>30 to ≤50 mL/minute	400 mg every 12 hours

≥15 to ≤30 mL/minute	300 mg every 12 hours
<15 mL/minute	200 mg every 12 hours
Hemodialysis, intermittent (thrice weekly) or Peritoneal dialysis	200 mg every 12 hours

Dosing: Hepatic Impairment: Adult
There are no dosage adjustments needed

Dosing: Altered Kidney Function: Pediatric
Infants, Children, and Adolescents <18 years: **Note:** Renal function estimated using the Schwartz equation.
CrCl >50 mL/minute/1.73 m^2: No adjustment necessary
CrCl ≤50 mL/minute/1.73 m^2: data is insufficient; use with caution, dosage adjustment may be necessary
Dosing: Hepatic Impairment: Pediatric
There are no dosage adjustments needed.

Contra-indications

Known serious hypersensitivity to ceftaroline, other members of the cephalosporin class, or any component of the formulation

Adverse Drug Reactions

>10%: Hematologic & oncologic: Positive direct Coombs test (10% to 18%; no evidence of hemolysis)
1% to 10%:
Cardiovascular: Bradycardia (adults: <2%), palpitations (adults: <2%), phlebitis (adults: 2%)
Dermatologic: Pruritus (infants, children, and adolescents: <3%), skin rash (3% to 7%), urticaria (adults: <2%)
Endocrine & metabolic: Hyperglycemia (adults: <2%), hyperkalemia (adults: <2%), hypokalemia (adults: 2%)
Gastrointestinal: Abdominal pain (adults: <2%), *Clostridioides difficile* colitis (adults: <2%), constipation (adults: 2%), diarrhea (5% to 8%), nausea (3% to 4%), vomiting (2% to 5%)
Hematologic & oncologic: Anemia (adults: <2%), eosinophilia (adults: <2%), neutropenia (adults: <2%; risk may be increased with high doses and prolonged use [>14 days]) (Sullivan 2019; Varada 2015), thrombocytopenia (adults: <2%)
Hepatic: Hepatitis (adults: <2%), increased serum alanine aminotransferase (infants, children, and adolescents: <3%), increased serum aspartate aminotransferase (infants, children, and adolescents: <3%), increased serum transaminases (adults: 2%)
Hypersensitivity: Anaphylaxis (adults: <2%), hypersensitivity reaction (adults: <2%)
Nervous system: Dizziness (adults: <2%), headache (infants, children, and adolescents: <3%), seizure (adults: <2%)
Renal: Renal failure syndrome (adults: <2%)
Miscellaneous: Fever (≤3%)

Monitoring Parameters

CBC (baseline and at least weekly); specimen for culture and susceptibility prior to the first dose; renal function; signs or symptoms of anaphylaxis during first dose and for neurotoxicity throughout therapy.

Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Sodium PicosulfateTyphoid Vaccine
Pregnancy and Lactation	**pregnancy category** B Adverse events have been observed in some animal reproduction studies. should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus It is not known if ceftaroline fosamil is excreted in breast milk. Caution be exercised when administering ceftaroline fosamil to nursing women.
Administration	**Administration: IV** Administer by slow IV infusion over 5 to 60 minutes **Preparation for Administration:** IV: Reconstitute 400 mg or 600 mg vial with 20 mL SWFI, NS, D5W, or LR; mix gently and ensure contents dissolve completely; resultant concentration is 20 mg/mL (400 mg vial) or 30 mg/mL (600 mg vial). Reconstituted solution should be further diluted for IV administration in a compatible solution to a final concentration not to exceed 12 mg/mL. Use of the same solution as used for reconstitution is suggested with the exception of SWFI; if SWFI was used for reconstitution, then appropriate infusion solutions include NS, $^{1}/_{2}$NS, D_5W, $D_{2.5}W$, or LR. Color of infusion solutions ranges from clear and light to dark yellow depending on concentration and storage conditions; potency is not affected. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hemolytic anemia: Seroconversion from a negative to a positive direct Coombs' test has been reported. Hemolytic anemia was not reported in clinical studies; however, if anemia develops during or after treatment, consider drug-induced hemolytic anemia. Diagnostic tests should include a direct Coombs' test. If hemolytic anemia is suspected, discontinue the drug and institute supportive care as clinically indicated. • Hypersensitivity: Serious hypersensitivity (anaphylactic) and skin reactions have occurred with ceftaroline. Use with caution in patients with a history of penicillin, cephalosporin, or carbapenem allergy. Maintain clinical supervision if given to penicillin or beta-lactam allergic patients; cross sensitivity among beta-lactam antibacterial agents has been reported. If a serious reaction occurs, discontinue the drug and institute supportive measures as clinically indicated. • Neurotoxicity: Neurological reactions have been reported, including encephalopathy and seizures. Risk may be increased in the presence of renal impairment; ensure dose adjusted for renal function, and discontinue therapy if patient develops neurotoxicity; effects are often reversible upon discontinuation of therapy. • Neutropenia: Neutropenia and agranulocytosis have been reported; risk may be increased with high doses and prolonged therapy (>14 days), patients with kidney dysfunction, and patients on concurrent antibiotics associated with neutropenia. Monitor CBC at baseline and at least weekly; limit duration of therapy when possible. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis (including fatalities); CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Renal impairment: Use with caution in patients with renal impairment (CrCl ≤50 mL/minute); dosage adjustments recommended. • Seizure disorders: Use with caution in patients with a history of seizure disorder; high levels, particularly in the presence of renal impairment, may increase risk of seizures.

Storage	Store unused vials at 25°C; excursions permitted between 15°C and 30°C. Diluted solutions in D2.5W, $^{1}/_{2}$NS, D5W, LR, or NS should be used within 6 hours when stored at room temperature or within 24 hours if refrigerated at 2°C to 8°C. Refer to manufacturer PIL if there are specific considerations.

2. Ceftolozane and Tazobactam

Reserve Group

Generic Name	Ceftolozane and Tazobactam
Dosage form/strengths	powder for solution Tazobactam 0.5 gm; Ceftolozane 1 gm
Route of administration	IV
Pharmacologic category	Cephalosporin's Combination ATC: J01DI54
Indications	**** Not recommended for routine empiric use.** Reserve use for patients with or at risk for certain multidrug-resistant gram-negative organisms (e.g., extensively drug-resistant P. aeruginosa) with limited treatment options **1-Intra-abdominal infection:** complicated intra-abdominal infection in patients ≥18 years of age, in combination with metronidazole **2-Pneumonia, hospital-acquired or ventilator-associated:** in patients ≥18 years of age. **3-Urinary tract infection, complicated (pyelonephritis or urinary tract infection with systemic signs/symptoms):** in patients ≥18 years of age
Dosage Regimen	**Dosing: Adult, Geriatric** **1-Intra-abdominal infection:** IV:1.5 to 3 g every 8 hours in combination with metronidazole for 4 to 14 days. **2-Pneumonia, hospital-acquired or ventilator-associated:** IV: 3 g every 8 hours; treatment is typically given for 7 days. **3-Urinary tract infection, complicated (pyelonephritis or urinary tract infection with systemic signs/symptoms):** IV: 1.5 g every 8 hours. Switch to an appropriate oral regimen once symptoms improve, for 5 to 14 days and depends on clinical response. **Dosing: Pediatric <18 years:** Safety and efficacy not established
Dosage adjustment	**Dosing: Renal Impairment: Adult**

CrCl (mL/minute)	If the usual recommended dose is 1.5 g every 8 hours	If the usual recommended dose is 3 g every 8 hours
>50 to 130 (usual recommended dosing schedule)	1.5 g every 8 hours	3 g every 8 hours
30 to 50	750 mg every 8 hours[c]	1.5 g every 8 hours[c]
15 to 29	375 mg every 8 hours[c]	750 mg every 8 hours[c]
<15 mL/minute not on dialysis	No suffecient data .	

[c]**Note:** May consider delaying dosage adjustment (eg, administer full doses for 48 hours after initiation) before decreasing the dose for acute kidney injury (AKI).

Hemodialysis, intermittent (thrice weekly): IV: Dialyzable (ceftolozane 66%; tazobactam 56%).

If the usual recommended dose is 1.5 g every 8 hours: Initial: 750 mg as a single dose, followed by 150 mg every 8 hours. Administer dose immediately after dialysis on dialysis days.

If the usual recommended dose is 3 g every 8 hours: Initial: 2.25 g as a single dose, followed by 450 mg every 8 hours. Administer dose immediately after dialysis on dialysis.

Dosing: Hepatic Impairment: Adult

No dosage adjustment necessary.

Contra-indications	Serious hypersensitivity to ceftolozane/tazobactam, piperacillin/tazobactam, other members of the beta-lactam class, or any component of the formulation.
Adverse Drug Reactions	**>10%:** Hematologic & oncologic: Positive direct Coombs test [HAP] and [VAP]: 31%; complicated intra-abdominal infections and UTIs: <1%) Hepatic: Increased serum transaminases (HAP and VAP: 12%) **1% to 10%:** Cardiovascular: Hypotension (≤2%), atrial fibrillation (≤1%) Central nervous system: Headache (3% to 6%), intracranial hemorrhage (HAP and VAP: 4%), insomnia (1% to 4%), anxiety (≤2%), dizziness (≤1%) Dermatologic: Skin rash (≤2%) Endocrine & metabolic: Hypokalemia (≤3%), increased gamma-glutamyl transferase (<2%) Gastrointestinal: Nausea (3% to 8%), diarrhea (2% to 6%), constipation (2% to 4%), *Clostridioides difficile* associated diarrhea (3%), vomiting (1% to 3%), abdominal pain (≤1%) Hematologic & oncologic: Anemia (≤2%), thrombocythemia (≤2%) Hepatic: Increased serum alanine aminotransferase (2%), increased serum alkaline phosphatase (<2%), increased serum aspartate aminotransferase (1% to 2%) Renal: Renal failure syndrome or renal insufficiency (HAP and VAP: ≤9%; complicated intra-abdominal infections and UTIs: <1%) Miscellaneous: Fever (2% to 6%)
Monitoring Parameters	Serum creatinine and CrCl at baseline and daily in patients with changing renal function.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine. ***Risk D: Consider therapy modification*** Probenecid: Sodium Picosulfate, Typhoid Vaccine
Pregnancy and Lactation	Pregnancy Category B. There are no adequate and well-controlled trials in pregnant women. It is not known if ceftolozane or tazobactam are present in breast milk.
Administration	Administer over 1 hour; for the treatment of multidrug-resistant gram-negative organisms and administration of 3 g doses, administer 3 g by IV infusion over 3 hours. **Preparation for Administration: Adult** Reconstitute the vial with 10 mL SWFI or NS and gently shake to dissolve. The final volume is approximately 11.4 mL. To prepare the required dose, withdraw the appropriate volume from the reconstituted vial(s). Add the withdrawn volume to an infusion bag containing 100 mL of NS or D5W. Infusions range from clear, colorless solutions to solutions that are clear and slightly yellow. Variations in color within this range do not affect the potency of the product. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity: Hypersensitivity and anaphylaxis (serious and sometimes fatal). • Superinfection: Use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Renal impairment: Exposure to ceftolozane is increased with increasing degrees of renal impairment; monitor creatinine clearance (CrCl) at least daily in patients with changing renal function and adjust the dose. In clinical trials, cure rates were lower in patients with a baseline CrCl of 30 to 50 mL/minute.

	Special population: • Higher incidence of adverse reactions was observed in patients age 65 years and older
Storage	• Intact vials: at 2°C to 8°C; protect from light. Diluted solution in D5W or NS: may be stored for 24 hours at room temperature or for 7 days at 2°C to 8°C. Do not freeze. • Refer to manufacturer PIL if there are specific considerations.

Macrolide

Watch Group

1. Azithromycin

Generic Name	Azithromycin
Dosage form/strengths	500 mg vial Tablets 500mg, 600mg, 1000mg Capsules 250mg, 500mg Suspension 100mg/5ml, 200mg/5ml, 2000mg/60ml, 2gm ER Eye drops 1%
Route of administration	Parenteral, Oral, ophthalmic
Pharmacologic action	Antibiotic, Macrolide Systemic ATC: J01FA10 Opthalmic ATC: S01AA26
Indications	**Oral, IV:** **Chancroid:** Treatment of genital ulcer disease (in men) **Chronic obstructive pulmonary disease, acute exacerbation:** Treatment of acute bacterial exacerbations of COPD ***Mycobacterium avium* complex:** Prevention of *Mycobacterium avium* complex (MAC) in patients with advanced HIV infection; treatment of disseminated MAC (in combination with ethambutol) in patients with advanced HIV infection **Otitis media, acute:** Treatment of acute otitis media **Pneumonia, community-acquired:** Treatment of community-acquired pneumonia (CAP) **Skin and skin structure infection, uncomplicated:** Treatment of uncomplicated skin and skin structure infections **Streptococcal pharyngitis (group A):** Treatment of pharyngitis/tonsillitis due to *S. pyogenes* as an alternative to first-line therapy **Urethritis/cervicitis:** Treatment of urethritis and cervicitis **Ophthalmic: Bacterial conjunctivitis**
Dosage Regimen	**Adult dosing:** **Chronic obstructive pulmonary disease, acute exacerbation:** *Acute exacerbation, treatment*: **Oral:** 500 mg in a single loading dose on day 1, followed by 250 mg once daily on days 2 to 5 **or** 500 mg once daily for 3 days **Mycobacterial (nontuberculous) infection:** *Mycobacterium avium complex (MAC) infection*: Disseminated disease in patients with HIV: Treatment: Oral: 500 to 600 mg daily as part of a combination therapy regimen Primary prophylaxis: **Oral:** 1.2 g once weekly (preferred) **or** 600 mg twice weekly Secondary prophylaxis: **Oral:** 500 to 600 mg daily as part of an appropriate combination regimen; **Pneumonia, community acquired:** Outpatient: **Oral:** 500 mg on day 1, followed by 250 mg once daily for 4 days **or** 500 mg once daily for 3 days. Inpatient: **Oral, IV:** 500 mg once daily for a minimum of 3 days, as part of an appropriate combination regimen **Sexually transmitted infections:**

	Oral: 1 g as a single dose. Given alone or in combination. **Streptococcal pharyngitis (group A) (alternative agent for severely penicillin-allergic patients): Oral:** 500 mg on day 1, followed by 250 mg once daily on days 2 through 5 **or** 500 mg once daily for 3 days **Ophthalmic: Bacterial conjunctivitis:** Ophthalmic: Instill 1 drop into affected eye(s) twice daily (8 to 12 hours apart) for 2 days, then 1 drop into affected eye(s) once daily for the next 5 days **Pediatric Dosing:** **General dosing, susceptible infection**: Infants, Children, and Adolescents: Oral: 10 to 12 mg/kg/dose once on day 1 (usual maximum dose: 500 mg/dose) followed by 5 to 6 mg/kg once daily (usual maximum dose: 250 mg/dose) for remainder of treatment duration. IV: 10 mg/kg once daily; maximum dose: 500 mg/dose **Ophthalmic: Bacterial conjunctivitis:** Children and Adolescents: Ophthalmic: Instill 1 drop in the affected eye(s) twice daily (8 to 12 hours apart) for 2 days, then 1 drop once daily for 5 days
Dosage adjustment	**Dosing: Renal Impairment:** Dosage adjustment not necessary. Use caution in severe renal impairment (GFR <10 mL/minute) because of limited data. **Dosing: Hepatic Impairment:** Azithromycin is predominantly hepatically eliminated. Use with caution due to potential for hepatotoxicity (rare); discontinue immediately for signs or symptoms of hepatitis
Contra-indications	• Hypersensitivity to azithromycin, erythromycin, other macrolide (eg, azalide or ketolide) antibiotics, or any component of the formulation.
Adverse Drug Reactions	**>10%:** Gastrointestinal: Diarrhea, nausea, vomiting
Monitoring Parameters	Liver function tests, CBC with differential QTc monitoring recommendations combined with hydroxychloroquine
Drug Interactions	***Risk X: Avoid combination*** Atorvastatin Bilastine Doxorubicin Fexinidazole Mizolastine Pazopanib Pimozideqt-Prolonging Strong CYP3A4 Inhibitors Rimegepant Topotecan Vincristine ***Risk D: Consider therapy modification*** Afatinib Betrixaban Colchicine Domperidone Edoxaban Lefamulin QT-prolonging Agents Sincalide Sirolimus Sodium Picosulfate Typhoid Vaccine Ubrogepant
Pregnancy and Lactation	**Pregnancy risk factor B.** Azithromycin is present in breast milk. should be used only if clearly needed. Breastfed infants should be monitored for gastrointestinal side effects (e.g., diarrhea, fungal infections, sensitization).
Administration	**Administration: IV** Infuse over 1 hour (2 mg/mL infusion) or over 3 hours (1 mg/mL infusion). Not for IM or IV bolus administration. **Preparation for Administration:** Parenteral: Reconstitute the 500 mg vial by adding 4.8 mL of SWFI; shake vial until drug is completely dissolved; resultant concentration: 100 mg/mL. The reconstituted

	solution should be further diluted to a concentration of 1 mg/mL (500 mL) to 2 mg/mL (250 mL) in NS, D5W, or LR. **Administration: Oral** Immediate release suspension and tablet may be taken without regard to food; extended release suspension should be taken on an empty stomach (at least 1 hour before or 2 hours following a meal), within 12 hours of reconstitution. do not administer with antacids that contain aluminum or magnesium. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity reactions: Allergic reactions have been reported (rare), including fatalities. • Altered cardiac conduction: Macrolides (especially erythromycin) have been associated with rare QTc prolongation and ventricular arrhythmias. • Cardiac risk. ***Disease-related concerns:*** • Bronchiolitis obliterans: When studied to prevent bronchiolitis obliterans syndrome in patients with hematologic malignancy who underwent allogeneic hematopoietic cell transplantation, rates of cancer relapse and mortality were increased among patients receiving long-term azithromycin. • Gonorrhea/syphilis: May mask or delay symptoms of incubating gonorrhea or syphilis, so appropriate culture and susceptibility tests should be performed prior to initiating a treatment regimen. • Hepatic impairment: Use with caution. • Myasthenia gravis: Use with caution in patients with myasthenia gravis; exacerbation and new onset of symptoms have occurred. • Renal impairment: Use with caution in patients with severe renal impairment (GFR <10 mL/minute); increased gastrointestinal adverse effects may occur. ***Special populations:*** • Infants: Use of azithromycin in neonates and infants <6 weeks of age has been associated with infantile hypertrophic pyloric stenosis (IHPS); the strongest association occurred with exposure during the first 2 weeks of life; observe for nonbilious vomiting or irritability with feeding. ***Dosage form specific issues:*** • Oral suspensions: Immediate release and extended release suspensions are not interchangeable
Storage	• Injection: Store intact vials at room temperature. • Reconstituted solution is stable for 24 hours when stored below 30°C. • The diluted solution is stable for 24 hours at or below room temperature (30°C) and for 7 days if stored under refrigeration (5°C) • Suspension, immediate release: Store dry powder below 30°C. Store reconstituted suspension at 5°C to 30°C and use within 10 days. • Suspension, extended release: Store dry powder ≤30°C. Following reconstitution, store at 25°C; excursions permitted to 15°C to 30°C; do not refrigerate or freeze. Should be consumed within 12 hours following reconstitution. • Tablet: Store between 15°C to 30°C • Refer to manufacturer PIL if there are specific considerations.

2. Clarithromycin

Watch Group

Generic Name	Clarithromycin
Dosage form/ strengths	Tablets 250mg, 500mg, 500mg SR, Granules or powder for Oral Suspension 125mg/5ml, 250mg/5ml, Powder for injection 500mg
Route of administration	*Oral, IV*
Pharmacologic action	Antibiotic, Macrolide ATC: J01FA09
Indications	**Chronic obstructive pulmonary disease, acute exacerbation:** Treatment of acute bacterial exacerbation of chronic bronchitis in adults ***Helicobacter pylori* eradication:** Eradication of *Helicobacter pylori* to reduce the risk of duodenal ulcer recurrence as a component of combination therapy (triple therapy) in adults with *H. pylori* infection and duodenal ulcer disease (active or 5-year history of duodenal ulcer). Limitations of use: Regimens that contain clarithromycin as the single antibacterial agent are more likely to be associated with the development of clarithromycin resistance. Clarithromycin-containing regimens should not be used in patients with known or suspected clarithromycin-resistant isolates (efficacy is reduced). **Mycobacterial (nontuberculous) infection:** Prophylaxis and treatment of disseminated mycobacterial infections **Otitis media:** Treatment of acute otitis media in pediatric patients due to susceptible *H. influenzae*, *M. catarrhalis*, or *S. pneumoniae.* **Pneumonia, community-acquired:** Treatment of community-acquired pneumonia **Skin/skin structure infection:** Treatment of uncomplicated skin/skin structure infection. **Streptococcal pharyngitis:** Treatment of pharyngitis/tonsillitis
Dosage Regimen	**Dosing: Adult** **General dosing note:** IR and ER formulations are available; 500 mg every 12 hours of immediate release is equivalent to 1 g of extended release (two 500 mg ER tablets) once daily. **Chronic obstructive pulmonary disease, acute exacerbation: Note:** Avoid use in patients with risk factors for *Pseudomonas* infection or poor outcomes (eg, ≥65 years of age with major comorbidities, FEV_1 <50% predicted, frequent exacerbations). **Oral:** Immediate release: 500 mg every 12 hours for 3 to 7 days ***Helicobacter pylori* eradication: Note:** Avoid clarithromycin-based therapy in patients with risk factors for macrolide resistance (eg, prior macrolide exposure, local clarithromycin resistance rates ≥15% [which is assumed in the United States] or eradication rates with clarithromycin triple therapy ≤85%).

	Oral: Immediate release: 500 mg twice daily for 7 to 14 days as part of an appropriate combination regimen **Pneumonia, community-acquired:** Inpatient: Oral: Immediate release: 500 mg twice daily as part of an appropriate combination regimen. Outpatient: **Oral:** 500 mg (immediate release) twice daily or 1 g (two 500 mg ER tablets) once daily. **Note:** Use as part of an appropriate combination regimen; if local pneumococcal macrolide resistance is <25%, monotherapy is an alternative approach for outpatients without comorbidities or risk factors for antibiotic-resistant pathogens. Duration of therapy: Minimum of 5 days; patients should be clinically stable with normal vital signs before therapy is discontinued **Dosing: Pediatric** **Note:** All pediatric dosing recommendations based on immediate release product formulations (tablet and oral suspension): **General dosing, susceptible infection, mild to moderate infection:** Infants, Children, and Adolescents: Oral: 15 mg/kg/day divided every 12 hours; maximum single dose: 500 mg
Dosage adjustment	**Dosing: Renal Impairment: adults** creatinine clearance under 30 ml/min: reduce normal dosage by 50% **Dosing: Renal Impairment: pediatrics** Renally adjusted dose recommendations are based on a dose 15 mg/kg/day divided twice daily. GFR ≥30 mL/minute/1.73 m^2: No dosage adjustment necessary GFR 10 to 29 mL/minute/1.73 m^2: 4 mg/kg/dose every 12 hours GFR <10 mL/minute/1.73 m^2: 4 mg/kg/dose once daily Hemodialysis: Administer after HD session is completed: 4 mg/kg/dose once daily Peritoneal dialysis: 4 mg/kg/dose once daily **Dosing: Hepatic Impairment: adults & pediatrics** No dosage adjustment necessary if renal function is normal; however, in patients with hepatic impairment and concomitant severe renal impairment, a dosage reduction or prolonged dosing intervals may be appropriate
Contra-indications	Hypersensitivity to clarithromycin, erythromycin, any of the macrolide antibiotics, or any component of the formulation; history of cholestatic jaundice/hepatic dysfunction associated with prior use of clarithromycin; concomitant use with cisapride, pimozide, ergot alkaloids (eg, ergotamine, dihydroergotamine), lomitapide, or HMG-CoA reductase inhibitors extensively metabolized by CYP3A4 (eg, lovastatin, simvastatin); concomitant use with colchicine in patients with renal or hepatic impairment Severe hepatic failure in combination with renal impairment; history of QT prolongation (congenital or documented acquired QT prolongation or ventricular cardiac arrhythmia, including torsades de pointes; hypokalemia; concomitant use with saquinavir, midazolam (oral), colchicine (regardless of hepatic/renal impairment), ticagrelor; concomitant use with astemizole, domperidone, terfenadine, or ranolazine (not available in Canada)
Adverse Drug Reactions	**1% to 10%:** **Central nervous system**: Headache (2%), insomnia **Dermatologic**: Skin rash (children 3%) **Gastrointestinal**: Dysgeusia (adults 3% to 7%), vomiting (children 6%), diarrhea (3% to 6%), nausea (adults 3%), abdominal pain (2% to 3%), dyspepsia (adults 2%) **Hematologic & oncologic:** Prolonged prothrombin time (adults 1%)

	Hepatic: Abnormal hepatic function tests **Hypersensitivity:** Anaphylactoid reaction **Infection**: Candidiasis (including oral) **Renal:** Increased blood urea nitrogen (4%)
Monitoring Parameters	BUN, creatinine; perform culture and sensitivity studies prior to initiating drug therapy as appropriate
Drug Interactions	**Long list of interactions must be checked before adminsterations includes:** ***Risk X: Avoid combination:*** Aprepitant, Budesonide (Topical), Doxorubicin, Everolimus, Fusidic Acid (Systemic), Ibrutinib, Irinotecan Products, Lopinavir, Lovastatin, Pimozide, Posaconazole, Simvastatin, Vincristine (Liposomal), ***Risk D: Consider therapy modification*** Calcium Channel Blockers Except Clevidipine, Colchicine, Fentanyl, Methylprednisolone, Midazolam, Rivaroxaban, Sildenafil, Sirolimus, Theophylline Derivatives
Pregnancy and Lactation	Pregnancy factor C Clarithromycin and its active metabolite (14-hydroxy clarithromycin) are present in breast milk in low levels. Decreased appetite, diarrhea, rash, and somnolence have been reported in breastfed infants exposed to macrolide antibiotics. should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother.
Administration	• Immediate Release tablets and granules for suspension: Administer with or without meals. Administer every 12 hours rather than twice daily to avoid peak and trough variation. Shake suspension well before each use. • Extended Release tablets: Administer with food. Do not break, crush, or chew. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** Altered cardiac conduction: Use has been associated with QT prolongation and infrequent cases of arrhythmias, including torsades de pointes (may be fatal); avoid use in patients with known prolongation of the QT interval, ventricular cardiac arrhythmia (including torsades de pointes), uncorrected hypokalemia or hypomagnesemia, clinically significant bradycardia, and patients receiving Class IA (eg, quinidine, procainamide) or Class III (eg, amiodarone, dofetilide, sotalol) antiarrhythmic agents or other drugs known to prolong the QT interval. • Hepatic effects: Elevated liver function tests and hepatitis (hepatocellular and/or cholestatic with or without jaundice) have been reported; usually reversible after discontinuation of clarithromycin. May lead to hepatic failure or death (rarely), especially in the presence of preexisting diseases and/or concomitant use of medications. Discontinue immediately if symptoms of hepatitis (eg, anorexia, jaundice, abdominal tenderness, pruritus, dark urine) occur. • Hypersensitivity reactions: Severe acute reactions have been reported, including anaphylaxis, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug rash with eosinophilia and systemic symptoms (DRESS), Henoch-Schönlein purpura (IgA vasculitis), and acute generalized exanthematous pustulosis; discontinue therapy and initiate treatment immediately for severe acute hypersensitivity reactions. • Superinfection: Use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment.

	Disease-related concerns: • CAD: Use with caution in patients with CAD. A clinical trial in patients with CAD demonstrated an increase in risk of all-cause mortality ≥1 year after the end of treatment in patients randomized to receive clarithromycin. Other epidemiologic studies evaluating this risk have variable results. • Myasthenia gravis: Use with caution in patients with myasthenia gravis; exacerbation of symptoms and new onset of symptoms has occurred. • Renal impairment: Use with caution in severe renal impairment; dosage adjustment required. ***Special populations:*** • Elderly: Use with caution; elderly patients may be at increased risk of torsades de pointes. • Patients with HIV: Decreased survival has been observed in patients with HIV with *Mycobacterium avium* complex (MAC) receiving clarithromycin doses above the maximum recommended dose; maximum recommended dosing should not be exceeded in this population. Development of resistance to clarithromycin has been observed when used as prophylaxis and treatment of MAC infection (Biaxin Canadian product labeling). ***Dosage form specific issues:*** • Extended release formulation: The presence of extended release tablets in the stool has been reported, particularly in patients with anatomic (eg, ileostomy, colostomy) or functional GI disorders with decreased transit times. Consider alternative dosage forms (eg, suspension) or an alternative antimicrobial for patients with tablet residue in the stool and no signs of clinical improvement. • Propylene glycol: Some dosage forms may contain propylene glycol; large amounts are potentially toxic and have been associated hyperosmolality, lactic acidosis, seizures, and respiratory depression; use caution ***Other warnings/precautions:*** • Appropriate use: *Helicobacter pylori* eradication: Short-term combination therapy (≤7 days) has been associated with a higher incidence of treatment failure. Current guidelines recommend 10 to 14 days of therapy (triple or quadruple) for eradication of *H. pylori* in pediatric and adult patients
Storage	• Tablets: Store at 20°C to 25°C; excursions are permitted between 15°C and 30°C. Protect from light. • Granules for suspension: Store at 25°C prior to and following reconstitution. Do not refrigerate. Use within 14 days of reconstitution • Refer to manufacturer PIL if there are specific considerations.

Watch Group

3. Erythromycin

Generic Name	Erythromycin
Dosage form/strengths	**Topical** gel/ointment/solution/lotion 2% **Tablets** 250mg, 500mg **powder for orl Suspension** 125mg/5ml, 200mg/5ml, 250mg/5ml, 400mg/5ml
Route of administration	Oral, topical
Pharmacologic action	Antibiotic, Macrolide Systemic ATC: J01FA01 Topical ATC: D10AF02
Indications	**Bacterial infections:** Treatment of susceptible bacterial infections, including *S. pyogenes*, some *S. pneumoniae,* some *S. aureus*, *M. pneumoniae*, *Legionella pneumophila*, diphtheria, pertussis, *Chlamydia*, erythrasma, *N. gonorrhoeae*, *E. histolytica*, syphilis and nongonococcal urethritis, and *Campylobacter* gastroenteritis; used in conjunction with neomycin for decontaminating the bowel **Surgical (preoperative) prophylaxis (colorectal):** Colorectal decontamination, in conjunction with other agents, prior to surgical intervention **Topical: Treatment of acne vulgaris**
Dosage Regimen	**Usual dosage range:** **Note:** Due to differences in absorption, 400 mg erythromycin ethylsuccinate produces the same serum levels as 250 mg erythromycin base or stearate. **Oral:** Base: 250 to 500 mg every 6 to 12 hours; maximum: 4 g daily. Ethylsuccinate: 400 to 800 mg every 6 to 12 hours; maximum: 4 g daily. **Dosing: Pediatric** **General dosing, susceptible infection:** Infants, Children, and Adolescents: Oral: Base, ethylsuccinate, stearate: 30 to 50 mg/kg/day divided every 6 to 8 hours usually; for severe infection may double dose; maximum daily dose: Mild to moderate infection: 2,000 mg/day; severe infection: 4,000 mg/day **Topical**: **Dosing: Adult and Adolescents** **Acne:** Topical: **Note:** The American Academy of Dermatology acne guidelines recommend erythromycin (topical) be used in conjunction with other therapies (not as monotherapy) due to the risk of bacterial resistance. Gel: Apply sparingly as a thin film over the affected area once or twice daily. Therapeutic response may take up to 6 to 8 weeks; discontinue use if no improvement after 6 to 8 weeks or if condition worsens. Ointment, solution: Apply to affected area twice daily (morning and evening); drying and peeling may be controlled by reducing the frequency of application.
Dosage adjustment	**Dosing: Renal Impairment: Adult** There are no dosage adjustments needed Dialysis: Slightly dialyzable (5% to 20%). Supplemental dose is not necessary in hemo- or peritoneal dialysis or in continuous arteriovenous or venovenous hemofiltration

	Dosing: Renal Impairment: Pediatric GFR ≥10 mL/minute/1.73 m^2: No adjustment required GFR <10 mL/minute/1.73 m^2: Intermittent hemodialysis, peritoneal dialysis: Not removed by peritoneal dialysis or hemodialysis: 10 to 17 mg/kg/dose every 8 hours **Dosing: Hepatic Impairment:** There are no dosage adjustments needed; use with caution
Contra-indications	Hypersensitivity to erythromycin, any macrolide antibiotics, or any component of the formulation Concomitant use with pimozide, cisapride, ergotamine or dihydroergotamine, terfenadine, astemizole, lovastatin, or simvastatin
Adverse Drug Reactions	**Frequency not defined:** **Cardiovascular:** QT_c prolongation, torsade de pointes, ventricular arrhythmia, ventricular tachycardia **Central nervous system:** Seizure **Dermatologic:** Erythema multiforme, pruritus, skin rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria **Gastrointestinal:** Abdominal pain, anorexia, diarrhea, nausea, oral candidiasis, pancreatitis, pseudomembranous colitis, pyloric stenosis (infantile hypertrophic), vomiting **Hepatic:** Abnormal hepatic function tests, cholestatic jaundice (most common with estolate), hepatitis **Hypersensitivity:** Anaphylaxis, hypersensitivity reaction **Local:** Injection site phlebitis **Neuromuscular & skeletal:** Weakness **Otic:** Hearing loss **Renal:** Interstitial nephritis Postmarketing and/or case reports: Hepatotoxicity
Monitoring Parameters	Assess results of culture and sensitivity tests and patient's previous allergy history prior to therapy. Obtain liver function tests and monitor for liver toxicity. Assess other medicines patient may be taking; alternate therapy or dosage adjustments may be needed. Assess for effectiveness of treatment. Test for *C. difficile* if patient develops diarrhea. May lead to ototoxicity when used in high doses with other ototoxic medications or in the elderly patient.
Drug Interactions	***Risk X: Avoid combination***: Amiodarone, Aprepitant, Bosutinib, Cholera Vaccine, Cisapride, Clindamycin (Topical), Domperidone, Doxorubicin (Conventional), Dronedarone, Ergot Derivatives, Fluconazole, Fosaprepitant, Ivabradine, Lovastatin, Quinidine, Simeprevir, Simvastatin ***Risk D: Consider therapy modification*** Budesonide (Systemic), Buspirone, Calcium Channel Blockers, Carbamazepine, Cilostazol, Colchicine, Edoxaban, Eplerenone, Everolimus, Fentanyl, Guanfacine, Methadone, Midazolam, Mitotane, Ranolazine, Rivaroxaban, Sildenafil, Sirolimus, Typhoid Vaccine,
Pregnancy and Lactation	**Pregnancy category B** Although Caution should be used if administered to a breastfeeding patient, erythromycin is considered compatible when used in usual recommended doses. Erythromycin is a preferred agent for the treatment of granuloma inguinale and lymphogranuloma venereum in breastfeeding patients. If systemic erythromycin is needed for the treatment of dermatologic conditions, only short-term use is recommended if breastfeeding. Topical erythromycin is considered to be compatible with breastfeeding.
Administration	**Administration: Oral** Administer base or stearate dosage forms on an empty stomach (2 hours before or after a meal); administer ethylsuccinate (EES) without regard to meals; may consider administering

	after food to decrease GI discomfort. **Topical**: Prior to treatment, thoroughly wash affected area with mild soap and warm water, rinse, and pat dry. Wash hands after use. Avoid contact with the eyes, nose, mouth and other mucous membranes, and broken skin. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Altered cardiac conduction: Macrolides have been associated with rare QTc prolongation and ventricular arrhythmias, including torsade de pointes; use with caution in patients at risk of prolonged cardiac repolarization; avoid use in patients with prolonged QT interval, uncorrected hypokalemia or hypomagnesemia, clinically significant bradycardia, or concurrent use of Class IA (eg, quinidine, procainamide) or Class III (eg, amiodarone, dofetilide, sotalol) antiarrhythmic agents. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Hepatic impairment: Use with caution in patients with preexisting liver disease; hepatic impairment, including hepatocellular and/or cholestatic hepatitis, with or without jaundice, has been observed. Discontinue if symptoms of malaise, nausea, vomiting, abdominal colic, and fever. • Myasthenia gravis: Exacerbation of and new onset of myasthenia gravis symptoms have been reported. ***Special populations:*** • Infants: Use of erythromycin has been associated with infantile hypertrophic pyloric stenosis (IHPS); observe for non-bilious vomiting or irritability with feeding. • Elderly: May be at increased risk of adverse events, including hearing loss and/or torsade de pointes, particularly if concurrent renal/hepatic impairment
Storage	• Granules: Prior to mixing, store at 20°C to 25°C. After mixing, store under refrigeration and use within 10 days. • Powder: Prior to mixing, store at <30°C. After mixing, store at ≤25°C and use within 35 days. • Tablet and Topicsl formulations: Store at 20°C to 25°C. Refer to manufacturer PIL if there are specific considerations.

4. Roxithromycin

Watch Group

Generic Name	Roxithromycin
Dosage form/strengths	Tablets: 100mg, 150 mg, 300mg
Route of administration	Oral
Pharmacologic category	a semi-synthethic macrolide antibiotic ATC: J01FA06
Indications	used to treat various infections caused by bacteria such as: • upper respiratory tract infection - acute pharyngitis, tonsillitis and sinusitis • dental infections • lower respiratory tract infection - acute bronchitis; acute exacerbations of chronic bronchitis and community acquired pneumonia • skin and skin structure infections • non-gonococcal urethritis.
Dosage Regimen	**Adults dosing:** Usual dosage: Roxithromycin 300 mg tablet daily or 150 mg twice daily. The usual duration of treatment is five to ten days depending on the indication and clinical response. The usual duration of treatment is five to ten days depending on the indication and clinical response. **Pediatric dosing:** Roxithromycin is administered twice daily at a dose of 5 to 8 mg/kg/day. For children≥ 40 kg: One 150 mg tablet morning and evening.
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary. **Dosing: Hepatic Impairment: Adult** 150 mg tablet once daily for patients with documented cirrhotic liver disease.
Contra-indications	known hypersensitivity to macrolide (such as azithromycin, clarithromycin or erythromycin), severely impaired hepatic function, concomitant therapy with vasoconstrictive ergot alkaloids.
Adverse Drug Reactions	Roxithromycin primarily causes gastrointestinal adverse events, such as diarrhoea, nausea, abdominal pain and vomiting. Less common adverse events include headaches, rashes, abnormal liver function values and alteration in senses of smell and taste
Monitoring Parameters	Signs of hypersensitivity to roxithromycin; development of superinfection or antibiotic-associated diarrhea
Drug Interactions	***Risk X: Avoid combination*** Ergotamine and derivatives, Terfenadine, Astemizole, cisapride, pimozide, Thioridizine, Dofetilide ***Risk D: Consider therapy modification*** Theophylline, Disopyramide, Warfarin, Digoxin and other cardiac glycosides, Midazolam,
Pregnancy and Lactation	Safety in this group of patients has not been determined. It passes to breast milk. This medicine is not recommended for use during pregnancy.

	low levels of roxithromycin in breastmilk, it would not be expected to cause adverse effects in breastfed infants. Monitor the infant for possible effects on the gastrointestinal flora, such as diarrhea, candidiasis (thrush, diaper rash)
Administration	**Oral**: should be taken at least 15 minutes before food or on an empty stomach (i.e. more than three hours after a meal). The film coated tablets must be swallowed whole with a drink. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Prolonged or repeated use of antibiotics including roxithromycin may result in superinfection by resistant organisms. In the event of superinfection, roxithromycin should be discontinued and appropriate therapy instituted**.** • Drugs that delay peristalsis, e.g. opiates and diphenoxylate with atropine, may prolong and/or worsen the condition and should not be used. • Drugs that delay peristalsis, e.g. opiates and diphenoxylate with atropine, may prolong and/or worsen the condition and should not be used. As with other macrolides, roxithromycin may have the potential to aggravate myasthenia gravis. • Cases of severe bullous skin reactions such as Stevens Johnson Syndrome or Toxic Epidermal Necrosis have been reported with roxithromycin (see Undesirable effects). If symptoms or signs of SJS or TEN (eg. progressive skin rash often with blisters or mucosal lesions) are present, roxithromycin treatment should be discontinued. • Severe vasoconstriction (“ergotism”) with possibly necrosis of the extremities has been reported when macrolide antibiotics have been associated with vasoconstrictive ergot alkaloids. Absence of treatment by these alkaloids must always be checked before prescribing roxithromycin. • Increased INR levels have been reported in patients when Arrow - Roxithromycin and coumarin anticoagulants are used concomitantly. Patients using Arrow - Roxithromycin and coumarin anticoagulants should be closely monitored. • Prolongation of the QT Interval Ventricular arrhythmias associated with prolonged QT interval, including ventricular tachycardia and torsades de pointes have been reported with macrolide antibiotics including roxithromycin.
Storage	Store in a cool, dry place where it stays below 25°C, and protect from light and moisture. Refer to manufacturer PIL if there are specific considerations.

5. Spiramycin

Watch Group

Generic Name	Spiramycin
Dosage form/strengths	Tablets 1.5 MIU, 3MIU
Route of administration	Oral
Pharmacologic category	Antibiotic, Macrolide ATC: J01FA02
Indications	Treatment of infections of the respiratory tract, buccal cavity, skin and soft tissues due to susceptible organisms. N. gonorrhoeae: as an alternate choice of treatment for gonorrhea in patients allergic to the penicillins. Before treatment of gonorrhea, the possibility of concomitant infection due to T. pallidum should be excluded
Dosage Regimen	**Dosing: Adult** **Mild to moderate infections:** Oral: 6 MIU to 9 MIU per day in 2 divided doses **Severe infections:** Oral: 12 MIU to 15 MIU per day in 2 divided doses **Gonorrhea:** Oral: 12 MIU to 13.5 MIU as a single dose **Acute toxoplasmosis in pregnancy (<18 weeks' gestation) (off-label use):** Oral: 1 g (3 MIU) every 8 hours to prevent transmission to fetus. At ≥18 weeks, if there is **no** evidence of transmission to the fetus, spiramycin can be continued until term. **Note:** If intrauterine fetal *Toxoplasma* infection is confirmed, treatment should be switched to pyrimethamine plus sulfadiazine and folinic acid **Dosing: Pediatric** **Susceptible infections:** Oral: Dosage by body weight; usual dosage 1.5 MIU/kg. Daily dose should be administered in 2 to 3 divided doses. **Note:** In severe infections, dosage may be increased by 50%.
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment required. **Dosing Hepatic impairment**: Use with caution in patients with pre-existing liver disease
Contra-indications	Hypersensitivity to spiramycin, other macrolides (eg, erythromycin) or any component of the formulation
Adverse Drug Reactions	**Frequency not defined.** Central nervous system: Paresthesia (transient) Dermatologic: Pruritus, skin rash, urticaria Gastrointestinal: Diarrhea, nausea, vomiting
Monitoring Parameters	Hepatic functions
Drug Interactions	**Risk X: Avoid combination** BCG (Intravesical) Mizolastine **Risk D: Consider therapy modification** Typhoid Vaccine: Sodium Picosulfate **Risk C: Monitor therapy** BCG Vaccine Carbidopa Lactobacillus and Estriol
Pregnancy	Spiramycin has not been found to be teratogenic and has been found to be safe in the pregnant woman, fetus, and newborn.

Administration	Administer without regard to meals. But Food may improve gastrointestinal tolerance. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Altered cardiac conduction: Macrolides have been associated with rare QT_c prolongation and ventricular arrhythmias, including torsade de pointes; use with caution in patients at risk of prolonged cardiac repolarization. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Hepatic impairment: Use with caution in patients with pre-existing liver disease; hepatic impairment, including hepatocellular and/or cholestatic hepatitis, with or without jaundice, has been observed. Discontinue if symptoms of malaise, nausea, vomiting, abdominal colic, and fever.
Storage	Store at 20°C to 25°C Refer to manufacturer PIL if there are specific considerations.

Miscellaneous

1. Aztreonam

Reserve Group

Generic Name	Aztreonam
Dosage form/strengths	**Powder for injection** :1gm
Route of administration	IV, IM
Pharmacologic category	Antibiotic, Monobactam ATC: J01DF01
Indications	Treatment of patients with urinary tract infections, lower respiratory tract infections, septicemia, skin/skin structure infections, intra-abdominal infections, and gynecological infections caused by susceptible gram-negative bacilli
Dosage Regimen	**Dosing: Adult** **Moderately severe systemic infections:** 1 g IV or IM or 2 g IV every 8 to 12 hours; maximum: 8 g/day. **Pneumonia:** - *Community-acquired pneumonia:* For empiric therapy of inpatients at risk of infection with a resistant gram-negative pathogen, including *P. aeruginosa:* IV: 2 g every 8 hours as part of an appropriate combination regimen. Total duration is for a minimum of 5 days. - *Hospital-acquired or ventilator-associated (alternative agent):* For empiric therapy or pathogen-specific therapy of resistant gram-negative pathogens, including *P. aeruginosa*: IV: 2 g every 8 hours for 7 days; may consider shorter or longer durations depending on rate of clinical improvement. **Severe systemic or life-threatening infections (eg, *Pseudomonas aeruginosa*)**: IV: 2 g every 6 to 8 hours; maximum: 8 g/day. **Urinary tract infection:** IM, IV: 500 mg to 1 g every 8 to 12 hours; maximum: 8 g/day. **Dosing: Pediatric** **General dosing, susceptible infection:** Infants, Children, and Adolescents: - Mild to moderate infection: IM, IV: 90 mg/kg/day in divided doses every 8 hours; maximum daily dose: 3,000 mg/day - Severe infection: IM, IV: 90 to 120 mg/kg/day in divided doses every 6 to 8 hours; maximum daily dose: 8 g/day **Cystic fibrosis *(Pseudomonas aeruginosa)*:** Infants, Children, and Adolescents: IV: 150 to 200 mg/kg/day in divided doses every 6 to 8 hours **Intra-abdominal infections, complicated:** Infants, Children, and Adolescents: IV: 90 to 120 mg/kg/day divided every 6 to 8 hours in combination with metronidazole; maximum dose: 2,000 mg **Peritonitis (peritoneal dialysis), treatment:** Infants, Children, and Adolescents: Intraperitoneal: Continuous: Loading dose: 1,000 mg per liter of dialysate; maintenance dose: 250 mg per liter **Surgical prophylaxis:** Children and Adolescents: IV: 30 mg/kg within 60 minutes before procedure; may repeat in 4 hours for prolonged procedure or excessive blood loss;

	maximum dose: 2,000 mg
Dosage adjustment	**Dosing: Renal Impairment: Adult** IM, IV: Adults: Following initial dose, maintenance doses should be given as follows: CrCl 10 to 30 mL/minute: 50% of usual dose at the usual interval CrCl <10 mL/minute: 25% of usual dosage at the usual interval **Dosing: Renal Impairment: Pediatric** Infants, Children, and Adolescents: IM, IV: The following adjustments have been recommended. **Note:** Renally adjusted recommendations are based on doses of 90 to 120 mg/kg/day divided every 8 hours. GFR ≥30 mL/minute/1.73 m^2: No adjustment required GFR 10-29 mL/minute/1.73 m^2: 15 to 20 mg/kg every 8 hours GFR <10 mL/minute/1.73 m^2: 7.5 to 10 mg/kg every 12 hours Intermittent hemodialysis: 7.5 to 10 mg/kg every 12 hours Peritoneal dialysis (PD): 7.5 to 10 mg/kg every 12 hours Continuous renal replacement therapy (CRRT): No adjustment required. **Dosing: Hepatic Impairment: Adult-pediatric** There are no dosage adjustments needed. Use with caution (minor hepatic elimination occurs).
Contra-indications	Hypersensitivity to aztreonam or any component of the formulation
Adverse Drug Reactions	**>10%:** **Hematologic & oncologic:** Neutropenia (children 3% to 11%; adults <1%) **Hepatic:** Increased serum transaminases (children, high dose: >3 times ULN: 15% to 20%; children, standard dose: increased serum AST 4%, increased serum ALT 7%) **Local:** Pain at injection site (children 12%, adults 2%) **1% to 10%:** Cardiovascular: Phlebitis, thrombophlebitis Dermatologic: Skin rash Gastrointestinal: Diarrhea, nausea, vomiting Hematologic & oncologic: Eosinophilia, thrombocythemia Local: Erythema at injection site, discomfort at injection site, swelling at injection site Renal: Increased serum creatinine Miscellaneous: Fever
Monitoring Parameters	Periodic renal and hepatic function tests; monitor for signs of anaphylaxis during first dose
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Sodium Picosulfate Typhoid Vaccine
Pregnancy and Lactation	**Pregnancy Risk Factor** B Aztreonam is present in breast milk in concentrations <1% of the corresponding maternal serum concentration. In general, antibiotics that are present in breast milk may cause nondose-related modification of bowel flora. The poor oral absorption of aztreonam from the gastrointestinal tract (<1%) may limit adverse effects to the infant.

Administration	**Preparation for Administration:** **IM**: Reconstitute vial with at least 3 mL SWFI, sterile bacteriostatic water for injection, NS, or bacteriostatic sodium chloride per gram of aztreonam to a final concentration of ≤333 mg/mL; immediately shake vigorously. Do not mix with any local anesthetic agent. **IV**: Bolus injection: Reconstitute vial with 6 to 10 mL SWFI; immediately shake vigorously **Infusion**: Reconstitute vial with at least 3 mL SWFI per gram of aztreonam; immediately shake vigorously. Reconstituted solutions are colorless to light yellow straw and may turn pink upon standing without affecting potency. Further dilute in an appropriate solution (eg, D5W, NS) for infusion to a final concentration not to exceed 20 mg/mL. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Beta-lactam allergy: Rare cross-allergenicity to penicillins, cephalosporins, or carbapenems may occur; use with caution in patients with a history of hypersensitivity to beta-lactams. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Renal impairment: Use with caution in patients with renal impairment; dosing adjustment required. ***Special populations:*** • Bone marrow transplantation: Use with caution in bone marrow transplant patients with multiple risk factors for toxic epidermal necrolysis (TEN) (eg, sepsis, radiation therapy, drugs known to cause TEN); rare cases of TEN in this population have been reported.
Storage	• Vials: store at room temperature; avoid excessive heat. • After reconstitution, solutions for infusion: should be used within 48 hours if stored at room temperature or within 7 days if refrigerated.; • solutions for infusion (prepared with other than SWFI or NS with a final concentration >20 mg/mL) must be used immediately after preparation. • Refer to manufacturer PIL if there are specific considerations.

2. Chloramphenicol

Access Group

Generic Name	Chloramphenicol
Dosage form/strengths	Eye ointmint 1% Eye drops 0.5% Capsule 250mg Ears drops 5% Oral Suspension 125 mg/5ml Suppository 500mg powder for injection 1g
Route of administration	*Oral IV Topical Ophthalmic*
Pharmacologic category	Antibiotic, Miscellaneous ATC (Topical, dermatological): D06AX02 ATC (Systemic): J01BA01 ATC (Ophthalmic): S01AA01, S03AA08
Indications	**Serious infections:** Treatment of serious infections, including cystic fibrosis exacerbations, bacterial meningitis, and bacteremia, caused by *Chlamydiaceae*, *Haemophilus influenzae*, *Rickettsia*, *Salmonella* spp. (acute infections), and other organisms when other less toxic agents are ineffective or contraindicated.
Dosage Regimen	**Dosing: Adult** Due to narrow therapeutic range it is recommended that plasma concentrations of chloramphenicol be monitored in all patients receiving the drug and dosage adjusted accordingly**.** Generally, adjust chloramphenicol dosage to maintain plasma concentrations of 5–20 mcg/mL (usually 10–20 mcg/mL). In pediatric patients beyond the neonatal period, AAP suggests adjusting dosage to maintain target plasma concentrations of 15–25 mcg/mL Chloramphenicol plasma concentrations >25 mcg/mL have been associated with toxicity **Serious infections:** IV: 50 to 100 mg/kg/day in divided doses every 6 hours; maximum daily dose: 4 g/day **Pediatric Patients** **General Dosage IV** **for Neonates** 25 mg/kg daily given in 4 equally divided doses every 6 hours usually provides and maintains blood and tissue concentrations adequate for most indications **for Pediatric Patients Beyond the Neonatal Period** 50 mg/kg daily given in 4 divided doses every 6 hours provides blood concentrations adequate for most indications in pediatric patients 50–100 mg/kg daily given in 4 divided doses for severe infections maximum daily dose: 4,000 mg/day
Dosage adjustment	**Dosing: Renal Impairment or Hepatic Impairment:** Use with caution, reduced dosage and serum concentration monitoring is recommended.
Contra-indications	Hypersensitivity to chloramphenicol or any component of the formulation; treatment of trivial or viral infections; bacterial prophylaxis
Adverse Drug Reactions	**Central nervous system**: Confusion, delirium, depression, headache **Dermatologic**: Skin rash, urticaria **Gastrointestinal**: Diarrhea, enterocolitis, glossitis, nausea, stomatitis, vomiting

	Hematologic & oncologic: Aplastic anemia, bone marrow depression, granulocytopenia, hypoplastic anemia, pancytopenia, thrombocytopenia **Hypersensitivity:** Anaphylaxis, angioedema, hypersensitivity reaction **Ophthalmic:** Optic neuritis **Miscellaneous:** Drug toxicity (Gray syndrome), fever
Monitoring Parameters	CBC with differential (baseline and every 2 days during therapy), periodic hepatic and renal function tests, serum drug concentration
Drug Interactions	• ***Risk X: Avoid combination*** Dipyrone, Cholera Vaccine, BCG (Intravesical), cladribine • ***Risk D: Consider therapy modification*** Ceftazidime, Cyclosporine, Deferiprone, Sodium Picosulfate, Tacrolimus (Systemic), Typhoid Vaccine • ***Risk C: Monitor therapy*** Alcohol ,Barbiturates, BCG Vaccine (Immunization), Carbocisteine, Chloramphenicol (Ophthalmic), Clozapine, Fosphenytoin, Actobacillus And Estrio, Phenytoin, Promazine, Rifampin, Sulfonylureas, Vitamin B12, Vitamin K Antagonists
Pregnancy and Lactation	**Pregnancy Risk Factor** C Due to the potential for serious adverse reactions in the breastfed infant, it is recommended to take a decision to discontinue breastfeeding or to discontinue the drug, taking into account the importance of treatment to the mother. Avoid use while breast-feeding, especially young infants (<34 weeks postconceptual age or <1 month of age) or when unusually large doses are needed.
Administration	**Parenteral**: IV push: Administer over at least 1 minute. Intermittent IV infusion: Infuse over 30 to 60 minutes. In neonates, some centers have administered as an intermittent IV infusion over 15 minutes Should not be administered IM; has been shown to be ineffective. **Preparation for Administration: Adult** IV push: Reconstitute with 10 mL SWFI or D5W for a concentration of 100 mg/mL. **Preparation for Administration: Pediatric** IV push: Reconstitute with 10 mL SWFI or D5W for a concentration of 100 mg/mL. Intermittent IV infusion (over 15-60 min): Further dilute in D5W to a final concentration not to exceed 20 mg/mL; in neonates, a higher maximum concentration of 25 mg/mL has been used Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Blood dyscrasias: [US Boxed Warning]: Serious and fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, and granulocytopenia) have occurred after both short-term and prolonged therapy; do not use for minor infections or when less potentially toxic agents are effective. Monitor CBC frequently in all patients; discontinue if evidence of myelosuppression. Irreversible bone marrow suppression may occur weeks or months after therapy. Avoid prolonged or repeated courses of treatment. • Gray syndrome: Characterized by cyanosis, abdominal distention, vasomotor collapse (often with irregular respiration), and death. Reaction appears to be associated with serum levels ≥50 mcg/mL. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. • Patients with Hepatic or Renal impairment: Use with caution; reduced dosage and serum concentration monitoring is recommended.

	• Glucose 6-phosphate dehydrogenase deficiency: Use with caution.
Storage	Store intact vials at 20°C to 25°C Refer to manufacturer PIL if there are specific considerations.

3. Clindamycin

Generic Name	Clindamycin
Dosage form/strengths	Capsules 150mg, 300mg, 600mg, Topical solution 1%, 10mg/30ml Topical jel or cream 1% Solution for injection 300mg 600mg Vaginal ovules 100mg, Vaginal cream2%
Route of administration	*Oral IV IM intravaginal*
Pharmacologic category	Antibiotic, Lincosamide ATC (Topical): D10AF01 ATC (Gynecological): G01AA10 ATC (systemic): J01FF01
Indications	**Bone and joint infections:** Treatment of bone and joint infections, including acute hematogenous osteomyelitis caused by *Staphylococcus aureus* and as adjunctive therapy in the surgical treatment of chronic bone and joint infections caused by susceptible organisms. **Gynecological infections:** Treatment of gynecologic infections, including endometritis, nongonococcal tubo-ovarian abscess, pelvic cellulitis, and postsurgical vaginal cuff infection caused by susceptible anaerobes. **Intraabdominal infections:** Treatment of intraabdominal infections, including peritonitis and intraabdominal abscess caused by susceptible anaerobic organisms. **Lower respiratory tract infections:** Treatment of lower respiratory tract infections, including pneumonia, empyema, and lung abscess **Septicemia:** Treatment of septicemia **Skin and soft tissue infection:** Treatment of skin and soft tissue infection
Dosage Regimen	**Adult Dosing:** **Serious Infections** Oral: 150–300 mg every 6 hours. IV or IM: 600 mg to 1.2 g daily in 2–4 equally divided doses. **More Severe Infections** Oral: 300–450 mg every 6 hours. IV or IM: 1.2–2.7 g daily in 2–4 equally divided doses. For life-threatening infections, IV dosage may be increased up 4.8 g daily **Dosing: Pediatric** **Note:** Dosage should be based on total body weight for obese children ≥2 years of age and adolescents. **General dosing, susceptible infection:** **IM, IV:** Infants, Children, and Adolescents 1 month to 16 years: ○ Weight-directed dosing: 20-40 mg/kg/day divided every 6-8 hours. ○ BSA-directed dosing: 350 to 450 mg/m^2/day divided every 6 to 8 hours. Alternate dosing (*Red Book* [AAP] 2012): Infants, Children, and Adolescents: ○ Mild to moderate infections: 20 mg/kg/day divided every 8 hours; maximum daily dose: 1,800 mg/**day**. ○ Severe infections: 40 mg/kg/day divided every 6 to 8 hours; maximum daily dose: 2,700 mg/**day**. **Oral:** Infants, Children, and Adolescents:

	○ Hydrochloride salt (capsule): 8 to 20 mg/kg/day divided every 6 to 8 hours. ○ Palmitate salt (solution): 8 to 25 mg/kg/day divided every 6 to 8 hours; minimum dose: 37.5 mg 3 times daily. Alternate dosing (*Red Book* [AAP]; 2012): Infants, Children, and Adolescents: ○ Mild to moderate infections: 10 to 25 mg/kg/day divided every 8 hours; maximum daily dose: 1,800 mg/**day**. ○ Severe infections: 30 to 40 mg/kg/day divided every 6 to 8 hours; maximum daily dose: 1,800 mg/**day**.
Dosage adjustment	**Dosing: Renal Impairment:** No dosage adjustment necessary. **Dosing: Hepatic Impairment:** There are no dosage adjustments available. Hepatic impairment significantly prolongs the elimination of clindamycin
Contra-indications	Hypersensitivity to clindamycin, lincomycin, or any component of the formulation. *Canadian labeling:* Additional contraindications (not in US labeling): Oral clindamycin: Infants <30 days of age.
Adverse Drug Reactions	**Cardiovascular**: Hypotension (rare; IV administration), thrombophlebitis (IV) **Central nervous system:** Metallic taste (IV) **Dermatologic:** Acute generalized exanthematous pustulosis, erythema multiforme (rare), exfoliative dermatitis (rare), maculopapular rash, pruritus, skin rash, Stevens-Johnson syndrome (rare), toxic epidermal necrolysis, urticaria, vesiculobullous dermatitis **Gastrointestinal**: Abdominal pain, antibiotic-associated colitis, *Clostridioides* (formerly *Clostridium*) *difficile*-associated diarrhea, diarrhea, esophageal ulcer, esophagitis, nausea, pseudomembranous colitis, unpleasant taste (IV), vomiting **Genitourinary:** Azotemia, oliguria, proteinuria, vaginitis **Hematologic & oncologic**: Agranulocytosis, eosinophilia (transient), neutropenia (transient), thrombocytopenia **Hepatic**: Abnormal hepatic function tests, jaundice **Hypersensitivity:** Anaphylactic shock, anaphylactoid reaction (rare), anaphylaxis, angioedema, hypersensitivity reaction **Immunologic:** DRESS syndrome **Local:** Abscess at injection site (IM), induration at injection site (IM), irritation at injection site (IM), pain at injection site (IM)
Monitoring Parameters	Observe for changes in bowel frequency. Monitor for colitis and resolution of symptoms. In severe liver disease monitor liver function tests periodically; during prolonged therapy monitor CBC, liver and renal function tests periodically.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine, Mecamylamine ***Risk D: Consider therapy modification*** Typhoid Vaccine, Sodium Picosulfate
Pregnancy and Lactation	Pregnancy factor B Clindamycin has the potential to cause adverse effects on the breastfed infant's gastrointestinal flora. If oral or intravenous clindamycin is required by a nursing mother, alternate drug may be preferred. Monitor the infant for possible effects on the gastrointestinal flora, such as diarrhea, candidiasis (thrush, diaper rash) or rarely, blood in the stool indicating possible antibiotic-associated colitis. Vaginal application is unlikely to cause infant side effects, although about 30% of a vaginal dose is absorbed. Infant side effects are unlikely with topical administration for acne; however, topical application to the breast may increase the risk of diarrhea if it is ingested by the infant.

Administration	**Administration: IM** Deep IM sites, rotate sites. Do not exceed 600 mg in a single injection. **Administration: IV** **Never administer undiluted as bolus**; administer by IV intermittent infusion over at least 10 to 60 minutes, at a maximum rate of 30 mg/minute (do not exceed 1,200 mg/hour). Final concentration for administration should not exceed 18 mg/mL. **Administration: Oral** Capsule should be taken with a full glass of water to avoid esophageal irritation; shake oral solution well before use; may administer with or without meals. **Preparation for Administration: Adult** Injection: Never administer undiluted as bolus. For IV infusion, dilute vials with 50 to 100 mL of compatible diluent (eg, D5W, NS); concentration of clindamycin for IV infusion should not exceed 18 mg/mL. Oral solution: Reconstitute bottles of 100 mL with 75 mL of water. Add a large portion of the water and shake vigorously; add the remainder of the water and shake until the solution is uniform. When reconstituted with water, each 5 mL of solution contains clindamycin palmitate hydrochloride equivalent to clindamycin 75 mg. **Preparation for Administration: Pediatric** Oral: Reconstitute powder for oral solution with appropriate amount of water as specified on the bottle. Shake vigorously until suspended. Parenteral: IV: Dilute with a compatible diluent (eg, D5W, NS) to a final concentration not to exceed 18 mg/mL Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Colitis: [US Boxed Warning]: Can cause severe and possibly fatal colitis. Should be reserved for serious infections where less toxic antimicrobial agents are inappropriate. It should not be used in patients with nonbacterial infections such as most upper respiratory tract infections. Hypertoxin-producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. *C. difficile*-associated diarrhea (CDAD) must be considered in all patients who present with diarrhea following antibiotic use. CDAD has been observed >2 months postantibiotic treatment. • Hypersensitivity: Severe hypersensitivity reactions, including severe skin reactions (eg, drug reaction with eosinophilia and systemic symptoms [DRESS], Stevens-Johnson syndrome [SJS], toxic epidermal necrolysis [TEN]), some fatal, and anaphylactic reactions, including anaphylactic shock, have been reported. Permanently discontinue treatment and institute appropriate therapy if these reactions occur. • Superinfection: Use may result in overgrowth of nonsusceptible organisms, particularly yeast. Should superinfection occur, appropriate measures should be taken as indicated by the clinical situation. ***Disease-related concerns:*** • GI disease: Use with caution in patients with a history of GI disease, particularly colitis. • Hepatic impairment: Use with caution in patients with moderate to severe liver disease, however, when administered at every-8-hour intervals, drug accumulation is rare. Monitor hepatic enzymes periodically as dosage adjustments may be necessary in patients with severe liver disease. ***Special populations:*** • Atopic patients: Use with caution in atopic patients. • Elderly: A subgroup of older patients with associated severe illness may tolerate diarrhea less well. Monitor carefully for changes in bowel frequency. ***Other warnings/precautions:*** • Administration (IV): Do not inject IV undiluted as a bolus. Product should be diluted in

	compatible fluid and infused over 10 to 60 minutes. • Appropriate use: Not appropriate for use in the treatment of meningitis due to inadequate penetration into the CSF.
Storage	• Oral: Store at 20°C to 25°C. Do not refrigerate the reconstituted oral solution (it will thicken); the solution is stable for 2 weeks at room temperature. • IV: Store intact vials and premixed bags at 20°C to 25°C. Infusion solution in NS or D5W solution is stable for 16 days at room temperature, 32 days refrigerated, or 8 weeks frozen. After initial use, discard any unused portion of vial after 24 hours. • Refer to manufacturer PIL if there are specific considerations.

4. Colistimethate

Reserve Group

Generic Name	Colistimethate
Dosage form/strengths	Powder for solution for injection or for nebulizer solution 1MIU Powder for oral solution 50000IU/ml, 750000 I.U./15ml Tablets 1.5 MIU
Route of administration	*Parentral, Oral*
Pharmacologic category	Antibiotic, Miscellaneous ATC: J01XB01
Indications	Treatment of acute or chronic infections due to sensitive strains of certain gram-negative bacilli (particularly Pseudomonas aeruginosa) which are resistant to other antibacterials or in patients allergic to other antibacterials
Dosage Regimen	**Dosing: Adult** **Note:** Dosage expressed in terms of mg of colistin base activity (CBA). CBA 1 mg is defined to be equivalent to colistimethate sodium (CMS) 30,000 units which is equivalent to ~2.4 mg CMS **--Pneumonia, hospital-acquired or ventilator-associated due to susceptible multidrug-resistant gram-negative bacilli (eg, *Pseudomonas aeruginosa*, *Acinetobacter spp*) or** **Severe infections (due to multidrug-resistant organisms susceptible to colistin):** **Intravenous or Intramuscular dosage** **IV**: Loading dose: 300 mg CBA followed by 300 to 360 mg CBA/day in divided doses twice daily. Begin maintenance dose 12 hours after the loading dose. Or 2.5 to 5 mg CBA/kg/day divided every 6 to 12 hours **Note:** This dosing should achieve a target average colistin steady-state plasma concentration of 2 mg/L. **Continuous Intravenous Infusion dosage** *Adults:* 2.5 to 5 mg/kg/day colistin base activity continuous IV infusion. Give one-half of the total daily dose IV over 3 to 5 minutes and follow 1 to 2 hours later with the remaining one-half of the total daily dose by continuous IV infusion over 22 to 23 hours. **Dosing: Pediatric** **Note:** Doses should be based on ideal body weight in obese patients **General dosing, susceptible infection:** Infants, Children, and Adolescents: Colistin base: **IM, IV**: 2.5 to 5 mg CBA/kg/day divided every 6 to 12 hours
Dosage adjustment	**Dosing: Renal Impairment: Adult** **IV:** **Loading dose**: 300 mg CBA, followed by a maintenance dose based on CrCl. Maintenance dose: The following total daily maintenance doses CrCl 80 mL/minute or more: No dosage adjustment needed. CrCl 50 to 79 mL/minute: 2.5 to 3.8 mg/kg/day colistin base activity IV or IM divided in 2 doses. CrCl 30 to 49 mL/minute: 2.5 mg/kg/day colistin base activity IV or IM once daily or divided in 2 doses. CrCl 10 to 29 mL/minute: 1.5 mg/kg colistin base activity IV or IM every 36 hours.

	Dosing: Renal Impairment: Pediatric There are no pediatric specific recommendations. Dosage adjustment is suggested in adult patients. **Dosing: Hepatic Impairment: Adult, pediatric** There are no dosage adjustments needed. **Dosing: Adjustment for Toxicity:** CNS toxicity: Dose reduction may reduce neurologic symptoms. Nephrotoxicity: Withhold treatment if signs of renal impairment occur during treatment.
Contra-indications	Hypersensitivity to colistimethate, colistin, or any component of the formulation
Adverse Drug Reactions	**>10%:** Genitourinary: Nephrotoxicity (18% to 26%) Renal: Acute renal failure (33% to 60%) **1% to 10%:** Central nervous system: Neurotoxicity (7%; higher incidence with high-dose IV use in cystic fibrosis) **Frequency not defined:** Central nervous system: Dizziness, oral paresthesia, paresthesia, peripheral paresthesia, seizures, slurred speech, vertigo Dermatologic: Pruritus, skin rash, urticaria Gastrointestinal: *Clostridioides* (formerly *Clostridium*) *difficile*-associated diarrhea, gastric distress Genitourinary: Decreased urine output Hypersensitivity: Anaphylaxis Renal: Decreased creatinine clearance, increased blood urea nitrogen, increased serum creatinine Respiratory: Apnea, respiratory distress Miscellaneous: Fever
Monitoring Parameters	Serum creatinine, BUN; urine output; signs of neurotoxicity; signs of bronchospasm (inhalation [off-label route]); colistin serum concentrations (to ensure adequate drug exposure particularly early in therapy). **Reference Range** Target serum concentration is 2 mg/L for susceptible organisms
Drug Interactions	***Risk X: Avoid combination*** Bacitracin (Systemic) BCG (Intravesical) Cholera Vaccine Mecamylamine Methoxyflurane ***Risk D: Consider therapy modification*** Neuromuscular-Blocking Agents, Sodium Picosulfate Typhoid Vaccine, Vancomycin
Pregnancy and Lactation	**Pregnancy Risk Factor** C Colistimethate is excreted into human milk in small amounts. The possibility of bowel flora modification and interference with culture results should be considered. caution should be used when administering colistimethate to breast-feeding women.
Administration	**Administration: IV** Infuse over 30 minutes to 1 hour **Administration: Pediatric** Parenteral: **IM**: Administer deep into a large muscle mass (eg, gluteal muscle or lateral part of the thigh).

	IV push: Administer over 3 to 5 minutes. **Intermittent IV infusion**: Administer over 30 minutes. **Continuous IV infusion**: Initially, one-half of the total daily dose is administered by direct IV injection over 3 to 5 minutes followed 1 to 2 hours later by the remaining one-half of the total daily dose diluted in a compatible IV solution infused over 22 to 23 hours. Infusion should be completed within 24 hours of preparation. **Preparation for Administration:** IV use: Reconstitute each vial containing 150 mg of colistin base activity with 2 mL of SWFI resulting in a concentration of 75 mg colistin base activity/mL; swirl gently to avoid frothing. May further dilute in D_5W or NS for IV infusion. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Bronchoconstriction: Use of inhaled colistimethate (off-label route) may result in bronchoconstriction. Use with caution in patients with hyperactive airways; consider administration of a bronchodilator (eg, albuterol) within 15 minutes prior to administration. • CNS toxicity: Transient, reversible neurological disturbances may occur. Patients must be cautioned about performing tasks which require mental alertness. Dose reduction may reduce neurologic symptoms; monitor closely. • Renal toxicity: Dose-dependent nephrotoxicity has been reported, generally reversible upon discontinuation of treatment. Withhold treatment if signs of renal impairment occur during treatment. • Respiratory arrest: Respiratory arrest has been reported with use; impaired renal function may increase the risk for neuromuscular blockade and apnea. • Superinfection: In Prolonged use. ***Disease-related concerns:*** • Renal impairment: Use with caution in patients with preexisting renal impairment; dosage adjustments are recommended. Impaired renal function may increase the risk for respiratory arrest. ***Other warnings/precautions:*** • Appropriate use: Inhalation (off-label route): Once mixed, colistimethate begins conversion to bioactive colistin, a component of which may result in severe pulmonary toxicity. Solutions for inhalation must be mixed immediately prior to administration and used within 24 hours to reduce the incidence of pulmonary toxicity. • Appropriate use: IV: Use only to prevent or treat infections strongly suspected or proven to be caused by susceptible bacteria to minimize development of bacterial drug resistance. • Safety: Potential for dosing errors due to lack of standardization in literature when referring to product and dose; colistimethate (inactive prodrug) and colistin base strengths are not interchangeable; verify prescribed dose is expressed in terms of colistin base activity prior to dispensing.
Storage	Store intact vials at 20-25°C; excursions permitted to 15-30°C. Reconstituted vials may be refrigerated at 2°C to 8°C or stored at 20°C to 25°C for up to 7 days. Solutions for infusion should be freshly prepared in D_5NS, D_5W, LR, or NS; do not use beyond 24 hours. Refer to manufacturer PIL if there are specific considerations.

5. Dapsone

Generic Name	Dapsone
Dosage form/strengths	Tablets 50mg, 100mg Topical Gel 5%
Route of administration	*Oral, Topical*
Pharmacologic category	Antibiotic, Miscellaneous ATC (Topical): D10AX05 Atc (Systemic): J04BA02
Indications	Treatment of leprosy (due to susceptible strains of Mycobacterium leprae) and dermatitis herpetiformis
Dosage Regimen	**Adult dosing** • **Dermatitis herpetiformis: Oral:** Start at 50 mg daily, increase to 300 mg daily, or higher to achieve full control, reduce to minimum maintenance dosage as soon as possible • **Leprosy: Oral:** ***Tuberculoid (paucibacillary):*** – National Hansen's Disease Program 2016: 100 mg daily in combination with rifampin for 12 months. – World Health Organization: 100 mg daily in combination with rifampin for 6 months (WHO 2012). ***Lepromatous (multibacillary):*** – National Hansen's Disease Program 2016: 100 mg daily in combination with rifampin and clofazimine for 24 months. – World Health Organization: 100 mg daily in combination with rifampin and clofazimine for 12 months (WHO 2012). **Dosing: Pediatric** • **Dermatitis herpetiformis:** **Infants, Children, and Adolescents:** **Oral: Initial**: 0.5 to 2 mg/kg/day in 1 to 2 divided doses; maximum initial daily dose in adults: 50 mg/day; increase dose as needed to achieve control; usual adult dose: 300 mg/dose; once lesions controlled, some have reported that dose may be decreased as tolerated for chronic therapy to a reported range: 0.125 to 0.5 mg/kg/day • **Leprosy (Hansen's disease):** **Note:** Treatment should be managed in consultation with a leprosy expert; use of multidrug therapy is important to prevent drug resistance. Recommended duration varies: **Paucibacillary (Tuberculoid) leprosy (1 to 5 patches):** – National Hansen's Disease Program Recommendations 2018: Infants, Children, and Adolescents: Oral: 1 mg/kg/dose once daily for 12 months; maximum dose: 100 mg/dose; use in combination with rifampin. – WHO Recommendations (WHO 2016): Infants and Children <10 years and weighing <20 kg: Oral: 2 mg/kg/dose once daily for 6 months; use in combination with rifampin Children ≥10 years and Adolescents ≤14 years: 20 to 40 kg: Oral: 25 mg once daily for 6 months; use in combination with rifampin >40 kg: Oral: 50 mg once daily for 6 months; use in combination with rifampin

	Adolescents >14 years: Oral: 100 mg once daily for 6 months; use in combination with rifampin **Multibacillary (Lepromatous) leprosy (≥6 patches):** – National Hansen's Disease Program Recommendations 2018: Infants, Children, and Adolescents: Oral: 1 mg/kg/dose once daily for 24 months; maximum dose: 100 mg/dose; use in combination with rifampin and clofazimine. – WHO Recommendations (WHO 2016): Infants and Children <10 years and weighing <20 kg: Oral: 2 mg/kg/dose once daily for 12 months; use in combination with rifampin and clofazimine Children ≥10 years and Adolescents ≤14 years: 20 to 40 kg: Oral: 25 mg once daily for 12 months; use in combination with rifampin and clofazimine >40 kg: Oral: 50 mg once daily for 12 months; use in combination with rifampin and clofazimine Adolescents >14 years: Oral: 100 mg once daily for 12 months; use in combination with rifampin and clofazimine
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments available; use with caution
Contra-indications	Hypersensitivity to dapsone or any component of the formulation. *Canadian labeling:* Additional contraindications (not in US labeling): Advanced amyloidosis of the kidneys.
Adverse Drug Reactions	>10%: **Hematologic**: Reticulocyte increase (2% to 12%), hemolysis (>10%; dose related; seen in patients with and without G6PD deficiency), hemoglobin decrease (>10%; 1-2 g/dL; almost all patients), methemoglobinemia (>10%), red cell life span shortened (>10%), Agranulocytosis, anemia, leukopenia, pure red cell aplasia (case report) **Cardiovascular:** Tachycardia **Central nervous system:** Fever, headache, insomnia, psychosis, vertigo **Dermatologic**: Bullous and exfoliative dermatitis, erythema nodosum, exfoliative dermatitis, morbilliform and scarlatiniform reactions, phototoxicity, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria **Endocrine & metabolic**: Hypoalbuminemia (without proteinuria), male infertility **Gastrointestinal:** Abdominal pain, nausea, pancreatitis, vomiting **Hepatic:** Cholestatic jaundice, hepatitis N**euromuscular & skeletal:** Lower motor neuron toxicity (prolonged therapy), lupus-like syndrome, peripheral neuropathy (rare, nonleprosy patients) O**phthalmic**: Blurred vision **Otic:** Tinnitus **Renal**: Albuminuria, nephrotic syndrome, renal papillary necrosis **Respiratory**: Interstitial pneumonitis, pulmonary eosinophilia **Miscellaneous:** Infectious mononucleosis-like syndrome (rash, fever, lymphadenopathy, hepatic dysfunction)
Monitoring Parameters	Check G6PD levels (prior to initiation); CBC (weekly for first month, monthly for 6 months and semiannually thereafter); reticulocyte counts; liver function tests (baseline and periodic). Monitor patients for signs of jaundice, hemolysis, and blood dyscrasias. If the patient is diabetic, consider alternative methods to monitor diabetes control other than HbA_{1C}
Drug Interactions	***Risk X: Avoid combination*** Cholera Vaccine, BCG (Intravesical) ***Risk D: Consider therapy modification***

	Antimalarial Agents, Dabrafenib, Enzalutamide, Mitotane, Sodium Picosulfate, Typhoid Vaccine ***Risk C: Monitor therapy*** BCG Vaccine (Immunization) Atazanavir CYP3A4 Inducers, Deferasirox Ivosidenib Lactobacillus And Estriol Local Anesthetics, Nitric Oxide, Prilocaine, Probenecid, Sarilumab Siltuximab, Sodium Nitrite, Tocilizumab, Trimethoprim
Pregnancy	**Pregnancy Risk Factor C** Hemolytic reactions have been reported in neonates. Due to the potential for serious adverse effects in a nursing infant, a decision should be made to discontinue nursing or discontinue the drug, taking into consideration the importance of the drug to the mother.
Administration	**Administration: Oral** Administer with meals if GI upset occurs. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Blood dyscrasias: Aplastic anemia, agranulocytosis and other severe blood dyscrasias (some fatal) have been reported; monitor for signs/symptoms (eg, fever, sore throat, pallor, purpura, jaundice). Closely monitor CBC and discontinue therapy if a significant reduction in leukocytes, platelets, or hemopoiesis is seen. • Dermatologic reactions: Serious dermatologic reactions, including toxic erythema, erythema multiforme, toxic epidermal necrolysis, morbilliform and scarlatiniform reactions, urticaria, and erythema nodosum have been reported rarely. Discontinue therapy if new or severe dermatologic reactions occur; leprosy reactional states (eg, erythema nodosum leprosum) do not require discontinuation. • Hepatic effects: Toxic hepatitis and cholestatic jaundice have been reported; hyperbilirubinemia may occur more frequently in G6PD deficient patients. Monitor liver function; discontinue use if abnormalities occur. • Peripheral neuropathy: Motor loss and muscle weakness have been reported; discontinue use if symptoms of peripheral neuropathy develop. Recovery after discontinuation is usually complete; some patients may tolerate retreatment at reduced doses. • Sulfonamide allergy: Use with caution in patients with hypersensitivity to other sulfonamides; sulfone reactions may also occur as potentially fatal hypersensitivity reactions, requiring drug discontinuation. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Anemia: Use with caution in patients with severe anemia; treat prior to therapy. • Diabetes mellitus: Dapsone may artificially lower HbA_{1C} by reducing erythrocyte survival time through hemolysis. ***Special populations:*** • G6PD deficiency: Use with caution in patients with G6PD deficiency; dose-related hemolysis and methemoglobinemia may occur. • Hemoglobin M deficiency: Use with caution in patients with hemoglobin M deficiency. • Methemoglobin reductase deficiency: Use with caution in patients with methemoglobin reductase deficiency
Storage	Store at 20°C to 25°C. Protect from light. Refer to manufacturer PIL if there are specific considerations.

6. Diloxanide

Generic Name	Diloxanide
Dosage form/strengths	Tablets 500mg
Route of administration	*oral*
Pharmacologic category	Antiprotozoal (systemic) ATC: P01AC01
Indications	Treatment of intestinal amoebiasis. It is given alone in the treatment of asymptomatic cyst passers or after an amoebicide that acts in the tissues, such as metronidazole, in patients with symptomatic (invasive) amoebiasis.
Dosage Regimen	**Usual adult and adolescent dose** Diloxanide furoate is given orally in a dosage of 500 mg three times daily for 10 days. The course of treatment may be repeated if necessary. **Usual pediatric dose** Children up to 12 years of age: Oral, 20 mg per kg of body weight per day given in three divided doses for ten days. (maximum: 1,500 mg/day).
Dosage adjustment	Elimination Renal (90%, rapidly excreted as glucuronide metabolite). 10% is excreted in the feces as diloxanide.
Contra-indications	Hypersensitivity.
Adverse Drug Reactions	Flatulence is the most common adverse effect during treatment with diloxanide furoate. Vomiting, pruritus, and urticaria may occasionally occur.
Monitoring Parameters	fecal examination may be required prior to treatment to establish the diagnosis; follow-up stool examinations should be done no earlier than 2 weeks after the end of treatment to determine efficacy of treatment
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	The safety of diloxanide in pregnancy and lactation has not been established. Use of other agents is preferred
Administration	Taking with meals to minimize gastrointestinal irritation Compliance with full course of therapy Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • CNS effects: May cause CNS effects such as dizziness or headache, which may impair physical or mental abilities; patients must be cautioned about performing tasks that require mental alertness (eg, operating machinery or driving).
Storage	preferably between 15 and 30 °C in a well-closed container. Protect from light Refer to manufacturer PIL if there are specific considerations.

7. Doxycycline

Access Group

Generic Name	Doxycycline
Dosage form/strengths	Capsules 100mg Tablets 50mg, 100mg, 200mg
Route of administration	*Oral*
Pharmacologic category	Antibiotic, Tetracycline Derivative ATC: J01AA02
Indications	**Acne:** Adjunctive therapy in severe acne. **Actinomycosis:** Treatment of actinomycosis caused by *Actinomyces israelii* when penicillin is contraindicated. **Acute intestinal amebiasis:** Adjunct to amebicides in acute intestinal amebiasis. **Anthrax, including inhalational anthrax (postexposure)** **Cholera:** Treatment of cholera infections caused by *Vibrio cholerae*. ***Clostridium:*** Treatment of infections caused by *Clostridium* spp. when penicillin is contraindicated. **Gram-negative infections:** Treatment of infections caused by *Escherichia coli*, *Enterobacter aerogenes*, *Shigella* spp., *Acinetobacter* spp., *Klebsiella* spp. (respiratory and urinary infections), and *Bacteroides* spp.; *Neisseria meningitidis* (when penicillin is contraindicated). **Gram-positive infections:** Treatment of infections caused by *Streptococcus* spp., when susceptible. **Listeriosis:** Treatment of listeriosis due to *Listeria monocytogenes* when penicillin is contraindicated. **Malaria, prophylaxis:** Prophylaxis of malaria due to *Plasmodium falciparum* in short-term travelers (under 4 months) to areas with chloroquine and/or pyrimethamine-sulfadoxine-resistant strains. **Mycoplasma pneumoniae:** Treatment of infections caused by *Mycoplasma pneumoniae*. **Ophthalmic infections:** Treatment of inclusion conjunctivitis or trachoma caused by *Chlamydia trachomatis*. **Relapsing fever:** Treatment of relapsing fever caused by *Borrelia recurrentis*. **Respiratory tract infections:** Treatment of respiratory infections caused by *Haemophilus influenzae*, *Klebsiella* spp., or *Mycoplasma pneumoniae*; treatment of upper respiratory tract infections caused by *Streptococcus pneumoniae*; respiratory infections caused by *Staphylococcus aureus* (doxycycline is not the drug of choice in the treatment of any type of staphylococcal infection). **Rickettsial infections:** Treatment of Rocky Mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox, and tick fevers caused by *Rickettsiae*. **Sexually transmitted infections** **Note:** The CDC sexually transmitted disease guidelines recommend dual antimicrobial therapy be used for uncomplicated gonorrhea due to *N. gonorrhea* resistance concerns; ceftriaxone is the preferred cephalosporin and doxycycline is an alternative option for the second antimicrobial only in cases of azithromycin allergy (CDC). **Skin and skin structure infections (Avidoxy only):** Treatment of skin and skin structure infections caused by *Staphylococcus aureus* (doxycycline is not the drug of choice in the treatment of any type of staphylococcal infection). **Vincent infection:** Treatment of Vincent infection caused by *Fusobacterium fusiforme* when penicillin is contraindicated.

	Yaws: Treatment of yaws caused by *Treponema pallidum* subspecies *pertenue* when penicillin is contraindicated. **Zoonotic infections**
Dosage Regimen	**Dosing: Adult** **Note:** Doxycycline is available as hyclate, monohydrate, and calcium salts. All doses are expressed as doxycycline base. **Usual dosage range:** **Oral:** IR and most ER formulations: 100 to 200 mg/day in 1 to 2 divided doses. **Note:** 120 mg of modified polymer coated tablet (Doryx MPC) is equivalent to 100 mg conventional delayed-release tablet. **Dosing: Pediatric** **Note:** Doxycycline is available as hyclate, monohydrate, and calcium salts. All doses are expressed as doxycycline base. **General dosing:** Children and Adolescents: Oral, IV: 2.2 mg/kg/dose every 12 hours, maximum dose: 100 mg/dose. **Note:** Use of doxycycline in children <8 years should be reserved for severe, potentially life-threatening infections, or when better alternatives are unavailable
Dosage adjustment	**Dosing: Renal Impairment:** No dosage adjustment necessary **Dosing: Hepatic Impairment: Adult** Severe hepatic impairment require caution. Specific dosage adjustments have not been studied
Contra-indications	○ Hypersensitivity to doxycycline, other tetracyclines, or any component of the formulation ○ Periostat, Apprilon [Canadian products]: Additional contraindications: Use in infants and children <8 years of age or during second or third trimester of pregnancy; breast-feeding
Adverse Drug Reactions	Cardiovascular: Hypertension (3%) Central nervous system: Anxiety (2%), pain (2%) Endocrine & metabolic: Increased lactate dehydrogenase (2%), increased serum glucose (1%) Gastrointestinal: Diarrhea (5%), upper abdominal pain (2%), abdominal distention (1%), abdominal pain (1%), xerostomia (1%) Hepatic: Increased serum aspartate aminotransferase (2%) Infection: Fungal infection (2%), influenza (2%) Neuromuscular & skeletal: Back pain (1%) Respiratory: Nasopharyngitis (5%), sinusitis (3%), nasal congestion (2%), sinus headache (1%
Monitoring Parameters	CBC, renal and liver function tests periodically with prolonged therapy. When used as part of alternative treatment for gonococcal infection, test of cure 7 days after dose
Drug Interactions	**Risk X: Avoid combination** Aminolevulinic Acid (Systemic) Methoxyflurane Cholera Vaccine BCG (Intravesical) Retinoic Acid Derivatives Strontium Ranelate Sodium Picosulfate **Risk D: Consider therapy modification** Antacids Bismuth Subcitrate Bismuth Subsalicylate Calcium Salts Fosphenytoin Carbamazepine Iron Preparations Magnesium Salts Multivitamins/Minerals (With AE, No Iron) Sucralfate Sucroferric Oxyhydroxide Typhoid Vaccine
Pregnancy and Lactation	**Pregnancy factor** D there is not likely to be harm in short-term use of doxycycline during lactation. avoid prolonged (>21 days) or repeat courses during nursing. Monitor the infant for rash and for possible effects on the gastrointestinal flora, such as diarrhea or candidiasis (thrush, diaper rash).

Administration	**Administration: Oral** In general, administer with meals to decrease GI upset; however, some manufacturer labeling recommends administration on an empty stomach. Administer capsule and tablet with at least glass of water and have patient sit up for at least 30 minutes or 1 to 2 hours after taking to reduce the risk of esophageal irritation and ulceration. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***concerns related to adverse effects:*** • GI inflammation/ulceration: Esophagitis and ulcerations (sometimes severe) may occur; patients with dysphagia and/or retrosternal pain may require assessment for esophageal lesions. • Hepatotoxicity: Rarely occurs; if symptomatic, assess LFTs and discontinue drug. • Hypersensitivity syndromes: Severe skin reactions (eg, exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms [DRESS]) have been reported. Discontinue therapy for serious hypersensitivity reactions. • Increased BUN: May be associated with increases in BUN secondary to antianabolic effects; this does not occur with use of doxycycline in patients with renal impairment. • Intracranial hypertension: Intracranial hypertension (pseudotumor cerebri) has been reported; headache, blurred vision, diplopia, vision loss, and/or papilledema may occur. Women of childbearing age who are overweight or have a history of intracranial hypertension are at greater risk. Intracranial hypertension typically resolves after discontinuation of treatment; however, permanent visual loss is possible. If visual symptoms develop during treatment, prompt ophthalmologic evaluation is warranted. Intracranial pressure can remain elevated for weeks after drug discontinuation; monitor patient until stable. • Photosensitivity: May cause photosensitivity; discontinue at first sign of skin erythema. Use skin protection and avoid prolonged exposure to sunlight and ultraviolet light. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. • Tissue hyperpigmentation: May induce hyperpigmentation in many organs, including nails, bone, skin (diffuse pigmentation as well as over sites of scars and injury), eyes, thyroid, visceral tissue, oral cavity (adult teeth, mucosa, alveolar bone), sclerae, and heart valves independently of time or amount of drug administration. ***Disease-related concerns*** • Oral candidiasis: Safety and effectiveness have not been established for treatment of periodontitis in patients with coexistent oral candidiasis; use with caution in patients with a history or predisposition to oral candidiasis. ***Special populations:*** • Pediatric: May cause tissue hyperpigmentation, tooth enamel hypoplasia, or permanent tooth discoloration (more common with long-term use, but observed with repeated, short courses) when used during tooth development (last half of pregnancy, infancy, and childhood ≤8 years of age). Recommended in prevention and treatment of anthrax, treatment of tickborne rickettsial diseases, and Q fever. ***Other warnings/precautions:*** • Appropriate use: Acne: The American Academy of Dermatology acne guidelines recommend doxycycline as adjunctive treatment for moderate and severe acne and forms of inflammatory acne that are resistant to topical treatments. Concomitant topical therapy with benzoyl peroxide or a retinoid should be administered with systemic antibiotic therapy (eg, doxycycline) and continued for maintenance after the antibiotic course is completed. • Limitations of use: Malaria prophylaxis: Doxycycline does not completely suppress asexual blood stages of *Plasmodium* strains; does not suppress *P. falciparum's* sexual blood stage gametocytes.

	Patients completing a regimen may still transmit the infection to mosquitoes outside endemic areas.
Storage	Capsule, tablet: Store at 20°C to 25°C; excursions permitted between 15°C and 30°C. Protect from light and moisture. Refer to manufacturer PIL if there are specific considerations.

8. Fosfomycin

Watch Group

Generic Name	Fosfomycin
Dosage form/strengths	Granules for Oral Solution: 3gm
Route of administration	oral
Pharmacologic category	Antibiotic, Miscellaneous ATC: J01XX01
Indications	**Cystitis, acute uncomplicated:** Treatment of uncomplicated urinary tract infections (acute cystitis) in women due to susceptible strains of *Escherichia coli* and *Enterococcus faecalis*.
Dosage Regimen	**Dosing: Adult** *Cystitis, acute uncomplicated or acute simple cystitis (infection limited to the bladder without signs/symptoms of upper tract, prostate, or systemic infection), treatment:* ***Oral:*** *3 g as a single dose* **Dosing: Pediatric** **Urinary tract infection, uncomplicated:** Limited data available: **Note:** Oral formulation should not be used for pyelonephritis or perinephric abscess. Children <12 years: Oral: 2 g as a single dose. Children ≥12 years and Adolescents: Oral: 3g as a single dose
Dosage adjustment	**Dosing: Altered Kidney Function: Adult** **Oral:** No dosage adjustment necessary for any degree of kidney dysfunction (expert opinion). However, elimination is significantly prolonged in patients with CrCl <50 mL/minute; monitor closely for adverse effects and tolerability, particularly with prolonged therapy. **Dosing: Hepatic Impairment: Adult** Oral: There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to fosfomycin or any component of the formulation
Adverse Drug Reactions	**1% to 10%:** Central nervous system: Headache (4% to 10%), pain (2%), dizziness (1% to 2%) Dermatologic: Skin rash (1%) Gastrointestinal: Diarrhea (9% to 10%), nausea (4% to 5%), abdominal pain (2%), dyspepsia (1% to 2%) Genitourinary: Vaginitis (6% to 8%), dysmenorrhea (3%) Neuromuscular & skeletal: Back pain (3%), weakness (1% to 2%) Respiratory: Rhinitis (5%), pharyngitis (3%)
Monitoring Parameters	No monitoring data needed.
Drug Interactions	**Risk X: Avoid combination** BCG (Intravesical) Cholera Vaccine **Risk D: Consider therapy modification** Sodium Picosulfate Typhoid Vaccine
Pregnancy and Lactation	**Pregnancy Category** B - No proven risk in humans. This drug should be used during pregnancy only if clearly needed and the benefit outweighs the risk. Due to the potential for serious adverse reactions in the breastfed infant, a decision should be made whether to discontinue breastfeeding or to discontinue the drug, taking into account the

	importance of treatment to the mother.
Administration	**Administration: Oral** Oral: Oral packet: Do not administer in its dry form; must be mixed with water prior to administration. May be administered without regard to meals. Pour contents of 3 g packet into 90 to 120 mL of water (not hot) and stir to dissolve; the resultant concentration is 25 to 33.3 mg/mL. Measure appropriate volume for desired dose and take immediately. Discard any remaining solution. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity: Hypersensitivity reactions, including anaphylactic shock, have been reported (rare). Discontinue use and institute supportive measures at the first sign(s) of a hypersensitivity reaction. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *Clostridioides difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment.
Storage	Oral packet: Store at 25°C; excursions are permitted between 15°C and 30°C Refer to manufacturer PIL if there are specific considerations.

9. Lincomycin

Watch Group

Generic Name	Lincomycin
Dosage form/strengths	Lincomycin 300 mg / ml ampoules
Route of administration	I.V ,I.M
Pharmacologic category	Antibiotic, Lincosamide ATC: J01FF02
Indications	-Treatment of serious infections caused by susceptible strains of streptococci, pneumococci, and staphylococci. -Use should be reserved for patients with penicillin allergy or other patients for whom a penicillin is inappropriate.
Dosage Regimen	**-Adult Dose:** **-Serious Bacterial infection:** **IM:** 600 mg every 12 to 24 hours **IV:** 600 mg to 1 g every 8 to 12 hours (maximum dose: 8 g daily) **-Pediatric Dose:** **-Serious Bacterial infection: Infants, Children, and Adolescents:** **-IM:** 10 mg/kg/dose every 12 to 24 hours. **-IV:** 10 to 20 mg/kg/day in divided doses every 8 to 12 hours
Dosage adjustment	**-Adult:** **-Renal Impairment:** -Mild to moderate impairment: no dosage adjustments availabla. -Severe impairment: Use with caution; decrease dose by 70% to 75% **-Hepatic impairment:** -No dosage adjustments available; use with caution
Contra-indications	-Hypersensitivity to lincomycin, clindamycin, or any component of the formulation.
Adverse Drug Reactions	-Frequency not defined: Gastrointestinal: Colitis, severe colitis
Monitoring Parameters	-Change in bowel frequency or consistency (eg, diarrhea) -Baseline serum creatinine and liver function tests (LFTs) -Periodical renal function and LFTs, complete blood cell count (CBC) with differential in case of prolonged therapy.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine, Erythromycin (Systemic), Mecamylamine ***Risk D: Consider therapy modification*** Sodium Picosulfate, Typhoid Vaccine
Pregnancy and Lactation	Pregnancy category C -Crosses the placenta at term and can be detected in cord blood and the amniotic fluid. No effects on the newborn were observed. - May also contain benzyl alcohol, which may cross the placenta. Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. Excreted into human milk but The effects in the nursing infant are unknown.

Administration	**-Adult:** **- IM:** Injection as deep IM into large muscle mass. **-I. V:** Dilute with compatible solution (eg, D_5W) to a final concentration of 6 to 10 mg/mL. Each gram of lincomycin for IV administration should be diluted with at least 100 mL of a compatible solution (eg, D5W) Administer as an intermittent infusion over at least 1 hour per gram **-Pediatric:** Same as adult but administer as an intermittent infusion over ≥1 hour Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Colitis: [US Boxed Warning]: *C. difficile*-associated diarrhea (CDAD) has been reported. May range in severity from mild to severe (and possibly fatal). Lincomycin therapy should be reserved for serious infections for which less toxic antimicrobial agents are inappropriate. • Hypersensitivity reactions: Hypersensitivity reactions, including anaphylaxis and severe cutaneous adverse reactions (including Stevens-Johnson syndrome [SJS], toxic epidermal necrolysis [TEN], acute generalized exanthematous pustulosis [AGEP], and erythema multiforme), have been reported. Discontinue use and institute appropriate therapy if allergic reaction occurs. • Superinfection: Prolonged use may result in bacterial or fungal superinfection, particularly yeasts. Concomitant antimonilial infection treatment should be given in patients with preexisting monilial infections. ***Disease-related concerns:*** • Allergies: Use with caution in patients with significant allergies. • Asthma: Use with caution in patients with a history of asthma. • Gastrointestinal disease: Use with caution in patients with a history of gastrointestinal disease (particularly colitis). • Hepatic impairment: Use with caution in patients with hepatic impairment; half-life may be prolonged 2-fold. • Renal impairment: Use with caution in patients with renal impairment; half-life may be prolonged; dosage adjustment necessary with severe impairment. ***Special populations:*** • Elderly: Use with caution in the elderly; monitor closely for bowel changes. ***Dosage form specific issues:*** • Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling. ***Other warnings/precautions:*** • Administration: Do not use undiluted as an IV bolus. • Appropriate use: Generally reserved for use when treatment with other antibiotics is inappropriate. Not appropriate for use in the treatment of meningitis due to inadequate penetration into the cerebrospinal fluid.
Storage	-Store at 20°C to 25°C. -Once diluted in dextran 6% in NS, D5NS, D10NS, D5W, D10W, or Ringer's, may store for 24 hours at room temperature. Refer to manufacturer PIL if there are specific considerations.

10. Linezolid

Reserve Group

Generic Name	Linezolid		
Dosage form/strengths	Oral suspension 100mg/5ml Tablets 200mg, 600mg Vial 600mg		
Route of administration	*IV, oral*		
Pharmacologic category	Antibiotic, Oxazolidinone ATC: J01XX08		
Indications	**Enterococcal infections (vancomycin-resistant):** Treatment of vancomycin-resistant *Enterococcus faecium* infections, including cases with concurrent bacteremia. **Pneumonia:** Treatment of community-acquired pneumonia caused by *Streptococcus pneumoniae*, including cases with concurrent bacteremia, or *Staphylococcus aureus* (methicillin-susceptible isolates only). Treatment of hospital-acquired or health care-associated pneumonia caused by *S. aureus* (methicillin-susceptible and methicillin-resistant isolates) or *S. pneumoniae*. **Skin and skin structure infections:** *Complicated:* Treatment of complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis. *Uncomplicated:* Treatment of uncomplicated skin and skin structure infections caused by *S. aureus* (methicillin-susceptible isolates) or *S. pyogenes*.		
Dosage Regimen	**Adult Dosing:** **General dose: IV/Oral:** 600mg/12 hr **Pediatric Patients** **General Dosage for Neonates** **Oral or IV** neonates <7 days of age: 10 mg/kg every 12 hours; may consider 10 mg/kg every 8 hours in those with inadequate response. All neonates ≥7 days of age: 10 mg/kg every 8 hours **General Dosage for Infants and Children** **Oral or IV** infants and children less than 12 years: 10 mg/kg every 8 hours adolescents ≥12 years of age :600 mg every 12 hours **Note**: Linezolid is not a preferred agent for the treatment of infections requiring prolonged therapy as the risk of serious hematologic and neurologic toxicity increases after >2 weeks and >4 weeks of therapy, respectively.		
Dosage adjustment	**Dosing: Renal Impairment:** Mild to severe impairment: No dosage adjustment necessary. The two primary metabolites accumulate in patients with renal impairment but the clinical significance is unknown; use with caution. Consider therapeutic drug monitoring in this population		

	Hemodialysis patients: Administer linezolid doses after dialysis session. **Dosing: Hepatic Impairment: Adult** Mild to moderate impairment: No dosage adjustment necessary. Severe impairment (Child-Pugh class C): Dosage adjustments has not been studied.
Contra-indications	Hypersensitivity to linezolid or any component of the formulation; concurrent use or within 2 weeks of MAO inhibitors
Adverse Drug Reactions	**>10%:** Gastrointestinal: Diarrhea (8% to 11%) Hematologic & oncologic: Decreased white blood cells, decreased platelet count **1% to 10%:** Central nervous system: Headache, dizziness, vertigo Dermatologic: Skin rash, pruritus Endocrine & metabolic: Increased amylase, increased lactate dehydrogenase Gastrointestinal: Vomiting, nausea, increased serum lipase, loose stools, abdominal pain, oral candidiasis, dysgeusia, tongue discoloration Genitourinary: Vulvovaginal candidiasis Hematologic & oncologic: Anemia, decreased neutrophils, thrombocytopenia, eosinophilia Hepatic: Increased serum ALT, increased serum bilirubin, increased serum AST, increased serum alkaline phosphatase, abnormal hepatic function tests Infection: Fungal infection Renal: Increased blood urea nitrogen, increased serum creatinine
Monitoring Parameters	Weekly CBC, peripheral sensory and visual function with extended therapy (≥3 months) or in patients with new onset neuropathic or visual symptoms, regardless of therapy length; in patients with renal impairment, monitor for hematopoietic (eg, anemia, leukopenia, thrombocytopenia) and neuropathic (eg, peripheral neuropathy, optic neuritis) adverse events when administering for extended periods. Periodic serum bicarbonate with extended therapy. Consider monitoring lactic acid in patients with renal dysfunction
Drug Interactions	***Risk X: Avoid combination*** Alcohol (Ethyl) Amphetamines Atomoxetine Atropine BCG (Intravesical) Buprenorphine Buspirone Carbamazepine Cholera Vaccine Codeine Cyclobenzaprine Cyproheptadine Dapoxetine Atomoxetine Atropine BCG (Intravesical) Bezafibrate Buprenorphine Buspirone Carbamazepine Cholera Vaccine Codeine Cyclobenzaprine Cyproheptadine Dapoxetine Deutetrabenazine Dexmethylphenidate Dextromethorphan Dihydrocodeine Diethylpropion Dipyrone Droxidopa Epinephrine (Oral Inhalation) Fenfluramine Guanethidine Hydromorphone Indoramin Isometheptene Levodopa-Containing Products Levomethadone Levonordefrin Maprotiline Meptazinol Mequitazine Methadone Methyldopa Methylene Blue Methylphenidate Metoclopramide Mianserin Monoamine Oxidase Inhibitors Morphine Nefazodone Levonordefrin Maprotiline Meptazinol Mequitazine Methadone Methyldopa Methylene Blue Methylphenidate Metoclopramide Mianserin Monoamine Oxidase Inhibitors Morphine Nefazodone Nefopam Normethadone Opicapone Opium Oxycodone Oxymorphone Ozanimod Pheniramine Pholcodine Pizotifen Reboxetine Selective Serotonin Reuptake Inhibitors Triptans Serotonin/Norepinephrine Reuptake Inhibitors Solriamfetol Sufentanil Tapentadol Tetrabenazine Tetrahydrozoline Tianeptine Tricyclic Antidepressants Tryptophan Valbenazine ***Risk D: Consider therapy modification*** Benzhydrocodone COMT Inhibitors Deferiprone DOPamine HYDROcodone Iohexol Iomeprol Iopamidol Lithium Remifentanil Reserpine Ropeginterferon Alfa-2b Serotonergic Opioids Sodium Picosulfate Sympathomimetics Typhoid Vaccine
Pregnancy and Lactation	**pregnancy category** C Animal reproduction studies have shown an adverse effect on the fetus and there are no

	adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. Use of this drug is not a reason to discontinue breastfeeding if it is required by the mother; alternate therapy may be preferred, especially if the nursing infant is premature or younger than 1 month.
Administration	**Administration: IV** Administer intravenous infusion over 30 to 120 minutes. When the same intravenous line is used for sequential infusion of other medications, flush line with D_5W, NS, or LR before and after infusing linezolid. The yellow color of the injection may intensify over time without affecting potency. **Administration: Oral** Administer without regard to meals. Oral suspension: Invert gently to mix prior to administration, do not shake. Single-use containers of linezolid injection for IV infusion should be administered without further dilution. Do not use the containers in series connections; do not introduce additives into the solution. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • **Lactic acidosis** • **Myelosuppression**: may be dependent on duration of therapy (generally >2 weeks of treatment). Weekly CBC monitoring is recommended; Thrombocytopenia is the most frequently observed blood dyscrasia. • **Peripheral and optic neuropathy (with vision loss)** • **Serotonin syndrome**: Symptoms of agitation, confusion, hallucinations, hyper-reflexia, myoclonus, shivering, and tachycardia may occur with concomitant proserotonergic drugs, agents which reduce linezolid's metabolism, or in patients with carcinoid syndrome. Avoid use in such patients unless clinically appropriate and under close monitoring for signs/symptoms of serotonin syndrome or neuroleptic malignant syndrome-like reactions. • **Superinfection**: Prolonged use ***Disease-related concerns:*** • Carcinoid syndrome: Use with caution and closely monitor for serotonin syndrome in patients with carcinoid syndrome. • Diabetes mellitus: Hypoglycemic episodes have been reported; Dose reductions/discontinuation of concurrent hypoglycemic agents or discontinuation of linezolid may be required. • Hypertension • Hyperthyroidism • Pheochromocytoma: closely monitor blood pressure in patients with pheochromocytoma • Seizure disorder ***Special populations:*** • Pediatric: It is not recommend to use linezolid for empiric treatment of pediatric CNS infections since therapeutic linezolid concentrations are not consistently achieved or maintained in the CSF of patients with ventriculoperitoneal shunts. ***Other warnings/precautions:*** • Appropriate use: Unnecessary use may lead to the development of resistance to linezolid; consider alternatives before initiating outpatient treatment.
Storage	• Infusion: Store at 25°C. Protect from light and freezing. Keep infusion bags in overwrap until ready for use.

- Oral suspension: Store at 25°C; following reconstitution store at room temperature and use suspension within 21 days. Protect from light.
- Tablet: Store at 25°C. Protect from light and moisture.
- Refer to manufacturer PIL if there are specific considerations.

11. Metronidazole

Access Group

Generic Name	Metronidazole
Dosage form/ strengths	Suppository 1gm Vaginal suppository 500mg Vaginal gel 0.75% Oral suspension 125mg/5ml, 200mg/5ml Tablets 250mg, 500mg Vial 500mg
Route of administration	IV, Oral, rectal, intravaginal
Pharmacologic category	Amebicide; Antiprotozoal, Nitroimidazole
Indications	Amebiasis, Anaerobic bacterial infections (caused by Bacteroides spp., including the B. fragilis group), Surgical prophylaxis (colorectal surgery), Trichomoniasis
Dosage Regimen	**Dosing: Adult** **Amebiasis, intestinal (acute dysentery) or extraintestinal (liver abscess): Oral:** 500 to 750 mg every 8 hours for 7 to 10 days **Intra-abdominal infection: Oral, IV:** 500 mg every 8 hours as part of an appropriate combination regimen. Duration of therapy is for 4 to 7 days following adequate source control **Intracranial abscess (brain abscess, intracranial epidural abscess): IV:** 7.5 mg/kg (usually 500 mg) every 6 to 8 hours for 6 to 8 weeks **Pelvic inflammatory disease (PID):** *Mild to moderate PID*: **Oral:** 500 mg twice daily for 14 days **Skin and soft tissue infection:in combination with other appropriate agents** Necrotizing infection: **IV:** 500 mg every 6 hours Surgical site infection, incisional (eg, intestinal or GU tract; axilla or perineum), warranting anaerobic coverage: **IV:** 500 mg every 8 hours **Surgical prophylaxis:** **IV:** 500 mg within 60 minutes prior to surgical incision in combination with other antibiotics. **Trichomoniasis (index case and sex partner):** Initial treatment: **Oral:** 500 mg twice daily for 7 days. Persistent or recurrent infection (ie, treatment failure of nitroimidazole [eg, metronidazole]): **Oral:** 500 mg twice daily for 7 days **Dosing: Pediatric** **Note:** Some clinicians recommend using adjusted body weight in obese children. Dosing weight = IBW + 0.45 (TBW-IBW) **General dosing, susceptible infection**: Infants, Children, and Adolescents: Oral: 15 to 50 mg/kg/day in divided doses 3 times daily; maximum daily dose: 2,250 mg/day. IV: 22.5 to 40 mg/kg/day in divided doses 3 or 4 times daily; maximum daily dose: 4,000 mg/day.
Dosage adjustment	**Dosing: Renal Impairment:** No dosage adjustment necessary however, monitor closely for adverse effects due to accumulation of metabolites, particularly with prolonged courses of therapy **Dosing: Hepatic Impairment:** Mild or moderate impairment (Child-Pugh class A or B): No dosage adjustment necessary; use with

	caution and monitor for adverse events. **Severe impairment (Child-Pugh class C):** Tablets, injection: Reduce dose by 50%
Contra-indications	Hypersensitivity to metronidazole, nitroimidazole derivatives, or any component of the formulation; pregnant patients (first trimester) with trichomoniasis; use of disulfiram within the past 2 weeks; use of alcohol or propylene glycol-containing products during therapy or within 3 days of therapy discontinuation Active neurological disorders; history of blood dyscrasia; hypothyroidism; hypoadrenalism
Adverse Drug Reactions	**>10%:** Central nervous system: Headache (18%) Gastrointestinal: Nausea (10% to 12%) Genitourinary: Vaginitis (15%)
Monitoring Parameters	Monitor CBC with differential at baseline, during, and after prolonged or repeated courses of therapy. Monitor LFTs in patients with Cockayne syndrome. Closely monitor elderly patients and patients with severe hepatic impairment or ESRD for adverse reactions. Observe patients carefully if neurologic symptoms occur and consider discontinuation of therapy.
Drug Interactions	***Risk X: Avoid combination*** Alcohol BCG (Intravesical) Carbocisteine Cholera Vaccine: Disulfiram Dronabinol Mebendazole Products Containing Propylene Glycol ***Risk D: Consider therapy modification*** Busulfan Lopinavir Sodium Picosulfate Typhoid Vaccine Vitamin K Antagonists ***Risk C: Monitor therapy*** BCG Vaccine (Immunization) Fluorouracil Products: Fosphenytoin Lactobacillus and Estriol Lithium Mycophenolate Phenobarbital Phenytoin Primidone Tipranavir Tolbutamide Vecuronium
Pregnancy and Lactation	**Pregnancy Category B** If metronidazole is given, breastfeeding should be withheld for 12 to 24 hours after a single 2 g dose. Use of lower maternal doses may provide lower concentrations of metronidazole in breast milk and use can be considered in patients who are breastfeedin
Administration	**IV**: Infuse intravenously over 30 to 60 minutes. Avoid contact of drug solution with equipment containing aluminum. **Oral**: Administer with food to minimize stomach upset. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Carcinogenic: **[US Boxed Warning]:** Possibly carcinogenic based on animal data. Reserve use for conditions described in Use; unnecessary use should be avoided. • CNS effects: Severe neurological disturbances, including aseptic meningitis (may occur within hours of a dose), cerebellar symptoms (ataxia, dizziness, dysarthria), convulsive seizures, encephalopathy, optic neuropathy, and peripheral neuropathy (usually of sensory type and characterized by numbness or paresthesia of an extremity) have been reported. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. Candidiasis infection (known or unknown) may be more prominent during metronidazole treatment, antifungal treatment required. ***Disease-related concerns:*** • Blood dyscrasias: Use with caution in patients with or history of blood dyscrasias; agranulocytosis, leukopenia, and neutropenia have occurred. Monitor CBC with differential at baseline, during and after treatment.

	• Cockayne syndrome: Severe hepatotoxicity/acute hepatic failure (has been fatal) has been reported with systemic metronidazole in patients with Cockayne syndrome; onset is rapid after initiation of treatment. Use metronidazole only after risk vs benefit assessment and if there are no appropriate alternatives in patients with Cockayne syndrome. Obtain LFTs prior to treatment initiation, within the first 2 to 3 days of initiation, frequently during therapy, and after treatment is complete. Discontinue treatment if elevated LFTs occur and monitor until LFTs return to baseline. • Hepatic impairment: Use with caution in patients with hepatic impairment due to potential accumulation; dosage adjustment recommended in patients with severe hepatic impairment. • Renal impairment: Use with caution in patients with severe renal impairment or ESRD due to potential accumulation. Accumulated metabolites may be rapidly removed by hemodialysis; supplemental doses may be needed. • Seizure disorder: Use with caution in patients with a history of seizure disorder. ***Concurrent drug therapy issues:*** • Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information. ***Dosage-form specific issues:*** • Injection: Use injection with caution in patients with heart failure, edema, or other sodium-retaining states, including corticosteroid treatment due to high sodium content. In patients receiving continuous nasogastric secretion aspiration, sufficient metronidazole may be removed in the aspirate to cause a reduction in serum levels.
Storage	Oral: Store at 15°C to 25°C. Protect the tablets from light. Injection: Store at 20°C to 25°C. Protect from light. Avoid excessive heat. Do not refrigerate. Do not remove unit from overwrap until ready for use. Discard unused solution. Refer to manufacturer PIL if there are specific considerations.

12. Nitrofurantoin

Generic Name	Nitrofurantoin
Dosage form/strengths	Tablets 100mg Capsules 50mg, 100mg, 100mg retard
Route of administration	Oral
Pharmacologic category	Antibiotic, Miscellaneous ATC: J01XE01
Indications	Urinary Tract Infections (UTIs) • Cystitis, acute uncomplicated, treatment • Cystitis, uncomplicated, prophylaxis for recurrent infection
Dosage Regimen	**Adults** **Urinary Tract Infections (UTIs)** **Oral** 50–100 mg 4 times daily given for 7 days or for ≥3 days after urine becomes sterile. If used for long-term suppressive therapy: states 50–100 mg once daily at bedtime may be adequate. Dual-release capsules: 100 mg every 12 hours for 7 days **Cystitis, uncomplicated, prophylaxis for recurrent infection** ***Continuous prophylaxis:*** Oral: 50 to 100 mg once daily at bedtime. *Postcoital prophylaxis:* Females with cystitis temporally related to sexual intercourse: Oral: 50 to 100 mg as a single dose taken within 2 hours of sexual intercourse **Dosage** **Pediatric Patients** **Urinary Tract Infections (UTIs) in Children ≥1 Month of Age** **Oral** Capsules containing macrocrystals or suspension containing microcrystals: 5–7 mg/kg daily in 4 divided doses given for 7 days or for ≥3 days after urine becomes sterile. If used for long-term suppressive therapy: 1 mg/kg daily given as a single dose or in 2 equally divided doses may be adequate. **Urinary Tract Infections (UTIs) in Children >12 Years of Age** **Oral** Dual-release capsules: 100 mg every 12 hours for 7 days. **UTI, prophylaxis:** Infants, Children, and Adolescents: Oral: 1 to 2 mg/kg/day in a single dose (at bedtime) or divided twice daily; maximum daily dose: 100 mg/day.
Dosage adjustment	**Dosing: Renal Impairment:** Contraindicated in those with anuria, oliguria, or significant renal impairment CrCl ≥60 mL/minute: No dosage adjustment necessary. CrCl <60 mL/minute: Use is contraindicated. **Dosing: Hepatic Impairment:** There are no dosage adjustments available. Nitrofurantoin is associated with hepatotoxicity and should be used cautiously in patients with hepatic impairment.

Contra-indications	• Anuria, oliguria, or significant impairment of renal function (creatinine clearance [CrCl] <60 mL/minute or clinically significant elevated serum creatinine) • previous history of cholestatic jaundice or hepatic dysfunction associated with prior nitrofurantoin use; hypersensitivity to drug or any component of the formulation. • Because of the possibility of hemolytic anemia caused by immature erythrocyte enzyme systems (glutathione instability), the drug is contraindicated in pregnant patients at term (38 to 42 weeks gestation), during labor and delivery, or when the onset of labor is imminent; also contraindicated in neonates younger than 1 month of age
Adverse Drug Reactions	**1% to 10%:** Central nervous system: Headache (6%) Endocrine & metabolic: Increased serum phosphate (1% to 5%) Gastrointestinal: Nausea (8%), flatulence (2%) Hematologic & oncologic: Decreased hemoglobin (1-5%), eosinophilia (1- 5%) Hepatic: Increased serum alanine aminotransferase (1% to 5%), increased serum aspartate aminotransferase (1% to 5%)
Monitoring Parameters	Liver function
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine Magnesium Trisilicate Norfloxacin ***Risk D: Consider therapy modification*** Sodium Picosulfate Typhoid Vaccine ***Risk C: Monitor therapy*** BCG Vaccine Dapsone Eplerenone Lactobacillus and Estriol Local Anesthetics Nitric Oxide Probenecid Prilocaine Sodium Nitrite
Pregnancy and Lactation	**Pregnancy Risk Factor B** World Health Organization states that nitrofurantoin is compatible with breastfeeding for healthy full-term infants with monitoring for adverse reactions (eg, jaundice, hemolysis). However, patients taking nitrofurantoin should avoid breastfeeding premature neonates or neonates <1 month of age.
Administration	Administration: Oral Administer with meals to improve absorption and decrease adverse effects Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hepatic reactions: Rare, but severe and sometimes fatal hepatic reactions (eg, cholestatic jaundice, hepatitis, hepatic necrosis) have been associated with use (onset may be insidious); discontinue immediately if hepatitis occurs. Monitor liver function tests periodically. Use is contraindicated in patients with a history of nitrofurantoin associated cholestatic jaundice or hepatic dysfunction. • Optic neuritis: Postmarketing cases of optic neuritis have been reported. • Peripheral neuropathy: Has been associated with peripheral neuropathy (rare); risk may be increased in patients with anemia, renal impairment (CrCl <60 mL/minute), diabetes, vitamin B deficiency, debilitating disease, or electrolyte imbalance; use caution. • Pulmonary toxicity: Acute, subacute, or chronic (usually after 6 months of therapy) pulmonary reactions (possibly fatal) have been observed; if these occur, discontinue therapy immediately. Monitor closely for malaise, dyspnea, cough, fever, radiologic evidence of diffuse interstitial pneumonitis or fibrosis.

	• Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months post antibiotic treatment. ***Disease-related concerns:*** • Hemolytic anemia: Use caution in patients with G6PD deficiency; may be at increased risk for hemolytic anemia. Discontinue therapy if occurs. • Renal impairment: Urinary nitrofurantoin concentrations are variable in patients with impaired renal function. The Beers Criteria recommends avoiding use in geriatric patients ≥65 years with a CrCl <30 mL/minute (Beers Criteria. ***Concurrent drug therapy issues:*** • Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information. • Sedatives: Effects may be potentiated when used with other sedative drugs or ethanol. ***Special populations:*** • Elderly: Use in elderly patients, particularly females receiving long-term prophylaxis for recurrent UTIs, has also been associated with an increased risk of hepatic and pulmonary toxicity and peripheral neuropathy. Monitor closely for toxicities during use. • Pediatric: Use is contraindicated in children <1 month of age (at increased risk for hemolytic anemia).
Storage	Capsules: Store at controlled room temperature, 15°C to 30°C. Dispense in a tight container using a child-resistant closure. Refer to manufacturer PIL if there are specific considerations.

Watch Group

13. Oxytetracycline

Generic Name	Oxytetracycline
Dosage form/strengths	Capsules 250 mg Topical ointment 3.330 gm/100g
Route of administration	Oral ,Topical
Pharmacologic category	Tetracycline antibiotic ATC (Topical): D06AA03 ATC (Systemic): J01AA06
Indications	**-Treatment of infections caused by oxytetracycline-sensitive organisms including:** **-Respiratory tract infections:** Pneumonia, whooping cough and other lower respiratory tract infections due to susceptible strains of Streptococcus pneumoniae, Haemophilus influenzae, Klebsiella pneumoniae and other organisms. Mycoplasma pneumoniae pneumonia. Treatment of chronic bronchitis (including the prophylaxis of acute exacerbations). **-Urinary tract infections:** caused by susceptible strains of the Klebsiella species. Enterobacter species, Escherichia coli, Streptococcus faecalis and other organisms. **-Sexually transmitted diseases:** Infections due to Chlamydia trachomatis including uncomplicated urethral, endocervical or rectal infections. Non-gonococcal urethritis caused by Ureaplasma urealyticum. Oxytetracycline is also indicated in chancroid, granuloma inguinale and lymphogranuloma venereum. Oxytetracycline is an alternative drug in the treatment of gonorrhoea and syphilis. **-Skin Infections:** Acne vulgaris when antibiotic therapy is considered necessary and severe rosacea. **-Ophthalmic infections:** Trachoma, although the infectious agent, as judged by immunofluorescence, is not always eliminated. Inclusion conjunctivitis may be treated with oral oxytetracycline alone or in combination with topical agents. **-Rickettsial infections:** Rocky Mountain spotted fever, typhus group, Q fever and Coxiella endocarditis and tick fevers. **-Other infections:** Stagnant loop syndrome. Psittacosis, brucellosis (in combination with streptomycin), cholera, bubonic plague, louse and tick-borne relapsing fever, tularaemia, glanders, melioidosis and acute intestinal amoebiasis (as an adjunct to amoebicides).
Dosage Regimen	Oral: Adults (including the elderly) and children over 12 years: -Skin infections: 250-500mg daily in single or divided doses should be administered for at least 3 months in the treatment of acne vulgaris and severe rosacea. -Streptococcal infections: A therapeutic dose of oxytetracycline should be administered for at least 10 days -Brucellosis: 500mg four times daily accompanied by streptomycin. - Sexually transmitted diseases: 500mg four times daily for 7 days in the following infections: uncomplicated gonococcal infections (except anorectal infections in men); uncomplicated urethra; endocervical or rectal infection caused by Chlamydia trachomatis; non-gonoccocal urethritis caused by Ureaplasma urealyticum. -Acute epididymo-orchitis caused by Chlamydia trachomatis, or Neisseria gonorroeae: 500mg four times daily for 10 days -Primary and Secondary syphilis: 500mg four times daily for 15 days.
Dosage	**-Renal impairment:**

adjustment	-In general, the drug contraindicated in renal impairment -only if use of this class of drug is deemed absolutely essential. Total dosage should be decreased by reduction of recommended individual doses and/or by extending time intervals between doses **-Hepatic Impairment:** Avoid in high doses
Contra-indications	-children below 12 years -Known hypersensitivity to any of the tetracyclines or any of ingredients in the formulation - Renal or hepatic impairment -Systemic lupus erythematosus -Pregnancy and breastfeeding women -Porphyria -Patients receiving vitamin A or retinoid therapy.
Adverse Drug Reactions	Gastrointestinal irritations ,nausea, abdominal discomfort, vomiting, diarrhoea, anorexia and dysphagia ,Pseudomembranous colitis, intestinal overgrowth of resistant organisms ,glossitis, rectal and vaginal irritation, tooth discolouration, pancreatitis , Hepatotoxicity (hepatitis, jaundice and hepatic failure), fatty liver degeneration , macropapular and erythematous rashes, photo-erythema, urticaria, angioneurotic oedema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus , Renal dysfunction.
Monitoring Parameters	-Renal, hepatic, and hematologic function test -Temperature, WBC, cultures and sensitivity -Appetite, mental status
Drug Interactions	***Risk D: Consider therapy modification*** Antacids , Calcium Salts , Iron Preparations , Magnesium Dimecrotate , Magnesium Salts , Multivitamins/Minerals (with ADEK, Folate, Iron , Zinc Salts)
Pregnancy and Lactation	Product should not be used in pregnancy unless absolutely essential. Tetracyclines cross the placenta and may have toxic effects on foetal tissues, particularly on skeletal development. The use of tetracycline compounds during pregnancy has been associated with reports of maternal liver toxicity. Tetracyclines are contraindicated during breastfeeding because of possible staining of infants' dental enamel or bone deposition of tetracyclines although milk levels are low and absorption by the infant is inhibited by the calcium in breastmilk. .
Administration	-Best taken on an empty stomach (1 hour before food or two hours after). - If gastric irritation occurs, tablets should be taken with food. - Tablets should be taken well before going to bed. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	-Drug shouldn't be administered in the following patients: -Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption -Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency -Photosensitivity reactions may occur in hypersensitive persons and such patients should be warned to avoid direct exposure to natural or artificial sunlight and to discontinue therapy at the first sign of skin discomfort.
Storage	-Store below 25°C. Refer to manufacturer PIL if there are specific considerations.

Watch Group

14. Rifaximin

Generic Name	Rifaximin
Dosage form/strengths	Tablets 200mg, 550mg
Route of administration	Oral
Pharmacologic category	Rifamycin ATC: A07AA11
Indications	**Hepatic encephalopathy:** Reduction in the risk of overt hepatic encephalopathy recurrence in adults. **Irritable bowel syndrome without constipation:** Treatment of moderate to severe irritable bowel syndrome without constipation in adults. **Travelers' diarrhea:** Treatment of travelers' diarrhea caused by noninvasive strains of *Escherichia coli* in adults and pediatric patients ≥12 years of age. Limitations of use: Rifaximin should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea caused by pathogens other than *E. coli*.
Dosage Regimen	**Dosage** **adult Patients** **Irritable bowel syndrome, moderate to severe, without constipation (alternative agent): Note:** Reserve for patients, particularly those with bloating, who have failed other therapies. Oral: 550 mg 3 times daily for 14 days **Travelers' diarrhea:** *Treatment, moderate to severe (alternative agent):* **Note:** Avoid in patients with fever or bloody diarrhea Oral: 200 mg 3 times daily for 3 days **Hepatic Encephalopathy** **Reduction of Risk of Recurrence of Overt Hepatic Encephalopathy** Oral: 550 mg twice daily. **Treatment of Hepatic Encephalopathy** Oral: 600–1200 mg daily (usually in 3 divided doses) for 7–21 days has been used **Dosage** **Pediatric Patients** **Travelers' Diarrhea Caused by Noninvasive Strains of E. coli** **Treatment** Oral: Adolescents ≥12 years of age: 200 mg 3 times daily for 3 days. If diarrhea worsens or persists >24–48 hours after drug initiated, discontinue and consider alternative anti-infective
Dosage adjustment	**Dosing: Renal Impairment: Adult** There are no dosage adjustments provided in the manufacturer's labeling (has not been studied). **Dosing: Hepatic Impairment: Adult** No dosage adjustment necessary. Use with caution in severe impairment (Child-Pugh class C); however, systemic absorption is limited and pharmacokinetic parameters are highly variable
Contra-indications	Hypersensitivity to rifaximin, other rifamycin antibiotics, or any component of the formulation
Adverse Drug	**>10%:**

Reactions	Cardiovascular: Peripheral edema (15%) Central nervous system: Dizziness (13%), fatigue (12%) Hepatic: Ascites (11%) Gastrointestinal: Nausea (14%; irritable bowel syndrome with diarrhea) Central nervous system: Headache, depression (7%) Dermatological: Pruritus (9%), skin rash (5%) Gastrointestinal: Abdominal pain (>2% to 9%), pseudomembranous colitis (<5%; travelers' diarrhea or irritable bowel syndrome with diarrhea <2%) Hematologic & oncologic: Anemia (8%) Hepatic: Increased serum ALT (irritable bowel syndrome with diarrhea 2%) Neuromuscular & skeletal: Muscle spasm (9%), arthralgia (6%), increased creatine phosphokinase (<5%; travelers' diarrhea or irritable bowel syndrome with diarrhea <2%) Respiratory: Nasopharyngitis (7%), dyspnea (6%), epistaxis (>2% to 5%) Miscellaneous: Fever (6%)
Monitoring Parameters	Hypersensitivity reactions, temperature, blood in stool, change in symptoms; monitor changes in mental status in hepatic encephalopathy
Drug Interactions	***Risk X: Avoid combination*** Lasmiditan BCG (Intravesical) ***Risk D: Consider therapy modification*** Sodium Picosulfate ***Risk C: Monitor therapy*** BCG Vaccine Erdafitinib Lactobacillus and Estriol Lumacaftor and Ivacaftor P-glycoprotein/ABCB1 Inhibitors
Pregnancy and Lactation	**Pregnancy Category C** Adverse events have been observed in some animal reproduction studies. Due to the limited oral absorption of rifaximin in patients with normal hepatic function, exposure to the fetus is expected to be low. It is not known if rifaximin is excreted in human milk. According to the manufacturer, the decision to breast-feed during therapy should take into account the risk of exposure to the infant and the benefits of treatment to the mother. Because of the limited oral absorption of rifaximin in patients with normal hepatic function, exposure to the nursing infant is expected to be low.
Administration	Oral: Administer with or without food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity: Hypersensitivity reactions (eg, exfoliative dermatitis, rash, urticaria, flushing, angioneurotic edema, pruritus, anaphylaxis) have occurred; these events have occurred as early as within 15 minutes of drug administration. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *Clostridioides* (formerly *Clostridium*) difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Diarrhea: Appropriate use: Avoid use in diarrhea with fever and/or blood in the stool and in the treatment of diarrhea due to pathogens other than *Escherichia coli*, including *Campylobacter jejuni*, *Shigellal* spp., and *Salmonella* spp. (efficacy has not been established). Consider alternative therapy if symptoms persist or worsen after 24 to 48 hours of treatment. • Hepatic impairment: Efficacy for prevention of encephalopathy has not been established in patients with a Model for End-Stage Liver Disease (MELD) score >25; use caution in patients with severe hepatic impairment (Child-Pugh class C). ***Concurrent drug therapy issues:***

	• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.
Storage	Store at 20°C to 25°C; excursions permitted to 15°C to 30°C Refer to manufacturer PIL if there are specific considerations.

15. Secnidazole

Access Group

Generic Name	Secnidazole
Dosage form/strengths	Tablets: 500 mg, 1gm
Route of administration	Oral
Pharmacologic category	Antiprotozoal, Nitroimidazole ATC: P01AB07
Indications	**Bacterial vaginosis**: Treatment of bacterial vaginosis in adult females. **Trichomoniasis**: Treatment of trichomoniasis caused by Trichomonas vaginalis in adults; treat partners of infected patients simultaneously to prevent reinfection.
Dosage Regimen	**Dosing: Adult** **Bacterial vaginosis**: **Oral:** 2 g single dose. **Trichomoniasis: Oral:** 2 g as a single dose; sexual partners should be treated at the same time.
Dosage adjustment	**Dosing: Renal Impairment: Adult** There are no dosage adjustments needed. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to secnidazole, other nitroimidazole derivatives, or component of formulation.
Adverse Drug Reactions	**1% to 10%:** Gastrointestinal: Diarrhea (3%), nausea (4%) Genitourinary: Vulvovaginal candidiasis (3% to 10%) Nervous system: Headache (4%) **Postmarketing**: Gastrointestinal: Dysgeusia
Monitoring Parameters	Monitor for adverse reactions.
Drug Interactions	***Risk X: Avoid combination*** Alcohol (Ethyl) BCG (Intravesical) Cholera Vaccine Products Containing Ethanol Products Containing Propylene Glycol ***Risk D: Consider therapy modification*** Sodium Picosulfate Typhoid Vaccine
Pregnancy and Lactation	Adverse events were not observed in animal reproduction studies. Information related to the use of secnidazole in pregnancy is limited. It is not known if secnidazole is present in breast milk. Due to the potential for adverse events, breastfeeding should be avoided during therapy and for 96 hours after the last dose.
Administration	**Administration: Oral:** Administer without regard to timing of meals Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • ***Carcinogenic:*** Carcinogenicity has been observed in mice and rats with nitroimidazole agents that are structurally similar to secnidazole in animal studies; it is unknown whether secnidazole is associated with carcinogenicity in humans. Avoid chronic use. ***Disease-related concerns:*** • ***Candidiasis:*** Vulvovaginal candidiasis may occur; antifungal treatment may be necessary if patient is symptomatic.

	Other warnings/precautions: • ***Ethanol use:*** Abdominal pain, diarrhea, dizziness, headache, nausea, and vomiting have been reported with secnidazole and concomitant alcohol consumption; avoid alcoholic beverages or products containing ethanol or propylene glycol during therapy and for at least 2 days after therapy completion.
Storage	Store at 20°C to 25°C; excursions permitted to 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.

16. Sulfamethoxazole and Trimethoprim

Generic Name	Sulfamethoxazole and Trimethoprim
Dosage form/strengths	Oral suspension Sulfamethoxazole 200 mg/5m, Trimethoprim 40 mg/5ml Tablets 400/80mg, 800/160mg
Route of administration	Oral
Pharmacologic category	Antibiotic, Miscellaneous; Antibiotic, Sulfonamide Derivative ATC: J01EE01
Indications	**Oral:** Treatment of urinary tract infections (UTIs) due to Escherichia coli, Klebsiella and Enterobacter spp, Morganella morganii, Proteus mirabilis, and Pro teus vulgaris; acute otitis media; acute exacerbations of chronic obstructive pulmonary disease due to susceptible strains of Haemophilus influenzae or Streptococcus pneumoniae; treatment and prophylaxis of Pneumocystis pneumonia (PCP); traveler's diarrhea due to enterotoxigenic E. coli; treatment of shigellosis caused by Shigella flexneri or Shigella sonnei.
Dosage Regimen	**Dosing: Adult** **General dosing guidelines:** **Oral:** 1 to 2 double-strength tablets every 12 to 24 hours. **Note:** Serum creatinine and potassium concentrations should be monitored in outpatients receiving high-dose therapy (>5 mg/kg/day [TMP component]). **Dosing: Pediatric** **Note:** Dosage recommendations are based on the trimethoprim (TMP) component**:** **General dosing, susceptible infection: Infants ≥2 months, Children, and Adolescents: Oral, IV:** 6 to 12 mg TMP/kg/day in divided doses every 12 hours; maximum single dose: 160 mg TMP/dose
Dosage adjustment	**Renal Impairment** **Oral** Adults with Cl_{cr} 15–30 mL/minute: Reduce dose to ~50% of usual dose. Adults with Cl_{cr} <15 mL/minute: Reduce dose to ~25 to 50% of usual dose. Use with caution and appropriate monitoring. **Dosing: Renal Impairment: Pediatric** Infants ≥2 months, Children, and Adolescents: Oral: CrCl >30 mL/minute: No adjustment required. CrCl 15 to 30 mL/minute: Administer 50% of recommended dose. CrCl <15 mL/minute: Use is not recommended. **Dosing: Hepatic Impairment:** • There are no dosage adjustments needed. Use with caution; use is contraindicated in cases of marked hepatic damage.
Contra-indications	Hypersensitivity to any sulfa drug, trimethoprim, or any component of the formulation; history of drug induced-immune thrombocytopenia with use of sulfonamides or trimethoprim; megaloblastic anemia due to folate deficiency; infants <2 months, infants <4 weeks; marked hepatic damage or severe renal disease (if patient not monitored); concomitant administration with dofetilide Additional contraindications: Blood dyscrasias; pregnancy; breastfeeding; premature infants; acute

	porphyria.
Adverse Drug Reactions	**Frequency not defined:** Cardiovascular: Allergic myocarditis, periarteritis nodosa (rare) Central nervous system: Apathy, aseptic meningitis, ataxia, chills, depression, fatigue, hallucination, headache, insomnia, nervousness, peripheral neuritis, seizure, vertigo Endocrine & metabolic: Hyperkalemia (generally at high dosages), hypoglycemia (rare), hyponatremia Gastrointestinal: Abdominal pain, anorexia, diarrhea, glottis edema, kernicterus (in neonates), nausea, pancreatitis, pseudomembranous colitis, stomatitis, vomiting Genitourinary: Crystalluria, diuresis (rare), nephrotoxicity (in association with cyclosporine), toxic nephrosis (with anuria and oliguria) Hematologic & oncologic: Agranulocytosis, anaphylactoid purpura (IgA vasculitis; rare), aplastic anemia, eosinophilia, hemolysis (with G6PD deficiency), hemolytic anemia, hypoprothrombinemia, leukopenia, megaloblastic anemia, methemoglobinemia, neutropenia, thrombocytopenia Hepatic: Cholestatic jaundice, hepatotoxicity (including hepatitis, cholestasis, and hepatic necrosis), hyperbilirubinemia, increased transaminases Hypersensitivity: Anaphylaxis, angioedema, hypersensitivity reaction, serum sickness Neuromuscular & skeletal: Arthralgia, myalgia, rhabdomyolysis (mainly in AIDS patients), systemic lupus erythematosus (rare), weakness Ophthalmic: Conjunctival injection, injected sclera, uveitis Otic: Tinnitus Renal: Increased blood urea nitrogen, increased serum creatinine, interstitial nephritis, renal failure Respiratory: Cough, dyspnea, pulmonary infiltrates Miscellaneous: Fever
Monitoring Parameters	CBC, serum potassium, creatinine, BUN
Drug Interactions	***Risk X: Avoid combination*** Aminolevulinic Acid Amodiaquine BCG (Intravesical) Cholera Vaccine Dofetilide Fexinidazole Leucovorin Calcium Mecamylamine Methenamine Metronidazole Potassium P-Aminobenzoate Procaine ***Risk D: Consider therapy modification*** Chloroprocaine Methotrexate Phenytoin Procainamide Sodium Picosulfate Typhoid Vaccine Vitamin K Antagonists ***Risk C: Monitor therapy*** Amantadine Aminolevulinic Acid Androgens Angiotensin Ii Receptor Blockers Angiotensin-Converting Enzyme Inhibitors Antidiabetic Agents Azathioprine Cyclosporine Dapsone Dexketoprofen Digoxin Eplerenone Hypoglycemia-Associated Agents Lactobacillus And Estriol Lamivudine Local Anesthetics Mercaptopurine Metformin Porfimer Prilocaine Prothionamide Rifampin Salicylates Sodium Nitrite
Pregnancy and Lactation	Avoidance of sulfamethoxazole/trimethoprim during the third trimester is recommended by some guidelines.
Administration	**Administration: Oral** Administer without regard to meals. Administer with food, water, or milk to minimize gastric irritation. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Blood dyscrasias: Fatalities associated with severe reactions including agranulocytosis, aplastic anemia, and other blood dyscrasias have occurred; discontinue use at first sign of rash or signs of serious adverse reactions. • Dermatologic reactions: Fatalities associated with severe reactions including Stevens-Johnson

	syndrome and toxic epidermal necrolysis have occurred; discontinue use at first sign of rash. • Hepatic necrosis: Fatalities associated with hepatic necrosis have occurred; discontinue use at first sign of rash or signs of serious adverse reactions. • Hyperkalemia: May cause hyperkalemia; potential risk factors for trimethoprim-induced hyperkalemia include high dosage (20 mg/kg/day of trimethoprim), renal impairment, older age, hypoaldosteronism, and concomitant use of medications causing or exacerbating hyperkalemia. • Hypoglycemia: May cause hypoglycemia, particularly in malnourished, or patients with renal or hepatic impairment. • Hyponatremia: Severe and symptomatic hyponatremia may occur, particularly in patients treated for *Pneumocystis jirovecii* pneumonia (PCP). • Sulfonamide ("sulfa") allergy: Traditionally, concerns for cross-reactivity have extended to all compounds containing the sulfonamide structure (SO_2NH_2). • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. • Thrombocytopenia: Immune mediated thrombocytopenia may occur. Severe cases which may be life-threatening or fatal have been reported. Thrombocytopenia usually resolves within 1 week following discontinuation of therapy. ***Disease-related concerns:*** • Asthma/allergies: Use with caution in patients with allergies or asthma. • Hepatic impairment: Use with caution in patients with hepatic impairment. • Renal impairment: Use with caution in patients with renal impairment; dosage adjustment recommended. Maintain adequate hydration to prevent crystalluria. • Thyroid dysfunction: Use with caution in patients with thyroid dysfunction. ***Concurrent drug therapy issues:*** • Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information. • Leucovorin: Avoid concomitant use when treating *Pneumocystis jirovecii* pneumonia (PCP) in patients with HIV; may increase risk of treatment failure and death. ***Special populations:*** • AIDS patients: Incidence of adverse effects appears to be increased in patients with AIDS. • Elderly: Use with caution in elderly patients; greater risk for more severe adverse reactions, including hyperkalemia associated with trimethoprim use. Elderly patients are at an increased risk for severe and potentially life-threatening hyperkalemia when trimethoprim is used concomitantly with medications known to cause or exacerbate hyperkalemia, such as spironolactone, ACE inhibitors, or ARBs. • G6PD deficiency: Use with caution in patients with G6PD deficiency; hemolysis may occur (dose-related). • Patients with potential for folate deficiency: Use with caution in patients with potential folate deficiency (malnourished, chronic anticonvulsant therapy, or elderly). • Porphyria: Use with caution in patients with porphyria. • Slow acetylators: May be more prone to adverse reactions
Storage	Store at controlled room temperature of 15°C to 25°C. Protect from light Refer to manufacturer PIL if there are specific considerations.

17. Tedizolid

Reserve Group

Generic Name	Tedizolid
Dosage form/strengths	Tablets: 200mg
Route of administration	Oral
Pharmacologic category	Antibiotic, Oxazolidinone ATC: J01XX11
Indications	Skin and soft tissue infections: Treatment of adults and pediatric patients ≥12 years of age with acute bacterial skin and soft tissue infections caused by susceptible isolates of the following gram-positive microorganisms
Dosage Regimen	**Dosing: Adult** **Skin and soft tissue infection (alternative agent):** **Note:** Reserve for patients with or at risk for methicillin-resistant *S. aureus* infection who cannot receive preferred agents. **Oral:** 200 mg once daily. Total duration of therapy is ≥5 days; may extend up to 14 days depending on severity and clinical response **Dosing: Pediatric** **Skin and skin structure infections:** Children ≥12 years and Adolescents: Oral: 200 mg once daily for 6 days
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary. **Dosing: Hepatic Impairment: Adult** No dosage adjustment necessary.
Contra-indications	Hypersensitivity to Tedizolid or any component of the formulation
Adverse Drug Reactions	**1% to 10%:** Cardiovascular: Flushing (<2%), hypertension (<2%), palpitations (<2%), phlebitis (adolescents: 3%), tachycardia (<2%) Dermatologic: Dermatitis (<2%), pruritus (<2%), urticaria (<2%) Endocrine & metabolic: Increased gamma-glutamyl transferase (<2%) Gastrointestinal: *Clostridioides difficile* colitis (<2%), diarrhea (4%), nausea (7%), oral candidiasis (<2%), vomiting (1% to 3%) Genitourinary: Vulvovaginal infection (fungal: <2%) Hematologic & oncologic: Anemia (<2%), decreased platelet count (<112,000/mm^3: 1% to 2%), decreased white blood cell count (<2%) Hepatic: Increased serum alanine aminotransferase (≤3%), increased serum aspartate aminotransferase (≤3%), increased serum transaminases (≤3%) Hypersensitivity: Hypersensitivity reaction (<2%) Local: Injection site reaction (≤4%) Nervous system: Dizziness (2%), facial nerve paralysis (<2%), headache (5%), hypoesthesia (<2%), insomnia (<2%), paresthesia (<2%), peripheral neuropathy (1%) Ophthalmic: Asthenopia (<2%), blurred vision (<2%), visual impairment (<2%), vitreous opacity (<2%) Miscellaneous: Infusion related reaction (≤4%)

Monitoring Parameters	Baseline complete blood count (CBC) with differential Monitor for improvement in infection, new opportunistic infections, development of severe diarrhea.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine Cladribine Dipyrone Fexinidazole Pazopanib Rimegepant Topotecan ***Risk D: Consider therapy modification*** Alpelisib Berotralstat Deferiprone Iohexol Iomeprol Iopamidol Sodium Picosulfate Typhoid Vaccine Ubrogepant
Pregnancy and Lactation	Adverse events were observed in animal reproduction studies. No information is available on the use of tedizolid during breastfeeding. Tedizolid is 70 to 90% bound in maternal plasma, so large amounts are not expected to appear in breastmilk. If tedizolid is required by the mother, it is not a reason to discontinue breastfeeding, but because there is no published experience with tedizolid during breastfeeding, an alternate drug may be preferred, especially while nursing a newborn or preterm infant.
Administration	**Administration: Oral** Administer with or without food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Neutropenia: Not recommended for use in patients with neutrophil counts <1000 cells/mm^3. Alternative therapies should be considered when treating patients with neutropenia and acute bacterial skin and skin structure infections
Storage	Store at 20°C to 25°C; excursions are permitted between 15°C and 30°C. Refer to manufacturer PIL if there are specific considerations.

18. Teicoplanin

Watch Group

Generic Name	Teicoplanin
Dosage form/strengths	Powder for solution for I.M or I.V Injection 200mg, 400mg
Route of administration	*IV IM*
Pharmacologic category	A glycopeptide antibacterial ATC: J01XA02
Indications	Indicated for use in serious gram+ve infections; serious staphylococcal infections in patients sensitive or unresponsive to penicillins and cephalosporins; CAPD (continuous ambulatory peritoneal dialysis) related peritonitis; prophylaxis in orthopaedic surgery at risk of Gram-positive infection
Dosage Regimen	**Adult Dosing** • The usual loading dose is 400 mg (equivalent to about 6 mg/kg) intravenously or intramuscularly, given every 12 hours for the first 3 doses, followed by 6 mg/kg once daily. • In more severe infections: 800 mg (equivalent to about 12 mg/kg) may be given intravenously every 12 hours for the first 3 to 5 doses, followed by 12 mg/kg intravenously or intramuscularly once daily. The duration of therapy should not exceed 4 months. • For the prophylaxis of Gram-positive infection in high-risk patients undergoing surgical procedures who are unable to receive penicillin, teicoplanin may be given in a single intravenous dose of 400 mg at induction of anaesthesia; a dose of 800 mg has been recommended for those undergoing skeletal stabilisation and definitive soft-tissue closure. • For *CAPD-associated peritonitis*, teicoplanin may be added to the dialysis solution at a concentration of 20 mg/litre; this dose should be given in each bag of solution in the first week, in alternate bags in the second week, and in the overnight dwell bag only during the third week. Patients should be given an initial loading dose of 400 mg intravenously. **Pediatric Dosing:** • IV for neonates (1-2month): a single loading dose of 16 mg/kg is followed by maintenance doses of 8 mg/kg once daily IV • for children from 1-2 month of age: IV: a loading dose of 10 mg/kg (maximum 400 mg) is given every 12 hours for three doses followed by maintenance doses of 6 mg/kg (maximum 400 mg) once daily; in severe infections, maintenance doses of 10 mg/kg once daily are recommended
Dosage adjustment	**Dosage adjustments in Renal disease:** Doses of teicoplanin should be adjusted in patients with renal impairment, though reduction is not required until the fourth day of treatment. Teicoplanin should be given in usual IV or IM doses for the first 3 days of therapy, thereafter the dose is adjusted according to creatinine clearance (CrCl): CrCl 30 to 80 mL/minute: half the maintenance dose given daily or the maintenance dose given every 2 days CrCl less than 30 mL/minute and for haemodialysed patients: one-third initial dose given daily or initial dose given every 3 days.

Contra-indications	Hypersensetivity to any of the drug components
Adverse Drug Reactions	Fever, rash and pruritus, and occasional bronchospasm and anaphylaxis erythema and flushing of the upper body have occurred. Other hypersensitivity reactions have included rigors, angioedema, and, rarely, severe skin reactions including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis. gastrointestinal disturbances, dizziness, headache, thrombocytopenia (especially at high doses), leucopenia, neutropenia, eosinophilia Disturbances in liver enzyme values, and thrombophlebitis abscess at the injection site. Rare cases of agranulocytosis have occurred. Renal impairment and ototoxicity have been reported
Monitoring Parameters	Renal and auditory function should be monitored during prolonged therapy in patients with pre-existing renal impairment, and in those receiving other ototoxic or nephrotoxic drugs, although opinions conflict as to whether increased risk of nephrotoxicity exists with combined therapy with drugs such as the aminoglycosides. In general, periodic blood counts and liver- and renal-function tests are advised during treatment
Drug Interactions	To be used with caution in conjunction with or sequentially with drugs of known nephrotoxic or ototoxic potential particularly streptomycin, neomycin, kanamycin, gentamicin, amikacin, tobramycin, cephaloridine, colistin.
Pregnancy and Lactation	**Pregnancy Category X** Limited data indicate that teicoplanin is poorly excreted into breastmilk. Because teicoplanin is not orally absorbed it is unlikely to adversely affect the breastfed infant.
Administration	• Given intravenously, as a bolus dose or by infusion over 30 minutes, or by intramuscular injection. • In children: after the loading doses have been given, the intramuscular route may be considered in children aged 1 month and over. • Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Prolonged use of teicoplanin may result in overgrowth of non-susceptible organisms. Repeated evaluation of patient's condition is essential. • Hypersensitivity Although there have been occasional reports of cross-sensitivity to teicoplanin in patients hypersensitive to vancomycin, the majority of reports suggest that cross-sensitivity is very rare and teicoplanin can usually be used in patients intolerant of vancomycin
Storage	• Store at a temperature of 2 -8 o C. Protect from light. • Refer to manufacturer PIL if there are specific considerations.

19. Tetracycline

Generic Name	Tetracycline
Dosage form/strengths	Topical ointment 3% Capsule 250mg Eye Ointment 1%
Route of administration	Oral topical
Pharmacologic category	Antibiotic, Tetracycline Derivative ATC (Topical): D06AA04 ATC (systemic): J01AA07 ATC (Ophthalmic): S01AA09, S03AA02
Indications	**Acute intestinal amebiasis:** Adjunctive therapy in acute intestinal amebiasis caused by *Entamoeba histolytica*. **Acne:** Adjunctive therapy for the treatment of severe acne. **Actinomycosis:** Treatment of actinomycosis caused by *Actinomyces* species when penicillin is contraindicated. **Anthrax:** Treatment of anthrax due to *Bacillus anthracis* when penicillin is contraindicated. **Campylobacter:** Treatment of infections caused by *Campylobacter fetus*. **Cholera:** Treatment of cholera caused by *Vibrio cholerae*. **Clostridium:** Treatment of infections caused by *Clostridium* spp. when penicillin is contraindicated. **Gram-negative infections:** Treatment of infections caused by *Escherichia coli*, *Klebsiella aerogenes* (formerly *Enterobacter aerogenes*), *Shigella* spp., *Acinetobacter* spp., *Klebsiella* spp., and *Bacteroides* spp. **Listeriosis:** Treatment of listeriosis due to *Listeria monocytogenes* when penicillin is contraindicated. **Ophthalmic infections:** Treatment of inclusion conjunctivitis or trachoma caused by *Chlamydia trachomatis*. **Relapsing fever:** Treatment of relapsing fever due to *Borrelia* spp. **Respiratory tract infection:** Treatment of respiratory tract infections caused by *Haemophilus influenzae* (upper respiratory tract only), *Klebsiella* spp. (lower respiratory tract only), *Mycoplasma pneumoniae* (lower respiratory tract only), *Streptococcus pneumoniae*, or *Streptococcus pyogenes*. **Rickettsial infections:** Treatment of Rocky Mountain spotted fever, typhus group infections, Q fever, and rickettsialpox caused by *Rickettsiae*. **Sexually transmitted diseases:** Treatment of lymphogranuloma venereum or uncomplicated urethral, endocervical, or rectal infections caused by *C. trachomatis*; chancroid caused by *Haemophilus ducreyi*; granuloma inguinale (donovanosis) caused by *Klebsiella granulomatis*; syphilis caused by *Treponema pallidum*, when penicillin is contraindicated. Limitations of use: Tetracycline is **not** a recommended alternative for uncomplicated gonorrhea according to the Centers for Disease Control and Prevention (CDC) sexually transmitted diseases guidelines. **Skin and skin structure infections:** Treatment of skin and skin structure infections caused by *Staphylococcus aureus* or *S. pyogenes*. **Urinary tract infections:** Treatment of urinary tract infections caused by susceptible gram-negative organisms (eg, *E. coli*, *Klebsiella* spp.).

	Vincent infection: Treatment of Vincent infection caused by *Fusobacterium fusiforme* when penicillin is contraindicated. **Yaws:** Treatment of yaws caused by *Treponema pertenue* when penicillin is contraindicated. **Zoonotic infections:** Treatment of psittacosis (ornithosis) due to *Chlamydophila psittaci*; plague due to *Yersinia pestis*; tularemia due to *Francisella tularensis*; brucellosis due to *Brucella* spp. (in conjunction with an aminoglycoside); bartonellosis due to *Bartonella bacilliformis*.
Dosage Regimen	**Dosing: Adult** **Usual dosage range: Oral:** 250 to 500 mg 4 times daily or 500 mg twice daily. **Acne vulgaris (moderate to severe, inflammatory):** **Note: Use as an adjunct to topical acne therapy.** **Oral:** Initial dose: 1 g daily in divided doses; reduce gradually to 125 to 500 mg/day once improvement is noted (alternate day or intermittent therapy may be adequate in some patients). Use the shortest possible duration to minimize risk of adverse effects and development of bacterial resistance; re-evaluate at 3 to 4 months **Cholera (*Vibrio cholerae*), treatment (adjunctive therapy for severely ill patients):** **Oral:** 500 mg 4 times daily for 3 days **Syphilis, penicillin-allergic patients: Note:** Limited data support use of alternatives to penicillin, and close serologic and clinical follow up is warranted. ***Early syphilis (primary, secondary, and early latent):*** **Oral**: 500 mg 4 times daily for 14 days. ***Latent syphilis (late latent):*** **Oral:** 500 mg 4 times daily for 28 days. **Tularemia (*Francisella tularensis*) (mild): Oral:** 500 mg 4 times daily for at least 14 days **Skin Infections** If tetracycline hydrochloride is used for the prevention or treatment of superficial infections of the skin, a small amount of the ointment should be applied to the cleansed affected area 2–3 times daily. **Dosing: Pediatric** **General dosing: Children ≥8 years and Adolescents:** Oral: 6.25 to 12.5 mg/kg/dose 4 times daily; maximum dose: 500 mg/dose
Dosage adjustment	**Dosing: Renal Impairment:** CrCl more than 90 mL/minute: no dosage adjustment needed. CrCl 51 to 90 mL/minute: extend dosing interval to every 8 to 12 hours. CrCl 10 to 50 mL/minute: extend dosing interval to every 12 to 24 hours. CrCl less than 10 mL/minute: extend dosing interval to every 24 hours. **Dosing: Hepatic Impairment:** Dose adjustment of tetracycline may be required in patients with hepatic impairment due to potential for reduced excretion and a prolonged half-life.
Contra-indications	Hypersensitivity to any of the tetracyclines or any component of the formulation.
Adverse Drug Reactions	**Frequency not defined:** Cardiovascular: Pericarditis Central nervous system: Bulging fontanel, idiopathic intracranial hypertension Dermatologic: Erythematous rash, maculopapular rash, skin photosensitivity, urticaria Endocrine & metabolic: Growth retardation (fibula) Gastrointestinal: Anorexia, diarrhea, dysphagia, enterocolitis, epigastric distress, glossitis, melanoglossia, nausea, vomiting Genitourinary: Inflammatory anogenital lesion (with monilial overgrowth) Hematologic & oncologic: Henoch-Schonlein purpura Hepatic: Hepatic failure, hepatotoxicity Hypersensitivity: Anaphylaxis, angioedema, hypersensitivity reaction Immunologic: Serum sickness-like reaction

	Neuromuscular & skeletal: Exacerbation of systemic lupus erythematosus
Monitoring Parameters	Renal, hepatic, and hematologic function test, temperature, WBC, cultures and sensitivity, appetite, mental status
Drug Interactions	***Risk X: Avoid combination*** Retinoic Acid Derivatives Methoxyflurane Mecamylamine BCG (Intravesical ***Risk D: Consider therapy modification*** Antacids Bismuth Subcitrate Bismuth Subsalicylate Calcium Salts CYP3A4 Inducers Dabrafenib Enzalutamide Iron Preparations Lanthanum Magnesium Salts Mitotane Multivitamins/Minerals Quinapril Sodium Picosulfate Sucralfate Typhoid Vaccine Zinc Salts
Pregnancy and Lactation	**Pregnancy Risk Factor** D As a class, tetracyclines have generally been avoided in nursing women due to theoretical concerns that they may permanently stain the teeth of the breastfeeding infant. Some sources note that breastfeeding can continue during tetracycline therapy but recommend use of alternative medications when possible.
Administration	**Administration: Oral** Administer on an empty stomach (ie, 1 hour prior to, or 2 hours after meals) to increase total absorption and with adequate amount of fluid to reduce risk of esophageal irritation and ulceration. Administer at least 1 to 2 hours prior to, or 4 hours after antacid because aluminum and magnesium cations may chelate with tetracycline and reduce its total absorption. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Increased BUN: May be associated with increases in serum urea nitrogen (BUN) secondary to antianabolic effects; use caution in patients with renal impairment. • Intracranial hypertension (eg, pseudotumor cerebri): Intracranial hypertension (headache, blurred vision, diplopia, vision loss, and/or papilledema) has been associated with use. Women of childbearing age who are overweight or have a history of intracranial hypertension are at greater risk. Concomitant use of isotretinoin (known to cause pseudotumor cerebri [PTC]) and tetracycline should be avoided. Intracranial hypertension typically resolves after discontinuation of treatment; however, permanent visual loss is possible. If visual symptoms develop during treatment, prompt ophthalmologic evaluation is warranted. Intracranial pressure can remain elevated for weeks after drug discontinuation; monitor patients until they stabilize. • Photosensitivity: May cause photosensitivity; discontinue if skin erythema occurs. Use skin protection and avoid prolonged exposure to sunlight; do not use tanning equipment. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *Clostridioides* (formerly *Clostridium*) *difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Hepatic impairment: Hepatotoxicity has been reported rarely; risk may be increased in patients with preexisting hepatic or renal impairment. • Renal impairment: Use with caution in patients with renal impairment; dosage adjustment recommended. ***Special populations:*** • Pediatric: May cause tissue hyperpigmentation, enamel hypoplasia, or permanent tooth discoloration; use of tetracyclines should be avoided during tooth development (children <8 years of age) unless other drugs are not likely to be effective or are contraindicated. ***Other warnings/precautions:*** • Appropriate use: Acne: The American Academy of Dermatology acne guidelines recommend tetracycline as adjunctive treatment for moderate and severe acne and forms of inflammatory acne that are resistant to topical treatments. Concomitant topical therapy with benzoyl peroxide

	or a retinoid should be administered with systemic antibiotic therapy (eg, tetracycline) and continued for maintenance after antibiotic course is completed
Storage	Store at 20°C to 25°C; protect from light. Refer to manufacturer PIL if there are specific considerations.

Access Group

20. Thiamphenicol

Generic Name	Thiamphenicol
Dosage form/strengths	Capsule 250mg Tablets 250mg Powder for Solution for Injection 750mg Oral Solution 250mg
Route of administration	IV, IM, Oral
Pharmacologic category	Antibacterial: Chloramphenicol ATC: J01BA02
Indications	Treatment of susceptible infections, including sexually transmitted diseases, gonorrhoea
Dosage Regimen	The usual oral dose is 1.5 g daily in divided doses; up to 3 g daily has been given initially in severe infections. Equivalent doses, expressed in terms of thiamphenicol base, may be given by intramuscular or intravenous injection as the more water soluble glycinate hydrochloride; 1.26 g of thiamphenicol glycinate hydrochloride is equivalent to about 1 g of thiamphenicol. A maximum daily dose of 1 g has been suggested for elderly patients. Doses should also be reduced in patients with renal impairment For the treatment of gonorrhoea, oral doses of thiamphenicol have ranged from 2.5 g daily for 1 or 2 days through to 2.5 g on the first day followed by 2 g daily on each of 4 subsequent days. The single daily dose may be most appropriate for male patients with uncomplicated gonorrhoea. **Administration in children** In children, oral doses may range from 30 to 100 mg/kg daily according to age and severity of infection. Similar doses may also be given by intramuscular or intravenous injection.
Dosage adjustment	**Administration in renal impairment** Doses of thiamphenicol should be reduced in patients with renal impairment according to creatinine clearance (CC). For the oral preparation, suggested reduced doses are: CC 30 to 60 mL/minute: 500 mg twice daily CC 10 to 30 mL/minute: 500 mg once daily Alternatively, for parenteral use the following doses have been suggested: CC 50 to 75 mL/minute: 500 mg every 12 hours CC 25 to 50 mL/minute: 500 mg every 18 hours CC 20 mL/minute: 500 mg every 24 hours CC 10 mL/minute: 500 mg every 48 hours **Administration in hepatic impairment:** no adjustments needed
Contra-indications	Hypersensetivity
Adverse Drug Reactions	Thiamphenicol is probably more liable to cause dose-dependent reversible depression of the bone marrow than chloramphenicol, particularly in the elderly or in those with impaired renal function, but it is not usually associated with aplastic anaemia. Thiamphenicol also appears to be less likely to cause the 'grey syndrome' in neonates. Doses of thiamphenicol should be reduced in patients with renal impairment. It is probably not necessary to reduce doses in patients with hepatic impairment.

Monitoring Parameters	CBC, Kideny functions
Drug Interactions	Although thiamphenicol is not metabolised in the liver and might not be expected to be affected by drugs that induce hepatic enzymes, it is reported to inhibit hepatic microsomal enzymes and may affect the metabolism of other drugs.
Pregnancy	**Category** C An alternate drug is preferred to chloramphenicol during breastfeeding, especially while nursing a newborn or preterm infant.
Administration	Oral, IV or IM Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	Thiamphenicol is probably more liable to cause dose-dependent reversible depression of the bone marrow than chloramphenicol, particularly in the elderly or in those with impaired renal function, but it is not usually associated with aplastic anaemia. Thiamphenicol also appears to be less likely to cause the 'grey syndrome' in neonates. Doses of thiamphenicol should be reduced in patients with renal impairment. It is probably not necessary to reduce doses in patients with hepatic impairment.
Storage	Refer to manufacturer PIL if there are specific considerations.

21. Tigecycline

Reserve Group

Generic Name	Tigecycline
Dosage form/strengths	Lyophilized Powder for Reconstitution for I.V Infusion: 50mg
Route of administration	IV
Pharmacologic category	Antibiotic, Glycylcycline ATC: J01AA12
Indications	**Intra-abdominal infection:** Treatment of complicated intra-abdominal infections in patients ≥18 years of age caused by susceptible organisms. **Pneumonia, community acquired:** Treatment of community-acquired bacterial pneumonia in patients ≥18 years of age caused by susceptible organisms. **Skin and skin structure infections, complicated:** Treatment of complicated skin and skin structure infections in patients ≥18 years of age caused by susceptible organisms. **Limitations of use:** Not indicated for treatment of diabetic foot infections. Not indicated for treatment of hospital-acquired or ventilator-associated pneumonia.
Dosage Regimen	**Dosing: Adult** **Note:** Given the increased mortality risk associated with tigecycline, reserve for use in situations when alternative treatments are not suitable. **Intra-abdominal infection (alternative agent):** **Note:** Not recommended for routine empiric use. Reserve use for patients with or at risk for certain multidrug-resistant organisms (eg, *K. pneumoniae* carbapenemase-producing Enterobacteriaceae, *Acinetobacter baumannii*). **IV:** 100 mg once, then 50 mg every 12 hours. Total duration of therapy is 4 to 5 days. **Pneumonia, community-acquired (alternative agent for patients unable to tolerate beta-lactams or fluoroquinolones):** Inpatients without risk factors for *Pseudomonas aeruginosa*; not recommended for routine empiric use. **IV:** 100 mg as a single dose, then 50 mg every 12 hours. Total duration (which may include oral step-down therapy) is a minimum of 5 days; patients should be clinically stable with normal vital signs before therapy is discontinued. **Skin/skin structure infection, complicated: IV:** Initial: 100 mg as a single dose; Maintenance dose: 50 mg every 12 hours for 5 to 14 days. **Dosing: Pediatric** **General dosing, susceptible infection:** Limited data available: **Note:** Use should be reserved for situations when no effective alternative therapy is available; should not be used in pediatric patients <8 years due to adverse effects on tooth development, unless no alternatives are available.
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary for any degree of kidney dysfunction **Dosing: Hepatic Impairment: Adult** Mild-to-moderate hepatic impairment (Child-Pugh class A or B): No dosage adjustment necessary.

	Severe hepatic impairment (Child-Pugh class C): Initial: 100 mg single dose; Maintenance: 25 mg every 12 hours. **Dosing: Renal and hepatic Impairment: Pediatric** There are no pediatric specific recommendations; data is insufficient.
Contra-indications	Hypersensitivity to tigecycline or any component of the formulation. Hypersensitivity to tetracycline class of antibiotics
Adverse Drug Reactions	**>10%:** Gastrointestinal: Diarrhea (12%), nausea (24% to 35%), vomiting (16% to 20%) **1% to 10%:** Cardiovascular: Phlebitis (3%), septic shock, thrombophlebitis Dermatologic: Pruritus, skin rash (3%) Endocrine & metabolic: Hypocalcemia, hypoglycemia, hyponatremia (2%), increased amylase (3%) Gastrointestinal: Abdominal pain (6%), abnormal stools, anorexia, dysgeusia, dyspepsia (2%) Genitourinary: Leukorrhea, vaginitis, vulvovaginal candidiasis Hematologic & oncologic: Anemia (5%), eosinophilia, hypoproteinemia (5%), increased INR, prolonged partial thromboplastin time, prolonged prothrombin time, thrombocytopenia Hepatic: Hyperbilirubinemia (2%), increased serum alanine aminotransferase (5%), increased serum alkaline phosphatase (3%), increased serum aspartate aminotransferase (4%), jaundice Hypersensitivity: Hypersensitivity reaction Infection: Abscess (2%), infection (7%), sepsis Local: Inflammation at injection site, injection site phlebitis, injection site reaction, pain at injection site, swelling at injection site Nervous system: Chills, dizziness (3%), headache (6%) Neuromuscular & skeletal: Asthenia (3%) Renal: Increased blood urea nitrogen (3%), increased serum creatinine Respiratory: Pneumonia (2%)
Monitoring Parameters	Hepatic function (periodically); coagulation parameters (including aPTT, PTT, fibrinogen) at baseline and regularly during therapy. Observe for signs and symptoms of anaphylaxis during administration.
Drug Interactions	**Risk X: Avoid combination** Aminolevulinic Acid (Systemic) BCG (Intravesical) Cholera Vaccine Mecamylamine Methoxyflurane Retinoic Acid Derivatives **Risk D: Consider therapy modification** Sodium Picosulfate Typhoid Vaccine
Pregnancy and Lactation	**pregnancy category D** **Tigecycline** may cause fetal harm when administered to a pregnant woman Although oral bioavailability is low and exposure to the breastfed infant is expected to be limited, breastfeeding is not recommended if maternal therapy is required for >3 weeks due to the potential risk of tooth discoloration and inhibition of bone growth in the infant.
Administration	**Administration: IV** Infuse over 30 to 60 minutes through dedicated line or via Y-site. If the same IV line is used for sequential infusion of several drugs, flush line with NS, D5W, or LR before and after Tigecycline administration. **Preparation for Administration:** Add 5.3 mL NS, D5W, or LR to each 50 mg vial. Swirl gently to dissolve. Resulting solution is 10 mg/mL. Reconstituted solution must be further diluted to allow IV administration. Transfer to 100 mL IV bag for infusion (final concentration should not exceed 1 mg/mL). Reconstituted

	solution should be yellow-orange; discard if not this color. Refer to manufacturer PIL if there are specific considerations.
Warnings /Precautions	***Concerns related to adverse effects:*** • Anaphylactic/Hypersensitivity reactions: May cause life-threatening anaphylaxis. Due to structural similarity with tetracyclines, avoid use in patients with known hypersensitivity to tetracycline-class antibiotics. • Antianabolic effects: May be associated with antianabolic effects observed with the tetracycline class (including increased BUN, azotemia, acidosis, and hyperphosphatemia). • Coagulopathy: May be associated with abnormalities of blood coagulation parameters, including prolongation of PT and aPTT and decreased fibrinogen that may be dose- and/or time-dependent, in particular in patients with renal and hepatic impairment; discontinue use when suspected. • Hepatotoxicity: Abnormal liver function tests (increased total bilirubin, prothrombin time, transaminases) have been reported. Isolated cases of significant hepatic dysfunction and hepatic failure have occurred. Closely monitor for worsening hepatic function in patients who develop abnormal liver function tests during therapy. Adverse hepatic effects may occur after drug discontinuation. • Pancreatitis: Acute pancreatitis (including fatalities) has been reported, including patients without known risk factors; discontinue use when suspected. • Photosensitivity: May be associated with photosensitivity due to structural similarities with tetracyclines. • Pseudotumor cerebri: May be associated with pseudotumor cerebri due to structural similarities with tetracyclines. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. • Treatment-related mortality: [US Boxed Warning]: In a meta analysis of Phase 3 and 4 clinical trials, an increase in all-cause mortality has been observed in tigecycline-treated patients versus comparator-treated patients. The cause of the mortality risk difference (0.6% [95% CI 0.1, 1.2]) has not been established. Use should be reserved for situations in which alternative treatments are not suitable. In general, deaths were the result of worsening infection, complications of infection, or underlying comorbidity. ***Disease-related concerns:*** • Hepatic impairment: Use with caution in patients with hepatic impairment; dosage adjustment recommended in severe hepatic impairment. • Intra-abdominal infections: Avoid use as monotherapy for patients with intestinal perforation (in the small sample of available cases, sepsis/septic shock occurred more frequently than patients treated with imipenem/cilastatin comparator). ***Special populations:*** • Pediatric: Safety and efficacy in children and adolescents <18 years of age have not been established due to increased mortality observed in trials of adult patients. Use only if no alternative antibiotics are available. Because of effects on tooth development (yellow-gray-brown discoloration), use in patients <8 years of age is not recommended. ***Other warnings/precautions:*** • Appropriate use: Do not use for diabetic foot infections; non-inferiority was not demonstrated in studies. Do not use for healthcare-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP); increased mortality and decreased efficacy have been reported in HAP and VAP trials.

Storage	Store intact vials at 20°C to 25°C; excursions are permitted between 15°C and 30°C. Reconstituted solutions may be stored at room temperature (not to exceed 25°C) for up to 6 hours in the vial or up to 24 hours if further diluted in NS, D5W, or LR. Alternatively, may be stored at 2°C to 8°C for up to 48 hours following immediate transfer of the reconstituted solution into NS or D5W. Refer to manufacturer PIL if there are specific considerations.

22. Vancomycin

Watch Group

Generic Name	Vancomycin
Dosage form/strengths	Powder for Solution for I.V Infusion 100mg, 500mg, 1gm, 10gm Hard Gelatin Capsules 250 mg
Route of administration	*Oral, IV*
Pharmacologic category	A glycopeptide antibacterial ATC (Oral): S01AA28 ATC (systemic): J01XA01
Indications	***Clostridioides* (formerly *Clostridium*) *difficile* infection (oral):** in adults and pediatric patients <18 years of age. **Endocarditis (injection):** Treatment of diphtheroid endocarditis in combination with either rifampin, an aminoglycoside, or both in early-onset prosthetic valve endocarditis caused by diphtheroids. *Enterococcal:* Treatment of endocarditis caused by enterococci (eg, *Enterococcus faecalis*), in combination with an aminoglycoside. *Staphylococcal:* Treatment of staphylococcal endocarditis. *Streptococcal:* Treatment of endocarditis due to *Streptococcus viridans* or *Streptococcus bovis,* as monotherapy or in combination with an aminoglycoside. **Enterocolitis (oral):** Treatment of enterocolitis caused by *Staphylococcus aureus* (including methicillin-resistant strains) in adults and pediatric patients <18 years of age. **Staphylococcal infections (injection):** Treatment of serious or severe infections (eg, bloodstream infections, bone infections, lower respiratory tract infections, skin and skin structure infections) caused by susceptible strains of methicillin-resistant (beta-lactam-resistant) staphylococci; empiric therapy of infections when methicillin-resistant staphylococci are suspected.
Dosage Regimen	**Dosing: Adult** **General Adult Dosage:** **Oral:** Ineffective for treating systemic infections: 125 to 500 mg 4 times daily. **Treatment of Life-threatening Systemic Infections** • *Intermittent infusion*: 15 to 20 mg/kg/dose (rounded to the nearest 250 mg) every 8 to 12 hours initially; for serious MRSA infections, adjust based on therapeutic monitoring. Early and frequent monitoring for dosage adjustments is recommended, especially when empiric doses exceed 4 g/day Loading dose: Seriously ill patients with documented/suspected MRSA infection: A loading dose of 20 to 35 mg/kg (based on actual body weight; maximum: 3 g/dose) may be considered to rapidly achieve target concentrations. After administration of the loading dose, initiate the maintenance dose 8 hours after the start of the loading dose). • *Continuous infusion*: **Note:** May be considered for critically ill patients who are unable to achieve AUC target with intermittent infusion dosing. Loading dose: 15 to 20 mg/kg, followed by a maintenance continuous infusion dose of 30 to 40 mg/kg/day (up to 60

mg/kg/day) to achieve a target steady state concentration of 20 to 25 mg/L

Pediatric Patients

General dosing, susceptible infection: Infants, Children, and Adolescents: IV: Initial: 45 to 60 mg/kg/day divided every 6 to 8 hours; dose and frequency should be individualized based on serum concentrations monitoring; doses require adjustment in renal impairment.

Neonates: Manufacturer recommends 15 mg/kg initially, followed by 10 mg/kg every 12 hours in neonates <1 week of age and 10 mg/kg every 8 hours in neonates 1 week to 1 month of age.

MRSA infection, serious; treatment:

Infants ≥3 months and Children <12 years: IV: Initial: 60 to 80 mg/kg/**day** in divided doses every 6 hours; initial maximum daily dose: 3,600 mg/**day**.

Children ≥12 years and Adolescents: IV: Initial: 60 to 70 mg/kg/**day** in divided doses every 6 to 8 hours; initial maximum daily dose: 3,600 mg**/day**.

Dosage adjustment

Dosing: Renal Impairment: Adult

Oral: There are no dosage adjustments provided in the manufacturer's labeling. However, dosage adjustment unlikely due to low systemic absorption.

IV:

Note: Initial IV dosing in nonobese patients should be based on actual body weight; subsequent dosing should generally be adjusted based on therapeutic monitoring

Altered kidney function:

Intermittent infusion:

CrCl (mL/minute)	Suggested loading dose (when applicable)	Suggested initial maintenance dose	Suggested dosing interval
>90 to <130	25 to 30 mg/kg	15 to 20 mg/kg	8 to 12 hours
50 to 90	20 to 25 mg/kg	15 to 20 mg/kg	12 hours
15 to <50	20 to 25 mg/kg	10 to 15 mg/kg	24 hours

IV: **Note:** Vancomycin levels should be monitored in patients with any renal impairment:

Pediatric:

The following adjustments have been recommended

Note: Renally-adjusted dose recommendations are based on IV doses of 10 mg/kg/dose every 6 hours or 15 mg/kg/dose every 8 hours.

GFR 30 to 50 mL/minute/1.73 m^2: 10 mg/kg/dose every 12 hours.

GFR 10 to 29 mL/minute/1.73 m^2: 10 mg/kg/dose every 18 to 24 hours.

GFR <10 mL/minute/1.73 m^2: 10 mg/kg/dose; redose based on serum concentrations.

Continuous renal replacement therapy (CRRT): 10 mg/kg/dose every 12 to 24 hours; monitor serum concentrations.

Dosing: Hepatic Impairment: Pediatric

There are no dosage adjustments provided in the manufacturer's labeling

Contra-indications

Hypersensitivity to vancomycin or any component of the formulation

Adverse Drug Reactions

Adverse Reactions (Significant): Considerations

Anaphylaxis

Clostridioides difficile infection

	Drug-induced immune thrombocytopenia Hypersensitivity reactions (delayed) Nephrotoxicity Neutropenia/pancytopenia Ototoxicity Vancomycin infusion reaction **IV:** Frequency not defined: Cardiovascular: Chest pain, flushing, hypotension, shock, vasculitis Dermatologic: Bullous dermatitis, erythema of skin, exfoliative dermatitis, pruritus, Stevens-Johnson syndrome, toxic epidermal necrolysis Gastrointestinal: *Clostridioides difficile* colitis Hematologic & oncologic: Agranulocytosis, eosinophilia, leukopenia, neutropenia (reversible), pancytopenia, thrombocytopenia Hypersensitivity: Anaphylaxis, hypersensitivity reaction, red man syndrome Local: Injection site phlebitis, irritation at injection site, pain at injection site Nervous system: Chills, dizziness, malaise, vertigo Neuromuscular & skeletal: Myalgia Otic: Hearing loss, ototoxicity, tinnitus Renal: Increased blood urea nitrogen, increased serum creatinine, interstitial nephritis, renal tubular necrosis Respiratory: Dyspnea, wheezing Miscellaneous: Fever **Oral:** **>10%:** Endocrine & metabolic: Hypokalemia Gastrointestinal: Abdominal pain, nausea **1% to 10%:** Cardiovascular: Peripheral edema Gastrointestinal: Diarrhea, flatulence, vomiting Genitourinary: Urinary tract infection Nervous system: Fatigue, headache Neuromuscular & skeletal: Back pain Renal: Nephrotoxicity Miscellaneous: Fever
Monitoring Parameters	**IV:** Periodic renal function tests, CBC, pregnancy test prior to use for formulation containing PEG 400 and NADA excipients, serum trough vancomycin concentrations in select patients (eg, aggressive dosing, life-threatening infection, seriously ill, unstable renal function, concurrent nephrotoxins, prolonged courses). AUC monitoring: Frequency of AUC monitoring should be based on clinical judgement; frequent or daily monitoring may be appropriate for hemodynamically unstable patients; hemodynamically stable patients may only require once-weekly monitoring **Reference Range** IV: Target concentrations: • Intermittent infusion: AUC/minimum inhibitory concentration determined by broth microdilution (MIC_{BMD}): 400 to 600, assuming MIC_{BMD} of 1 mg/L. When MIC_{BMD} is >1 mg/L, probability of attaining an

	AUC/MIC target of ≥400 is low with conventional dosing; higher doses may risk unnecessary toxicity. When MIC_{BMD} is <1 mg/L, decreasing the dose to achieve the AUC/MIC target is not recommended Trough: 10 to 20 mg/L; target within this range depends on site and severity of infection, as well as clinical response. The American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines for hospital-acquired pneumonia and the IDSA meningitis guidelines also recommend trough concentrations of 15 to 20 mg/L • Continuous infusion: Target steady-state concentration: 20 to 25 mg/L. Concentrations associated with toxicity: Serum concentration >80 mg/L **Oral therapy:** Serum sample monitoring is not typically required; systemic absorption of enteral vancomycin may occur in patients with mucosal disruption due to colitis, especially in patients with renal failure. Monitoring serum vancomycin levels may be considered for patients with renal failure who have severe colitis and require a prolonged course of enteral vancomycin
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Bile Acid Sequestrants Colistimethate Sodium Picosulfate Typhoid Vaccine
Pregnancy and Lactation	**IV vancomycin injection is as category C.** Vancomycin is present in breast milk following IV administration. Limited information indicates that vancomycin produces low levels in milk and because vancomycin is poorly absorbed orally, it is not likely to reach the bloodstream of the infant or cause any adverse effects in breastfed infants. No special precautions are required.
Administration	**Administration: IV** Administer vancomycin with a final concentration not to exceed 5 mg/mL by IV intermittent infusion over at least 60 minutes (recommended infusion period of ≥30 minutes for every 500 mg administered, in adult patients in need of fluid restriction, a concentration up to 10 mg/mL may be used, but risk of infusion-related reactions is increased. Not for IM administration. If a maculopapular rash appears on the face, neck, trunk, and/or upper extremities (vancomycin infusion reaction [formerly "red man syndrome"]), slow the infusion rate to over $1^1/_2$ to 2 hours and increase the dilution volume. Hypotension, shock, and cardiac arrest (rare) have also been reported with too rapid of infusion. Administration of antihistamines prior to infusion may prevent or minimize this reactionIrritant; ensure proper needle or catheter placement prior to and during infusion. Avoid extravasation. **Extravasation management:** If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); remove needle/cannula; elevate extremity. Information conflicts regarding the use of dry cold or dry warm compresses; however, dry warm compresses may be of benefit in increasing local blood flow to enhance drug removal from the extravasation site. Intradermal hyaluronidase may be considered for refractory cases **Administration: Oral** Reconstituted powder for injection (not premixed solution) may be diluted and used for oral administration; common flavoring syrups may be added to improve taste. The unflavored, diluted solution may also be administered via nasogastric tube. **Preparation for Administration: Adult** IV: Reconstitute 500 mg and 1 g vials with a compatible diluent to a final concentration of 50

	mg/mL. Reconstituted solution must be further diluted with at least 100 mL of a compatible diluent per 500 mg of vancomycin prior to parenteral administration. **Preparation for Administration: Pediatric** Parenteral: Reconstitute vials with SWFI to a final concentration of 50 mg/mL (see manufacturer's labeling for specific details). Further dilute the reconstituted solution in a compatible diluent (eg, D5W, NS) to a final concentration ≤5 mg/mL. In fluid restricted patients, a concentration of 10 mg/mL may be used, but the risk of infusion reactions increases. **Oral Solution** Using a vial of vancomycin powder for injection (reconstituted to 50 mg/mL), add the appropriate volume for the dose to 30 mL of water and administer orally or via NG tube. For oral administration, common flavoring syrups may be added to improve taste. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Extravasation and thrombophlebitis: If thrombophlebitis occurs, slow infusion rates, dilute solution (eg, 2.5 to 5 g/L) and rotate infusion sites. • Nephrotoxicity • Neutropenia: Prolonged therapy and use of concomitant drugs that causes neutropenia may increase the risk; monitor leukocyte counts periodically in these patients. • Ototoxicity: It has been most frequently reported in older patients, patients receiving excessive doses, those who have underlying hearing loss, or those receiving concomitant ototoxic drugs (eg, aminoglycosides). Ototoxicity may be transient or permanent; discontinue treatment if signs of ototoxicity occur. • Superinfection: Prolonged use. ***Disease-related concerns:*** • Inflammatory bowel disease: in case of oral vancomycin (multiple doses) for the treatment of *C. difficile*-associated diarrhea. consider monitoring serum trough concentrations, especially with renal insufficiency, severe colitis, and concurrent enteral vancomycin administration. • Pregnancy: [US Boxed Warning]: The formulation of vancomycin injection containing the excipients, polyethylene glycol (PEG 400) and N-acetyl D-alanine (NADA), is not recommended for use during pregnancy. PEG 400 and NADA have caused fetal malformations in animal reproduction studies. If use of vancomycin is needed during pregnancy, use other available formulations of vancomycin. • Renal impairment: Use with caution in patients with renal impairment or those receiving other nephrotoxic drugs; dosage modification required and close monitoring is recommended in patients with preexisting renal impairment and those at high risk for renal impairment. Accumulation may occur after multiple oral doses of vancomycin in patients with renal impairment; consider monitoring serum concentrations in this circumstance. ***Concurrent drug therapy issues:*** • Drug-drug interactions: Potentially significant interactions may exist. ***Other warnings/precautions:*** • Appropriate use: Oral vancomycin is only indicated for the treatment of CDI or enterocolitis due to *S. aureus* and is not effective for systemic infections; parenteral vancomycin is not effective for the treatment of enterocolitis. • Infusion reactions: Rapid IV administration (eg, over <60 minutes) may result in hypotension, flushing, erythema, urticaria, pruritus, wheezing, dyspnea, and, rarely, cardiac arrest. Reactions usually cease promptly after infusion is stopped. Frequency of infusion reactions may increase with concomitant administration of anesthetics. If used in conjunction with anesthesia, complete the vancomycin infusion prior to anesthesia

	induction.
Storage	Vials: Store intact vials at 20°C to 25°C. Reconstitute vial using an appropriate diluent; recommendations may vary by product. Capsules: Store at 20°C to 25°C; excursions permitted to 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.

Penicillins

1. Amoxicillin

Access Group

Generic Name	Amoxicillin
Dosage form/strengths	Powder for Oral suspension 125mg/5ml, 200mg/5ml, 250mg/5ml, 400mg/5ml Capsule 250mg, 500mg Tablet 125mg, 875mg, 1g, Extended Release Tablets: 775 mg Powder for injection 250mg, 500mg, 1g Oral drops 100mg/ml
Route of administration	Oral, IV
Pharmacologic category	Antibiotic, Penicillin J01CA04
Indications	Ear, nose, and throat infections (pharyngitis/tonsillitis, otitis media) Genitourinary tract infections Helicobacter pylori eradication Lower respiratory tract infections (including pneumonia) Rhinosinusitis, acute bacterial: Skin and skin structure infections.
Dosage Regimen	**Adult Dosing: Usual dosage range:** ***Oral:*** Immediate release: 500 mg to 1 g every 8 to 12 hours. Extended release: 775 mg once daily. • ***Helicobacter pylori* eradication: Oral:** ○ *Different regimens containing* Amoxicillin 1 g twice daily with different agents e.g clarithromycin 500 mg twice daily, a standard-dose or double-dose proton pump inhibitor, metronidazole or tinidazole 500 mg twice daily or levofloxacin 500 mg once daily. regimen is for 10 to 14 days. ○ *High-dose dual therapy (salvage regimen)*: Amoxicillin 750 mg 4 times daily **or** 1 g 3 times daily; in combination with a standard-dose or double-dose proton pump inhibitor 3 to 4 times daily for 14 days • **Otitis media, acute (alternative agent): Oral:** 500 mg every 8 hours. Some experts use 1 g every 8 hours for patients at high risk of severe infection or resistant *Streptococcus pneumoniae*. Duration is 5 to 7 days for mild to moderate infection and 10 days for severe infection • **Pneumonia, community acquired, outpatient empiric therapy (patients without comorbidities or risk factors for antibiotic resistant pathogens):** **Oral:** 1 g 3 times daily; some experts prefer use of amoxicillin in combinations. Duration is for a minimum of 5 days. • **Rhinosinusitis, acute bacterial:** **Oral:** 500 mg every 8 hours **or** 875 mg every 12 hoursfor 5 to 7 days • **Skin and soft tissue infection:** *Erysipelas, mild:* **Oral:** 500 mg 3 times **or** 875 mg every 12 hours for 5 days, for up to 14 days *Erysipeloid, localized cutaneous:* **Oral:** 500 mg 3 times daily for 5 to 10 days • **Streptococcal pharyngitis (group A):** **Oral:** 500 mg twice daily **or** 1 g once daily for 10 days. Extended release: 775 mg once daily for 10 days.

	• **Urinary tract infection:** **Note:** Not recommended for empiric therapy. **Oral:** 500 mg every 8 hours for 4 to 7 days. **Dosing: Pediatric:** – **General dosing, susceptible infection:** **Mild to moderate infection:** **Infants ≤3 months: Oral**: 30 mg/kg/day divided into 2 doses. **Infants >3 months, Children, and Adolescents:** Oral: 20 to 40 mg/kg/day in divided doses every 8 hours (maximum dose: 500 mg/dose) **or** 25 to 45 mg/kg/day in divided doses every 12 hours (maximum dose: 875 mg/dose). **Severe infection (as step-down therapy): Infants, Children, and Adolescents**: **Oral**: 80 to 90mg/kg/day in divided doses every 12 hours; maximum dose: 500 mg/dose for most indications.
Dosage adjustment	**Renal Impairment: Adult** Oral: **If the normal recommended dose is 250 to 500 mg every 8 hours** GFR >30 mL/minute: No dosage adjustment necessary. GFR 10 to 30 mL/minute: 250 to 500 mg every 12 hours GFR <10 mL/minute: 250 to 500 mg every 12 to 24 hours Hemodialysis, intermittent: 250 to 500 mg every 12 to 24 hours Peritoneal dialysis: 250 to 500 mg every 12 hours **If the normal recommended dose is 1 g every 8 hours** GFR >30 mL/minute: No dosage adjustment necessary. GFR 10 to 30 mL/minute: 1 g every 12 hours GFR <10 mL/minute: 500 mg every 12 hours Hemodialysis, intermittent: 500 mg every 12 hours Peritoneal dialysis: 500 mg every 12 hours Avoid extended release 775 mg tablet and immediate release 875 mg tablet in patients with GFR <30 mL/minute or patients requiring hemodialysis **Renal Impairment in pediatrics** The following guidelines have been used by some clinicians: Oral: *Immediate release*: Infants, Children, and Adolescents: Mild to moderate infection: Dosing based on 25 to 50 mg/kg/day divided every 8 hours: GFR >30 mL/minute/1.73 m^2: No adjustment required GFR 10 to 29 mL/minute/1.73 m^2: 8 to 20 mg/kg/dose every 12 hours GFR <10 mL/minute/1.73 m^2: 8 to 20 mg/kg/dose every 24 hours Hemodialysis: Moderately dialyzable (20% to 50%); ~30% removed by 3-hour hemodialysis: 8 to 20 mg/kg/dose every 24 hours; give after dialysis Peritoneal dialysis: 8 to 20 mg/kg/dose every 24 hours Severe infection (high dose): Dosing based on 80 to 90 mg/kg/day divided every 12 hours: GFR >30 mL/minute/1.73 m^2: No adjustment required GFR 10 to 29 mL/minute/1.73 m^2: 20 mg/kg/dose every 12 hours; do not use the 875 mg tablet GFR <10 mL/minute/1.73 m^2: 20 mg/kg/dose every 24 hours; do not use the 875 mg tablet Hemodialysis: Moderately dialyzable (20% to 50%); ~30% removed by 3-hour hemodialysis: 20 mg/kg/dose every 24 hours; give after dialysis Peritoneal dialysis: 20 mg/kg/dose every 24 hours *Extended release*: Children ≥12 years and Adolescents: CrCl <30 mL/minute: Not recommended

	Dosing: Hepatic Impairment: There are no dosage adjustments needed.
Contra-indications	Serious hypersensitivity to amoxicillin or to other beta-lactams, or any component of the formulation
Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** Antibiotic-associated (non–Clostridioides difficile) diarrhea Clostridioides difficile diarrhea Hypersensitivity reactions (immediate and delayed) **1% to 10%:** CNS: Headache (1%) Gastrointestinal: Diarrhea (2%), nausea (1%), vomiting (1%) Genitourinary: Vulvovaginal infection (2%)
Monitoring Parameters	Obtain CBC with differential, renal function tests, and liver function tests periodically with prolonged therapy. Screen patients for history of renal impairment, liver impairment, or active mononucleosis. Assess for signs of anaphylaxis during first dose. Assess for signs and symptoms of opportunistic infections
Drug Interactions	***Risk X: Avoid combination:*** BCG (Intravesical), Cholera Vaccine ***Risk D: Consider therapy modification:*** Typhoid Vaccine, Sodium Picosulfate ***Risk C: Monitor therapy:*** Acemetacin, Allopurinol, Aminoglycosides, BCG Vaccine (Immunization), Dichlorphenamide. Lactobacillus and Estriol. Methotrexate, Mycophenolate, Probenecid, Tetracyclines, warfarin May interfere with urinary glucose tests
Pregnancy	**Pregnancy Risk Factor** B Amoxicillin is present in breast milk. In general, antibiotics that are present in breast milk may cause non-dose-related modification of bowel flora. Monitor infants for GI disturbances, such as thrush or diarrhea.
Administration	Oral: Immediate release: May be administered on an empty or full stomach; may be mixed with formula, milk, cold drink, or juice; administer dose immediately after mixing; shake suspension well before use Extended release: Administer within 1 hour of finishing a meal; do not chew or crush tablet. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/Precautions	• Anaphylactic/hypersensitivity reactions: Serious and occasionally severe or fatal. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. **Disease-related concerns:** • Infectious mononucleosis: A high percentage of patients with infectious mononucleosis develop an erythematous rash during amoxicillin therapy; avoid use in these patients. **Geriatric Considerations** Resistance to amoxicillin has been a problem in patients on frequent antibiotics or in nursing homes. Alternative antibiotics may be necessary in these populations. Adjust dose based on renal function. - May be administered on an empty or full stomach;

Storage	Store at room temperature. Reconstituted oral suspension remains stable for 14 days at room temperature or refrigerated (refrigeration preferred). Refer to manufacturer PIL if there are specific considerations.

2. Amoxicillin and Clavulanic acid

Access Group

Generic Name	Amoxicillin and Clavulanate
Dosage form/strengths	**Tablet (film coated, dispersible or chewable):** 125/31.25 mg, 200/28.5 mg, 250/62.5 mg, 250/125mg, 500/125 mg, 652.78/50.4 mg, 875/125 mg, 875/148.9 mg **Powder for Oral Suspension:** 50/12.5 mg, 125/31.25 mg, 200/28.5 mg, 200/30 mg, 250/62.5 mg, 400/57 mg, 400/60 mg, 600/42.9 mg, 1000/125 mg **Powder for injection:** 500/100 mg, 1000/200 mg
Route of administration	*Oral, IV*
Pharmacologic category	Antibiotic, Penicillin ATC: J01CR02
Indications	**Oral:** Otitis media, acute Pneumonia Rhinosinusitis, acute bacterial Skin and skin structure infections. Urinary tract infections **IV**: Treatment of severe upper respiratory infections, chronic bronchitis (acute exacerbation), CAP, cystitis, pyelonephritis, skin and soft tissue infections, osteomyelitis, intra-abdominal infections, and female genital infections caused by susceptible organisms in adults and pediatric patients; surgical prophylaxis in procedures involving the GI tract, pelvic cavity, head and neck, or biliary tract in adults.
Dosage Regimen	**Adult:** **Usual dosing range:** **Oral**: Immediate release: 500 mg every 8 to 12 hours **or** 875 mg every 12 hours; **IV**: 1 g every 8 hours or 2 g every 8 to 12 hours **Duration**: 5 to 7 days for mild to moderate infection and 10 days for severe infection • **Otitis media(acute); community acquired (mild); Community acquired (outpatient with comorbidities, as part of an appropriate combination regimen): Oral**: Immediate release: 875 mg twice daily **or** 500 mg every 8 hours. • **Rhinosinusitis, acute bacterial: Oral** Standard dose: Immediate release: 500 mg every 8 hours **or** 875 mg every 12 hours for 5 to 7 days • **Urinary tract infection (UTI) (alternative agent)** ○ **acute simple cystitis:** **Oral**: Immediate release: 500 mg twice daily ○ **Complicated UTI (including pyelonephritis):** **Oral**: 875 mg twice daily for 10 to 14 days **Note:** Oral therapy should follow appropriate parenteral therapy. **Pediatric** • Children weighing <40 kg should *not* receive film-coated tablets containing 250 mg of amoxicillin since this preparation contains a high dose of clavulanic acid. • The oral suspension containing 125 mg of amoxicillin/5 mL is the only preparation recommended for use in neonates and infants <12 weeks (3 months) of age.

Frequency of dosing generally based on ratio of amoxicillin to clavulanate:
• 2:1 formulation is dosed 3 times daily amoxicillin/clavulanate (250 mg/ 125 mg): should only be used in patients ≥40 kg, due to the amoxicillin to clavulanate ratio.

• 4:1 formulation is dosed 3 times daily amoxicillin/clavulanate (125 mg/ 31.25 mg; 250 mg/ 62.5 mg; 500 mg/ 125 mg).

• 7:1 formulation is dosed 2 times daily amoxicillin/clavulanate (200 mg/ 28.5 mg; 400 mg/ 57 mg; 875 mg/ 125 mg).

• 14:1 formulation is dosed 2 times daily amoxicillin/clavulanate (600 mg/ 42.9 mg).

General dosing, susceptible infection:
Note: Dosing determined by formulations amoxicillin/clavulanate ratio:
Infants, Children, and Adolescents: Oral:

4:1 formulation: 20 to 40 mg amoxicillin/kg/day in divided doses 3 times daily; maximum daily dose: 1,500 mg/day.

7:1 formulation: 25 to 45 mg amoxicillin/kg/day in divided doses twice daily; maximum daily dose: 1,750 mg/day.

14:1 formulation: 90 mg amoxicillin/kg/day in divided doses twice daily; maximum daily dose: 4,000 mg/day.

IV dosing:
5:1 formulation:
Infants <3 months or weighing <4 kg: IV: 25 mg amoxicillin/kg/dose every 12 hours.
Infants ≥3 months weighing ≥4 kg, Children, and Adolescents: IV: 25 mg amoxicillin/kg/dose every 8 hours; maximum dose: 1,000 mg amoxicillin/dose.

Dosage adjustment

Dosing: Renal Impairment: Adult
Oral: Note: Renally adjusted dose recommendations are based on the amoxicillin 250 mg/clavulanate 125 mg and amoxicillin 500 mg/clavulanate 125 mg tablets. Avoid IR 875 mg tablet.
CrCl ≥30 mL/minute: No dosage adjustment necessary.
CrCl 10 to <30 mL/minute: 250 to 500 mg every 12 hours.
CrCl <10 mL/minute; Hemodialysis, intermittent (thrice weekly):
250 to 500 mg every 12 to 24 hours
Peritoneal dialysis: 250 to 500 mg every 12 hours

IV: **Note:** Dose based on amoxicillin component.
CrCl ≥30 mL/minute: No dosage adjustment necessary.
CrCl 10 to 30 mL/minute: Initial: 1 g followed by 500 mg every 12 hours.
CrCl <10 mL/minute; Hemodialysis, intermittent (thrice weekly):
Initial: 1 g followed by 500 mg every 12 to 24 hours (expert opinion).
Peritoneal dialysis: Initial: 1 g followed by 500 mg every 12 hours

Dosing: Renal Impairment: Pediatric

	Oral: ○ *Mild to moderate infection*: Dosing based on 20 to 40 mg amoxicillin/kg/day divided every 8 hours or 25 to 45 mg amoxicillin/kg/day divided every 12 hours: GFR >30 mL/minute/1.73 m^2: No adjustment required. GFR 10-29 mL/minute/1.73 m^2: 8- 20 mg amoxicillin/kg/dose every 12 hours. GFR <10 mL/minute/1.73 m^2: 8-20 mg amoxicillin/kg/dose every 24 hours. Hemodialysis: 8-20 mg amoxicillin/kg/dose every 24 hours; given after dialysis. Peritoneal dialysis: 8-20 mg amoxicillin/kg/dose every 24 hours. ○ *Severe infection (high dose)*: do not use the 875 mg tablet. Dosing based on 80 to 90 mg amoxicillin/kg/day divided every 12 hours: CrCl >30 mL/minute/1.73 m^2: No adjustment required. CrCl 10-29 mL/minute/1.73 m^2: 20 mg amoxicillin/kg/dose every 12 hours. CrCl <10 mL/minute/1.73 m^2: 20 mg amoxicillin/kg/dose every 24 hours. Hemodialysis: 20 mg amoxicillin/kg/dose every 24 hours; give after dialysis. Peritoneal dialysis: 20 mg amoxicillin/kg/dose every 24 hours; do not use the 875 mg tablet. **IV**: *5:1 formulation:* preferred formulation in case of kidney impairment. ○ Infants, Children, and Adolescents weighing <40 kg: CrCl >30 mL/minute: No dosage adjustment necessary. CrCl 10 to 30 mL/minute: 25 mg amoxicillin/kg every 12 hours. CrCl <10 mL/minute: 25 mg amoxicillin/kg every 24 hours. Hemodialysis: 25 mg amoxicillin/kg every 24 hours; give an additional dose of 12.5 mg amoxicillin/kg at the end of each dialysis session. ○ Children and Adolescents weighing ≥40 kg: CrCl >30 mL/minute: No dosage adjustment necessary. CrCl 10 to 30 mL/minute: 1,000 mg amoxicillin followed by 500 mg amoxicillin every 12 hours. CrCl <10 mL/minute: 1,000 mg amoxicillin followed by 500 mg amoxicillin every 24 hours. Hemodialysis: 1,000 mg amoxicillin followed by 500 mg amoxicillin every 24 hours; give an additional 500 mg at the end of each dialysis session. **Dosing: Hepatic Impairment: Adult, pediatric** There are no dosage adjustments available. Use caution and monitor liver function during therapy.
Contra-indications	Hypersensitivity to amoxicillin, clavulanic acid, other beta-lactam antibacterial drugs (eg, penicillins, cephalosporins), or any component of the formulation; history of cholestatic jaundice or hepatic dysfunction with amoxicillin/clavulanate potassium therapy.
Adverse Drug Reactions	**>10%:** Gastrointestinal: Diarrhea (3% to 34%; incidence varies upon dose and regimen used) **1% to 10%:** Dermatologic: Diaper rash, skin rash, urticaria Gastrointestinal: Abdominal distress, loose stools, nausea, vomiting Genitourinary: Vaginitis Infection: Candidiasis, vaginal mycosis
Monitoring Parameters	Assess patient at beginning and throughout therapy for infection; with prolonged therapy, monitor renal, hepatic, and hematologic function periodically; in patients with hepatic impairment, monitor liver function tests at regular intervals; monitor for signs of anaphylaxis during first dose
Drug Interactions	***Risk X: Avoid combination:*** BCG (Intravesical), Cholera Vaccine,

	***Risk D: Consider therapy modification*:** Tolvaptan, Typhoid Vaccine, Sodium Picosulfate: ***Risk C: Monitor therapy*:** Allopurinol, Acemetacin, Aminoglycosides, BCG Vaccine (Immunization), Dichlorphenamide, Lactobacillus and Estriol, Methotrexate, Mycophenolate, Probenecid, Teriflunomide, Tetracyclines, Vitamin K Antagonists
Pregnancy and Lactation	**Pregnancy Risk Factor** B Amoxicillin is present in breast milk following administration amoxicillin/clavulanate. amoxicillin/clavulanate is considered compatible with caution during breastfeeding when used in usual recommended doses. Monitor infants for GI disturbances, such as thrush and diarrhea
Administration	**Administration: IV** Administer by slow IV injection over 3 to 4 minutes (1 g dose **only**) or as an infusion over 30 to 40 minutes. **Administration: Oral** Administer around-the-clock to promote less variation in peak and trough serum levels. Administer with food to increase absorption and decrease stomach upset; shake suspension well before use. **Administration: Pediatric** Oral: Can be given without regard to meals. Administer at the start of a meal to decrease the frequency or severity of GI side effects; may mix with milk, formula, or juice; shake suspension well before use. IV: Administer as an infusion over 30 to 40 minutes. In infants ≥3 months, children, and adolescents, 5:1 formulation (500/100 mg and 1,000/200 mg) may also be administered by slow IV injection over 3 to 4 minutes. **Preparation for Administration:** • Oral: Reconstitute powder for oral suspension with appropriate amount of water as specified. Shake vigorously until suspended. • IV: 500 mg vial: Reconstitute with 10 mL of SWFI; within 15 minutes, further dilute to 50 mL in a compatible solution (eg, SWFI, NS). 1 g or 2 g vial: Reconstitute with 20 mL SWFI; within 15 minutes, further dilute in a compatible solution (eg, SWFI, NS) to a final concentration of 10 to 20 mg amoxicillin/mL (ie, 1,000 to 2,000 mg in 100 mL for larger patients). **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Anaphylactic/hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy, especially with a history of beta-lactam hypersensitivity, or history of sensitivity to multiple allergens. • Diarrhea: Incidence of diarrhea is higher than with amoxicillin alone. • Hepatic effects: Although rarely fatal, hepatic dysfunction (eg, cholestatic jaundice, hepatitis) has been reported. Patients at highest risk include those with serious underlying disease or concomitant medications. Hepatic toxicity is usually reversible. Monitor LFTs at regular intervals in patients with hepatic impairment. • Prolonged therapy: Monitor renal, hepatic, and hematopoietic function if therapy extends beyond approved duration times.

	• Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *Clostridioides* (formerly *Clostridium) difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Hepatic impairment: Use with caution in patients with hepatic impairment and monitor LFTs at regular intervals. • Infectious mononucleosis: A high percentage of patients with infectious mononucleosis have developed rash during therapy; ampicillin-class antibiotics not recommended in these patients. • Renal impairment: Dosage adjustment recommended in patients with CrCl ≤30 mL/minute.
Storage	• Powder for oral suspension: Store dry powder at or below 25°C. Reconstituted oral suspension should be kept in refrigerator. Discard unused suspension after 10 days (consult manufacturer's labeling). Unit-dose antibiotic oral syringes are stable under refrigeration for 24 hours. • Tablet: Store at or below 25°C. Dispense in original container. • IV: Store intact vials at 15°C to 30°C. Solutions diluted for infusion should be used within 1 hour if stored at 25°C or within 4 hours if stored at 4°C; recommendations may vary based on solution used for dilution, refer to manufacturer's PIL for detailed information. • Refer to manufacturer PIL if there are specific considerations.

3. Ampicillin

Generic Name	Ampicillin
Dosage form/strengths	Capsules: 250mg, 500mg Oral suspension: 125mg/5ml, 250mg/5ml Vial: 250 mg, 500 mg, 1g
Route of administration	*Oral, IV, IM*
Pharmacologic category	Antibiotic, Penicillin ATC: J01CA01
Indications	Oral: **GI tract infections:** Treatment of GI tract infections. **Note:** Ampicillin is **not** recommended by CDC as a first-line agent for shigellosis, salmonellosis (nontyphoid), or *Salmonella enterica* species (typhoid fever) due to development of resistance. **GU tract infections:** Treatment of GU tract infections. **Note:** Ampicillin is **not** recommended by the CDC as a first-line agent in the treatment of gonorrhea. **Respiratory tract infections:** Treatment of respiratory tract infections. Injection: **Bloodstream infection** **Endocarditis, treatment:** caused by susceptible gram-positive organisms **GI infections:** Treatment of GI infections. **Note:** Ampicillin is **not** recommended as a first-line agent for shigellosis, salmonellosis (nontyphoid), or *S. enterica* species (typhoid fever) due to development of resistance. **Meningitis, bacterial** **Respiratory tract infections** **Urinary tract infections**.
Dosage Regimen	**Adult Dosing** • **Endocarditis:** 12 g daily (by continuous IV infusion or in 6 equally divided IV doses) in conjunction with IM or IV gentamicin (1 mg/kg every 8 hours). Treatment with both drugs generally should be continued for 4–6 weeks • **Meningitis and Other CNS Infections** **IV, then IM** 150–200 mg/kg daily in divided doses every 3–4 hours. Use IV initially, may switch to IM after 3 days. • **Respiratory Tract Infections** **Oral** 250 mg 4 times daily. **IV or IM** Adults weighing <40 kg: 25–50 mg/kg daily in divided doses every 6–8 hours. Adults weighing ≥40 kg: 250–500 mg every 6 hours. • **Septicemia** **IV or IM** 150–200 mg/kg daily • **Urinary Tract Infections (UTIs)** **Oral** 500 mg 4 times daily.[1]

IV or IM
Adults weighing <40 kg: 50 mg/kg daily in divided doses every 6–8 hours.[2]
Adults weighing ≥40 kg: 500 mg every 6 hours

Dosing: Pediatric
General dosing, susceptible infection: **Infants, Children, and Adolescents:**
Mild to moderate infection:
Oral: 50 to 100 mg/kg/day divided every 6 hours; maximum daily dose: 2,000 mg/day.
IM, IV: 50 to 200 mg/kg/day divided every 6 hours; maximum daily dose: 8 g/day.
Severe infection (eg, meningitis, endocarditis): IM, IV: 300 to 400 mg/kg/**day** divided every 4 to 6 hours; maximum daily dose: 12 g/day.

Dosage adjustment

Dosing: Renal Impairment, Adult: IV:
Note: The following recommendations are based primarily on expert opinion.

Ampicillin Dose Adjustments in Altered Kidney Function

CrCl (mL/minute)	If usual recommended dose is 1 to 2 g every 6 hours	If usual recommended dose is 2 g every 4 hours
50 to <130	1 to 2 g every 6 hours	2 g every 4 hours
30 to <50	1 to 2 g every 8 hours	2 g every 6 hours
15 to <30	1 to 2 g every 12 hours	2 g every 8 hours
<15	1 to 2 g every 24 hours	2 g every 12 hours
Hemodialysis, intermittent (thrice weekly)[c]	1 to 2 g every 24 hours	2 g every 12 hours
Peritoneal dialysis	1 to 2 g every 24 hours	2 g every 12 hours

Dosing: Renal Impairment: Pediatric
Infants, Children, and Adolescents: The following adjustments have been recommended.
Note: Renally adjusted dose recommendations are based on IM, IV doses of 100 to 200 mg/kg/day divided every 6 hours: IM, IV:
GFR 30 to 50 mL/minute/1.73 m^2: 35 to 50 mg/kg/dose every 6 hours
GFR 10 to 29 mL/minute/1.73 m^2: 35 to 50 mg/kg/dose every 8 to 12 hours
GFR <10 mL/minute/1.73 m^2: 35 to 50 mg/kg/dose every 12 hours
Intermittent hemodialysis: 35 to 50 mg/kg/dose every 12 hours
Peritoneal dialysis (PD): 35 to 50 mg/kg/dose every 12 hours
Continuous renal replacement therapy (CRRT): 35 to 50 mg/kg/dose every 6 hours
Dosing: Hepatic Impairment:
There are no dosage adjustments needed

Contra-indications

Hypersensitivity (eg, anaphylaxis) to ampicillin, any component of the formulation, or other penicillins; infections caused by penicillinase-producing organisms

Adverse Drug Reactions	Frequency not defined. **Central nervous system**: Brain disease (penicillin-induced), glossalgia, seizure, sore mouth **Dermatologic:** Erythema multiforme, exfoliative dermatitis, skin rash, urticaria **Note:** Appearance of a rash should be carefully evaluated to differentiate (if possible) nonallergic ampicillin rash from hypersensitivity reaction. Incidence is higher in patients with viral infection, *Salmonella* infection, lymphocytic leukemia, or patients that have hyperuricemia. **Gastrointestinal**: Diarrhea, enterocolitis, glossitis, melanoglossia, nausea, oral candidiasis, pseudomembranous colitis, stomatitis, vomiting **Hematologic & oncologic**: Agranulocytosis, anemia, eosinophilia, hemolytic anemia, immune thrombocytopenia, leukopenia **Hepatic**: Increased serum AST **Hypersensitivity**: Anaphylaxis **Immunologic**: Serum sickness-like reaction **Renal**: Interstitial nephritis (rare) **Respiratory**: Stridor **Miscellaneous**: Fever
Monitoring Parameters	With prolonged therapy, monitor renal, hepatic, and hematologic function periodically; observe signs and symptoms of anaphylaxis during first dose
Drug Interactions	***Risk X: Avoid combination:*** BCG (Intravesical), Cholera Vaccine ***Risk D: Consider therapy modification:*** Chloroquine, Sodium Picosulfate, Typhoid Vaccine, ***Risk C: Monitor therapy:*** Allopurinol, Aminoglycosides, Atenolol, BCG Vaccine (Immunization), Dichlorphenamide, Lactobacillus and Estriol, Methotrexate, Mycophenolate, Probenecid, Tetracyclines, Vitamin K Antagonists (eg, warfarin)
Pregnancy and lacatation	**Pregnancy Risk Factor** B Ampicillin is considered compatible with breastfeeding when used in usual recommended doses. Monitor infants for GI disturbances, such as thrush or diarrhea.
Administration	**Administration: Oral** Administer around-the-clock to promote less variation in peak and trough serum levels. Administer on an empty stomach with a full glass of water (ie, 30 minutes prior to or 2 hours after meals) to increase total absorption. **Administration: IM** Inject deep IM into a large muscle mass **Administration: IV** Direct IV bolus: Administer over 3 to 5 minutes (125 to 500 mg) or over 10 to 15 minutes (1 to 2 g). More rapid infusion may cause seizures. Infusion: Rapid infusion may cause seizures. Adjust rate of infusion so that the total dose is administered before admixture stability expires. **Preparation for Administration:** **IM**: Dissolve contents of vial in sterile water for injection or bacteriostatic water for injection; final concentration for IM injection is 125 mg/mL or 250 mg/mL. Solutions for IM injection should be freshly prepared and used within 1 hour. **IV**: *Direct IV use*: Dissolve contents of 125 mg, 250 mg, or 500 mg vial in 5 mL SWFI or bacteriostatic water for injection. Alternatively, dissolve contents of 1 g or 2 g vial in 7.4 or 14.8 mL SWFI or bacteriostatic water for injection, respectively. *Intermittent infusion*: Minimum volume: Concentration should not exceed 30 mg/mL due to concentration-dependent stability restrictions. Usual diluent: 500 mg/50 mL NS; 1 g/50 mL NS;

	2 g/100 mL NS. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity/anaphylactoid reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy, especially with a history of beta-lactam hypersensitivity or a history of sensitivity to multiple allergens. Serious anaphylactoid reactions require emergency treatment and airway management. Appropriate treatments must be readily available. • Rash: Appearance of a rash should be carefully evaluated to differentiate a nonallergic ampicillin rash from a hypersensitivity reaction; rash occurs in 5% to 10% of children and is a generalized dull red, maculopapular rash, generally appearing 3 to 14 days after the start of therapy. It normally begins on the trunk and spreads over most of the body. It may be most intense at pressure areas, elbows, and knees. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *Clostridioides* (formerly *Clostridium*) *difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment **Geriatric Considerations** Resistance to ampicillin has been a problem in patients on frequent antibiotics or in nursing homes. Alternative antibiotics may be necessary in these populations. Adjust dose for renal function. **Warnings: Additional Pediatric Considerations** Ampicillin has been shown to prolong the bleeding time in neonates in 2 prospective studies
Storage	• Capsules: Store at 20°C to 25°C. • Oral suspension: Store dry powder at 20°C to 25°C. Once reconstituted, oral suspension is stable for 14 days under refrigeration. • Vials: Store intact vials at 20°C to 25°C. • Solutions for IM or direct IV should be used within 1 hour. • Stability of parenteral admixture in NS at 25°C is 8 hours (concentrations up to 30 mg/mL) and at 4°C is 24 hours (concentration of 30 mg/mL) or 48 hours (concentrations up to 20 mg/mL). Protect from freezing. • Refer to manufacturer PIL if there are specific considerations.

4. Ampicillin and sulbactam

Access Group

Generic Name	Ampicillin and Sulbactam
Dosage form/strengths	Powder for Injection: 2000/1000mg, 1000/500mg, 500/250mg, 250/125 mg
Route of administration	*IM, IV*
Pharmacologic category	Antibiotic, Penicillin ATC: J01CR01
Indications	Treatment of skin and skin structure, intra-abdominal, and gynecological infections caused by susceptible bacteria; spectrum is that of ampicillin plus organisms producing beta-lactamases such as Staphylococcus aureus, Haemophilus influenzae, Escherichia coli, Klebsiella, Acinetobacter, Enterobacter, and anaerobes.
Dosage Regimen	**Dosing: Adult** **Note:** Adult dosage recommendations are expressed as total grams of ampicillin/sulbactam. **Usual dosage range:** IM, IV: 1.5 to 3 g every 6 hours (maximum: ampicillin/sulbactam 12 g daily); for the treatment of infections caused by *Acinetobacter* spp., higher doses have been described. **Dosing: Pediatric** **General dosing, susceptible infection:** Infants, Children, and Adolescents: **Mild to moderate infection**: IV: 100 to 200 mg ampicillin/kg/day divided every 6 hours; maximum dose: 2,000 mg ampicillin/dose. may also be administered IM **Severe infection** (eg, meningitis, resistant *Streptococcus pneumonia*): IV: 200 to 400 mg ampicillin/kg/day divided every 6 hours; maximum dose: 2,000 mg ampicillin/dose; may also be administered IM **Surgical prophylaxis:** Children and Adolescents: IV: 50 mg ampicillin/kg/dose within 60 minutes prior to procedure; may repeat in 2 hours if lengthy procedure or excessive blood loss; maximum dose: 2,000 mg ampicillin/dose
Dosage adjustment	**Dosing: Renal Impairment: Adult** **Note:** Renally adjusted dose recommendations are based on a usual recommended dose of 1.5 to 3 g every 6 hours. **Altered kidney function**: **IV:** CrCl ≥30 mL/minute: No dosage adjustment necessary. CrCl 15 to 29 mL/minute: 1.5 to 3 g every 12 hours. CrCl 5 to 14 mL/minute: 1.5 to 3 g every 24 hours. **Hemodialysis, intermittent (thrice weekly):** Dialyzable (39% to 63%): **IV:** 1.5 to 3 g every 12 to 24 hours; administer after dialysis when scheduled dose falls on dialysis days. **Peritoneal dialysis: IV:** 1.5 g every 12 hours or 3 g every 24 hours. **CRRT:** Drug clearance is dependent on the effluent flow rate, filter type, and method of renal replacement. CVVH/CVVHD/CVVHDF: **IV:** 3 g every 8 to 12 hours. **PIRRT (eg, sustained, low-efficiency diafiltration):** Drug clearance is dependent on the effluent flow rate, filter type, and method of renal replacement. Appropriate dosing requires consideration of adequate drug concentrations (eg, site of infection) and consideration of initial loading doses. Close monitoring of response and adverse reactions (eg, neurotoxicity) due to drug accumulation is important.

	IV: Initial: 3 g followed by 1.5 to 3 g every 8 to 12 hours. Where possible, give one dose after PIRRT session. **Dosing: Renal Impairment: Pediatric** Children and Adolescents: IV: CrCl ≥30 mL/minute/1.73 m^2: No dosage adjustment required. CrCl 15 to 29 mL/minute/1.73 m^2: Administer every 12 hours. CrCl 5 to 14 mL/minute/1.73 m^2: Administer every 24 hours. **Dosing: Hepatic Impairment: Pediatric** There are no dosage adjustments needed
Contra-indications	Hypersensitivity (eg, anaphylaxis or Stevens-Johnson syndrome) to ampicillin, sulbactam, or to other beta-lactam antibacterial drugs (eg, penicillins, cephalosporins), or any component of the formulations; history of cholestatic jaundice or hepatic dysfunction associated with ampicillin/sulbactam
Adverse Drug Reactions	**>10%:** Local: Pain at injection site (IM; 16%) **1% to 10%:** Cardiovascular: Thrombophlebitis (3%), phlebitis (1%) Dermatologic: Skin rash (<2%) Gastrointestinal: Diarrhea (3%) Local: Pain at injection site (IV; 3%)
Monitoring Parameters	With prolonged therapy, monitor hematologic, renal, and hepatic function; monitor for signs of anaphylaxis during first dose. In patients with preexisting hepatic impairment, monitor hepatic function at regular intervals
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine ***Risk D: Consider therapy modification*** Chloroquine, Sodium Picosulfate, Typhoid Vaccine, ***Risk C: Monitor therapy:*** Acemetacin, Allopurinol, Aminoglycosides, Atenolol, BCG Vaccine (Immunization), Dichlorphenamide, Lactobacillus and Estriol, Methotrexate, Mycophenolate, Probenecid, Tetracyclines, Vitamin K Antagonists (eg, warfarin)
Pregnancy and Lactation	**Pregnancy category B** Ampicillin and sulbactam are present in breast milk. Ampicillin is considered compatible with breastfeeding when used in usual recommended doses. In general, antibiotics that are present in breast milk may cause nondose-related modification of bowel flora. Monitor infants for GI disturbances
Administration	**Administration:** Parenteral: **IM**: Administer by deep IM injection. Administer within 1 hour of preparation. **IV**: Administered by slow IV injection over 10 to 15 minutes or by intermittent IV infusion over 15 to 30 minutes Ampicillin and gentamicin should not be mixed in the same IV tubing. Concurrent Y-site administration with aminoglycosides should be avoided (penicillins have been shown to inactivate aminoglycosides *in vitro,* while amikacin has shown greater stability against inactivation*)* **Preparation for Administration: Adult** Direct IV administration and IV infusion: Reconstitute with sterile water for injection (SWFI).

	Sodium chloride 0.9% (NS) is the diluent of choice for IV infusion use. IM administration: Reconstitute with SWFI **or** 0.5% or 2% lidocaine hydrochloride injection. **Preparation for Administration: Pediatric** **IV**: Use within several hours after preparation. Reconstitute with SWFI. Further dilute with a compatible solution; sodium chloride 0.9% (NS) is the diluent of choice; final concentration should not exceed (30 mg/mL of ampicillin and 15 mg/mL of sulbactam) **IM**: Reconstitute with SWFI or lidocaine (0.5% or 2%) to a final concentration of 375 mg/mL (ie, 250 mg/mL of ampicillin and 125 mg/mL of sulbactam). Administer within 1 hour of preparation. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** Anaphylactoid/hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy, especially with a history of beta-lactam hypersensitivity or a history of sensitivity to multiple allergens. If an allergic reaction occurs, discontinue and institute appropriate therapy. • Hepatic dysfunction: Hepatitis and cholestatic jaundice have been reported (including fatalities). Toxicity is usually reversible. Monitor hepatic function at regular intervals in patients with hepatic impairment. • Rash: Appearance of a rash should be carefully evaluated to differentiate a nonallergic ampicillin rash from a hypersensitivity reaction; rash occurs in 5% to 10% of children and is a generalized dull red, maculopapular rash, generally appearing 3-14 days after the start of therapy. It normally begins on the trunk and spreads over most of the body. It may be most intense at pressure areas, elbows, and knees. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment.
Storage	• Prior to reconstitution, store at 20°C to 25°C. • IM: Concentration of 375 mg/mL (250 mg ampicillin/125 mg sulbactam) should be used within 1 hour after reconstitution. • Intermittent IV infusion: Refer to manufacturer's labeling for specific storage instructions after reconstitution and dilution (varies by concentration and diluent) • Refer to manufacturer PIL if there are specific considerations.

5. Benzylpenicillin [Penicillin G]

Access Group

Generic Name	Benzylpenicillin [Penicillin G]		
Dosage form/strengths	Vial 1 M.I.U		
Route of administration	IV, IM		
Pharmacologic category	Antibiotic, Penicillin ATC: J01CE01		
Indications	**Anthrax:** Treatment of anthrax caused by *Bacillus anthracis.* **Actinomycosis, severe or extensive:** Treatment of actinomycosis (cervicofacial disease and thoracic and abdominal disease) caused by *Actinomyces israelii.* **Bloodstream infection:** Treatment of bloodstream infection caused by *Streptococcus* spp., *Listeria monocytogenes*, *Neisseria meningitidis*, and *Pasteurella multocida*. **Botulism, wound:** Treatment of botulism caused by *Clostridium* spp. as an adjunctive agent following antitoxin administration. **Diphtheria:** Treatment of diphtheria caused by *Corynebacterium diphtheriae* as an adjunctive agent following antitoxin administration. **Endocarditis, treatment:** Treatment of endocarditis caused by *Streptococcus* spp. and *Erysipelothrix rhusiopathiae*. **Meningitis, bacterial:** Treatment of meningitis caused by *L. monocytogenes, N. meningitidis, P. multocida,* and *Streptococcus* spp. **Neurosyphilis (including ocular and otosyphilis):** Treatment of syphilis (congenital and neurosyphilis) caused by *Treponema pallidum.* **Odontogenic infection:** Treatment of pyogenic odontogenic infection, including severe infections of the oropharynx, caused by *Fusobacterium* spp. and spirochetes. **Rat bite fever:** Treatment of rat bite fever (including Haverhill fever) caused by *Spirillum minus* or *Streptobacillus moniliformis.* **Tetanus:** Treatment of tetanus caused by *Clostridium tetani* as an adjunctive agent following tetanus immune globulin and vaccine administration. **Toxic shock syndrome:** Treatment of toxic shock syndrome caused by *Streptococcus* spp		
Dosage Regimen	**Dosing: Adult** **Note:** For ease of outpatient administration, the total daily dose may be administered as a 24-hour continuous infusion **Actinomycosis, severe or extensive: IV:** 10 to 20 million units/day as a continuous infusion or in divided doses every 4 to 6 hours for 4 to 6 weeks followed by appropriate long-term oral therapy. **Bloodstream infection:** – *Pathogen-directed therapy for Listeria monocytogenes*: **IV:** 24 million units/day in divided doses every 4 hours; use in combination with gentamicin for nonpregnant patients. Duration should be individualized usually continued for at least 2 weeks; – *Pathogen directed therapy for beta-hemolytic streptococci:* **IV:** 18 to 24 million units/day in divided doses every 4 hours. Duration of therapy is generally 14 days; some experts suggest a shorter course (eg, 10 days) for patients with rapid clearance of bacteremia and clinical improvement.		

- *Pathogen-directed therapy for group D streptococci (Streptococcus bovis/Streptococcus equinus complex) (alternative agent)*: **IV:** 12 to 24 million units/day in divided doses every 4 hours. Duration of therapy is 14 days.

Botulism, wound (adjunctive agent following antitoxin administration): IV: 18 to 20 million units/day in divided doses every 4 to 6 hours in combination with wound debridement; duration depends on extent of the wound.

Diphtheria (adjunctive agent following antitoxin administration) (alternative agent): IV: 2 to 3 million units/day in divided doses every 4 to 6 hours for 10 to 12 days

Endocarditis, treatment:

12–24 million units daily in divided doses every 4 hours for 4-6 weeks. In case of relatively resistant strains, taken in conjunction with gentamicin (3–6 mg/kg daily IV in divided doses every 8 hours given concomitantly during first 2 weeks of penicillin G treatment)

Meningitis, bacterial:

Pathogen-directed therapy for Cutibacterium acnes, L. monocytogenes, Neisseria meningitidis (with MIC <0.1 mcg/mL), Streptococcus agalactiae, or Streptococcus pneumoniae (with MIC ≤0.06 mcg/mL): **IV:** 4 million units every 4 hours. For treatment of *L. monocytogenes,* use as part of an appropriate combination regimen. Treatment duration is 7 to 21 days, depending on causative pathogen(s) and clinical response.

Neurosyphilis (including ocular and otosyphilis): Note: Penicillin desensitization and treatment is recommended in patients with a history of severe penicillin allergy.

IV: 18 to 24 million units/day as a continuous infusion or in divided doses every 4 hours for 10 to 14 days.

Odontogenic infection, pyogenic (alternative agent): IV: 2 to 4 million units every 4 to 6 hours in combination with metronidazole; total duration (including oral step-down therapy) is 7 to 14 days

Rat bite fever:

Uncomplicated infection: **IV:** 200,000 units every 4 hours; if patient clinically improves, may switch to an oral antibiotic after 5 to 7 days to complete a 14-day course.

Serious invasive infection (including bacteremia, meningitis, endocarditis, and other focal organ involvement): **IV:** 12 to 18 million units/day as a continuous infusion or in divided doses every 4 to 6 hours; may increase dose to 24 million units/day in patients with an isolate that is not highly penicillin-susceptible (eg, MIC >0.1 mcg/mL). Treatment duration is 4 weeks.

Tetanus (*Clostridium tetani* infection) (adjunctive agent following tetanus immune globulin and vaccine administration) (alternative agent): IV: 2 to 4 million units every 4 to 6 hours for 7 to 10 days.

Toxic shock syndrome, streptococcal: IV: 4 million units every 4 hours in combination with clindamycin. Duration of therapy depends on extent and severity of infection and response to treatment; treat patients who are bacteremic for ≥14 days.

Dosing: Pediatric

General dosing, susceptible infection (non-CNS):

Infants, Children and Adolescents, IM, IV:

Mild to moderate infections: 100,000–150,000 units/kg daily in 4 divided doses.

Severe infections: 200,000–300,000 units/kg daily in 4–6 divided doses. maximum daily dose: 24 million units/day.

Anthrax, systemic; treatment:

- Non-CNS infection; preferred agent for penicillin-susceptible strains: Infants, Children, and Adolescents: IV: 400,000 units/kg/day in divided doses every 4 hours; maximum dose: 4 million units/dose; use in combination with clindamycin, linezolid, doxycycline, or rifampin for ≥14 days until clinical stability is achieved; treatment must be followed by prophylaxis for a total antibiotic course of 60 days.

– Meningitis; preferred agent for penicillin-susceptible strains: Infants, Children, and Adolescents: IV: 400,000 units/kg/day in divided doses every 4 hours; maximum dose: 4 million units/dose; use in combination with a fluoroquinolone plus linezolid, clindamycin, rifampin, or chloramphenicol for ≥2 to 3 weeks until clinical stability is achieved; treatment must be followed by prophylaxis for a total antibiotic course of 60 days.

Clostridial myonecrosis (gas gangrene): Infants, Children, and Adolescents: IV: 250,000 to 400,000 units/kg/day in divided doses every 4 to 6 hours with or without clindamycin.

Diphtheria: Infants, Children, and Adolescents: IM, IV: 150,000 to 250,000 units/kg/day in divided doses every 6 hours for 7 to 10 days for 14 days.

Endocarditis, bacterial; treatment: Children and Adolescents: IV: 200,000 to 300,000 units/kg/day in divided doses every 4 hours; maximum daily dose: 24 million units/day; treat for at least 4 weeks; longer durations may be necessary; may use in combination with gentamicin for some resistant organisms.

Note: For endocarditis from rat-bite fever/haverhill fever, a lower dose of 150,000 to 250,000 units/kg/day in divided doses every 4 hours is recommended; maximum daily dose: 20 million units/day.

Lyme disease: Infants, Children, and Adolescents: IV: 200,000 to 400,000 units/kg/day in divided doses every 4 hours; maximum daily dose: 24 million units/day.

Meningitis: Note: Dosing varies based on organism being treated.

Group B *streptococcus*: Infants: IV: 450,000 to 500,000 units/kg/day divided every 6 hours.

S. pneumoniae: Infants, Children, and Adolescents: IV: 250,000 to 400,000 units/kg/day divided every 4 to 6 hours.

Other susceptible organisms (including health care-associated ventriculitis/meningitis): Infants, Children, and Adolescents: IV: 300,000 to 400,000 units/kg/day divided every 4 to 6 hours; maximum daily dose: 24 million units/day.

Meningococcal disease: Infants, Children, and Adolescents: IV: 300,000 units/kg/day in divided doses every 4 to 6 hours; maximum daily dose: 12 million units/day.

Pneumonia, community-acquired (CAP): Infants >3 months and Children:

Empiric treatment or *S. pneumoniae* (moderate to severe; MICs to penicillin ≤2.0 mcg/mL): IV: 200,000 to 250,000 units/kg/day divided every 4 to 6 hours.

Alternate dosing (AAP recommendation): IV: 250,000 to 400,000 units/kg/day divided every 4 to 6 hours; maximum daily dose: 24 million units/day.

Group A *Streptococcus* (moderate to severe): IV: 100,000 to 250,000 units/kg/day divided every 4 to 6 hours.

Skin and soft tissue necrotizing infections due to Clostridium species: Infants, Children, and Adolescents: IV: 60,000 to 100,000 units/kg/dose every 6 hours; use in combination with clindamycin and continue until patient has clinically improved, and patient is afebrile for 48 to 72 hours.

Streptococcal skin infections, including skin and soft tissue necrotizing infections: Infants, Children, and Adolescents: IV: 60,000 to 100,000 units/kg/dose every 6 hours; maximum dose: 4 million units/dose; use in combination with clindamycin for necrotizing infections and continue until patient has clinically improved, and patient is afebrile for 48 to 72 hours.

Syphilis:

Congenital: Infants and Children: IV: 50,000 units/kg/dose every 4-6 hours for 10 days.

Neurosyphilis (including ocular syphilis):

Infants and Children: IV: 50,000 units/kg/dose every 4 to 6 hours for 10 to 14 days; maximum daily dose: 24 million units/day.

Adolescents: IV: 3 to 4 million units every 4 hours or as a continuous infusion for 10 to 14 days; maximum daily dose: 24 million units/day.

Tetanus; treatment: Infants, Children, and Adolescents: IV: 100,000 units/kg/day in divided

	doses every 4 to 6 hours for 7 to 10 days; maximum daily dose: 12 million units/day.
Dosage adjustment	**Dosing: Renal Impairment:** Uremic patients with CrCl >10 mL/minute/1.73 m^2: Administer a usual recommended dose followed by 50% of the usual recommended dose every 4 to 5 hours. CrCl <10 mL/minute/1.73 m^2: Administer a normal dose followed by 50% of the normal dose every 8 to 10 hours. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to any penicillin or any component of the formulation Documentation of allergenic cross-reactivity for beta-lactams (eg, penicillins and cephalosporins) is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty.
Adverse Drug Reactions	**Frequency not defined:** Cardiovascular: Local thrombophlebitis, localized phlebitis Central nervous system: Coma (high doses), hyperreflexia (high doses), myoclonus (high doses), seizure (high doses) Dermatologic: Exfoliative dermatitis, maculopapular rash, skin rash Endocrine & metabolic: Electrolyte disorder (high doses) Gastrointestinal: *Clostridioides difficile* associated diarrhea, *Clostridioides difficile* colitis Hematologic & oncologic: Neutropenia, positive direct Coombs test (rare, high doses) Hypersensitivity: Anaphylaxis, angioedema, hypersensitivity reaction (immediate and delayed), serum sickness-like reaction Immunologic: Jarisch-Herxheimer reaction Local: Pain at injection site Renal: Acute interstitial nephritis (high doses), renal tubular disease (high doses)
Monitoring Parameters	Periodic electrolyte, hepatic, renal, cardiac and hematologic function tests during prolonged/high-dose therapy; observe for signs and symptoms of anaphylaxis during first dose. In older adults, especially those with decreased renal function, monitor for seizure activity.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Sodium Picosulfate Typhoid Vaccine Probenecid Teriflunomide Tetracyclines Vitamin K Antagonists (eg, warfarin)
Pregnancy and Lactation	**Pregnancy Category** B Penicillin is considered compatible with breastfeeding when used in usual recommended doses. Monitor infants for GI disturbances, such as thrush or diarrhea.
Administration	**Administration:** Parenteral: **IM**: Administer IM by deep injection in the upper outer quadrant of the buttock. Administer injection around-the-clock to promote less variation in peak and trough levels. **IV**: Usually administered by intermittent infusion. The potassium or sodium content of the dose should be considered when determining the infusion rate. – Intermittent IV: Infuse over 15 to 30 minutes

	– Continuous IV infusion: Daily dose may be administered as a continuous infusion over 24 hours, or smaller increments (eg, 24-hour dose divided into two 12-hour infusions) **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Anaphylactic/hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactic) reactions have been reported, especially in patients with a history of beta-lactam hypersensitivity (including cephalosporins) or history of sensitivity to multiple allergens. Use with caution in asthmatic patients. If a serious reaction occurs, discontinue treatment and institute supportive measures. • Neurovascular damage: Avoid intra-arterial administration or injection into or near major peripheral nerves or blood vessels since such injections may cause severe and/or permanent neurovascular damage. • Severe cutaneous adverse reactions: Severe cutaneous adverse reactions (SCAR) (eg, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, acute generalized exanthematous pustulosis) have been reported; discontinue immediately if SCAR is suspected. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Renal impairment: Use with caution in patients with renal impairment; dosage adjustment recommended. In the presence of concomitant hepatic impairment, further dosage adjustment may be needed. • Seizure disorders: Use with caution in patients with a history of seizure disorder; high levels, particularly in the presence of renal impairment, may increase risk of seizures. ***Special populations:*** • Neonates: Neonates may have decreased renal clearance of penicillin and require frequent dosage adjustments depending on age. ***Other warnings/precautions:*** • Electrolyte imbalance: Product contains sodium and potassium; high doses of IV therapy may alter serum levels. If high doses (eg, >10 million units) are used, administer at a slower rate (eg, >30 minutes for intermittent IV infusion).
Storage	Penicillin G powder for injection should be stored at 25°C. Once reconstituted, it is recommended to be used immediately Store at temperature not exceeding 30 °C, protect from light. Refer to manufacturer PIL if there are specific considerations.

6. Cloxacillin

Access Group

Generic Name	Cloxacillin
Dosage form/strengths	In combinations: capsule, suspension
Route of administration	*Oral*
Pharmacologic category	Antibiotic, Penicillin ATC: J01CF02
Indications	**Bacterial infections:** Treatment of bacterial infections including endocarditis, pneumonia, bone and joint infections, skin and soft-tissue infections, and sepsis that are caused by susceptible strains of penicillinase-producing staphylococci. Limitations of use: Exhibits good activity against *Staphylococcus aureus*; has activity against many streptococci, but is less active than penicillin and is generally not used in clinical practice to treat streptococcal infections. Not effective against methicillin-resistant staphylococci.
Dosage Regimen	**Dosing: Adult** **Susceptible infections:** Oral: 250 to 500 mg every 6 hours (maximum adult dose: 6 g/day) **Note:** Dose and duration of therapy can vary depending on infecting organism, severity of infection, and clinical response of patient. Treat severe staphylococcal infections for at least 14 days; endocarditis and osteomyelitis require an extended duration of therapy for 4 to 6 weeks. **Dosing: Pediatric** **Susceptible infections:** Oral: Children ≤20 kg: 25 to 50 mg/kg/day in divided doses every 6 hours Children and Adolescents >20 kg: Refer to adult dosing.
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments necessary
Contra-indications	Hypersensitivity to cloxacillin, other penicillins, cephalosporins, or any component of the formulation
Adverse Drug Reactions	**Frequency not defined** Cardiovascular: Hypotension, thrombophlebitis Central nervous system: Confusion, lethargy, myoclonus, seizure (high doses and/or renal failure), twitching Dermatologic: Pruritus, skin rash, urticaria Gastrointestinal: Abdominal pain, diarrhea, epigastric distress, flatulence, hairy tongue, loose stools, melanoglossia, nausea, oral candidiasis, pseudomembranous colitis, stomatitis, vomiting Genitourinary: Hematuria, proteinuria Hematologic & oncologic: Agranulocytosis, anemia, bone marrow depression, eosinophilia, granulocytopenia, hemolytic anemia, immune thrombocytopenia, leukopenia, neutropenia, thrombocytopenia Hepatic: Increased serum alkaline phosphatase, increased serum ALT & AST, hepatotoxicity Hypersensitivity: Anaphylaxis, angioedema, hypersensitivity reaction (immediate and

	delayed) Immunologic: Serum sickness-like reaction Neuromuscular & skeletal: Laryngospasm Renal: Interstitial nephritis, renal insufficiency, renal tubular disease Respiratory: Bronchospasm, laryngeal edema, sneezing, wheezing Miscellaneous: Fever
Monitoring Parameters	Observe for signs and symptoms of anaphylaxis during first dose; CBC with differential (prior to initiating therapy and weekly thereafter), periodic urinalysis, BUN, creatinine, hepatic function
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Sodium Picosulfate Typhoid Vaccine
Pregnancy and Lactation	**Pregnancy category** B Cloxacillin is considered compatible with breastfeeding when used in usual recommended doses. Monitor infants for GI disturbances, such as thrush or diarrhea.
Administration	**Administration: Oral** Administer with water 1 hour before or 2 hours after meals. Powder for oral solution: Prior to mixing, store powder at room temperature not exceeding 25°C. Refrigerate oral solution after reconstitution; discard after 14 days. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Anaphylactoid/hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy, especially with a history of beta-lactam hypersensitivity, history of sensitivity to multiple allergens, or previous IgE-mediated reactions (eg, anaphylaxis, angioedema, urticaria). Use with caution in asthmatic patients. • Hematologic effects: Penicillin use has been associated with hematologic disorders (eg, agranulocytosis, neutropenia, thrombocytopenia) believed to be a hypersensitivity phenomenon. Reactions are most often reversible upon discontinuing therapy. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Renal impairment: Use with caution in patients with renal impairment; rate of elimination is reduced. • Seizure disorders: Use with caution in patients with a history of seizure disorder; high serum levels, particularly in the presence of renal impairment, may increase risk for seizures. ***Special populations:*** • Neonates: May have decreased renal clearance of cloxacillin; frequent evaluation of serum levels and of clinical status for adverse effects as well as frequent dosage adjustments may be necessary in this patient population.
Storage	Capsule: Store at room temperature not exceeding 25°C Refer to manufacturer PIL if there are specific considerations.

7. Flucloxacillin

Access Group

Generic Name	Flucloxacillin
Dosage form/strengths	In cominations: Capsule, tablet, oral suspension & vial.
Route of administration	IV, IM & oral
Pharmacologic category	Antibiotic, Penicillin ATC: **J01CF05**
Indications	Flucloxacillin is an isoxazolyl penicillin used primarily for the treatment of infections due to staphylococci resistant to benzylpenicillin. These include bone and joint infections, endocarditis, pneumonia, skin infections (including soft-tissue infections), and toxic shock syndrome. Flucloxacillin is used in children, often to treat ear infections and chest infections.
Dosage Regimen	**Adult dosing:** Flucloxacillin is given parenterally and orally as the sodium or magnesium salt. All doses are expressed as flucloxacillin; 1.18 g of flucloxacillin magnesium and 1.09 g of flucloxacillin sodium are each equivalent to about 1 g of flucloxacillin. The usual adult dose **orally or by intramuscular** injection is 250 mg four times daily Flucloxacillin is given **intravenously** in a dose of 0.25 to 1 g four times daily by slow injection over 3 to 4 minutes or by intravenous infusion. All systemic doses may be doubled in severe infections. Up to 8 g daily in 3 or 4 divided doses may be given for osteomyelitis; in endocarditis a dose of 8 g daily in 4 divided doses may be given to patients weighing up to 85 kg, and 12 g daily in 6 divided doses may be used in those weighing more. In severe renal impairment a reduction in dosage may be necessary. **Administration in children** Flucloxacillin may be given to neonates and children for the treatment of infections caused by susceptible organisms and may be given orally, by intramuscular or slow intravenous injection, or by intermittent intravenous infusion over 30 to 60 minutes. In the UK, the BNFC suggests the following: For infections due to beta-lactamase-producing staphylococci including **in otitis externa, pneumonia, impetigo, and cellulitis:** **neonates**: 25 mg/kg *orally* or*intravenously*, given twice daily for those under 7 days of age, 3 times daily for those 7 to 20 days of age, and 4 times daily for those 21 to 28 days of age; intravenous doses may be doubled for severe infection children from 1 month to 1 year of age: 62.5 to 125 mg; 2 to 9 years, 125 to 250 mg; 10 years and older, 250 to 500 mg; all doses to be given*orally* 4 times daily *or* **children from 1 month of age**: 12.5 to 25 mg/kg *intramuscularly* (to a maximum of 500 mg) or *intravenously* (to a maximum of 1 g) every 6 hours; intravenous dose may be doubled for severe infection **For osteomyelitis, cerebral abscess, and staphylococcal meningitis**: neonates: 50 to 100 mg/kg *intravenously*, given every 12 hours for those under 7 days of age, every 8 hours for those 7 to 20 days of age, and every 6 hours for those 21 to 28 days of age children from 1 month of age: 50 mg/kg (maximum 2 g) *intravenously* every 6 hours **For endocarditis**: children from 1 month of age: 50 mg/kg (maximum 2 g) intravenously every 6 hours **For *prevention* of staphylococcal lung infection in cystic fibrosis**: for primary prevention, flucloxacillin is given orally to neonates and children up to 3 years of age in a dose of 125 mg twice daily

	for secondary prevention in children from 1 month of age an oral dose of 50 mg/kg (to a maximum of 1 g) twice daily is given **For the*treatment* of staphylococcal lung infection in cystic fibrosis,** infants and children from 1 month of age may be given an oral dose of 100 mg/kg (to a maximum of 4 g) daily in 3 or 4 divided doses; alternatively, it may be given intravenously in a dose of 50 mg/kg (to a maximum of 2 g) every 6 hours.
Dosage adjustment	In children with severe renal impairment (creatinine clearance less than 10 mL/min), the normal dose should be given no more frequently than every 8 hours
Contra-indications	Hypersensitivity reaction to flucloxacillin
Adverse Drug Reactions	Hepatitis and cholestatic jaundice
Monitoring Parameters	Liver enzymes
Drug Interactions	• Probenecid, Anticoagulants (warfarin), Hormonal contraceptives • Other antibacterials such as chloramphenicol and tetracyclines and may be incompatible *in vitro* with other drugs, including some other antibacterials.
Pregnancy and Lactation	Maternal use of penicillins has generally not resulted in an increased risk of adverse fetal effects. Use during pregnancy only if potential benefits outweigh possible risks. Flucloxacillin is considered compatible with breastfeeding when used in usual recommended doses. Monitor infants for GI disturbances, such as thrush or diarrhea.
Administration	• Oral: Take flucloxacillin on an empty stomach. This means 30 to 60 minutes before a meal or snack, or at least 2 hours after. • Swallow flucloxacillin capsules whole with a drink of water. Do not chew or break them. **N.B**. Hypersensitivity test must be done before using injection form of this medicine. • Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	Hepatitis and cholestatic jaundice have been reported occasionally with flucloxacillin and may be delayed in onset for up to 2 months after treatment has been stopped; older patients and those receiving flucloxacillin for more than 2 weeks are at greater risk. **Effects on metabolism** Use of flucloxacillin, often with paracetamol, has been associated with accumulation of pyroglutamic acid resulting in pyroglutamic aciduria (5–oxoprolinuria) and high-anion gap metabolic acidosis **Porphyria** The Drug Database for Acute Porphyria, compiled by the Norwegian Porphyria Centre (NAPOS) and the Porphyria Centre Sweden, classifies flucloxacillin as possibly porphyrinogenic; it should be used only when no safer alternative is available and precautions should be considered in vulnerable patients.
Storage	• Capsules: Store in original package at controlled room temperature; protect from moisture • Oral suspension: Store at ≤25°C prior to reconstitution. After reconstitution, store in refrigerator at 2°C to 8°C. • Solution for injection: Store below ≤25°C prior to reconstitution. Protect from light. • Refer to manufacturer PIL if there are specific considerations.

Access Group

8. Penicillin G Benzathine

Generic Name	Penicillin G Benzathine
Dosage form/strengths	Vial 1.2M IU
Route of administration	IM
Pharmacologic category	Antibiotic, Penicillin ATC: J01CE08
Indications	**Acute glomerulonephritis:** Prophylaxis (secondary) in patients with a history of acute glomerulonephritis **Respiratory tract infections:** Treatment of mild to moderate upper respiratory tract infections (including pharyngitis) caused by streptococci susceptible to low, prolonged serum concentrations of penicillin G **Rheumatic fever and chorea:** Prophylaxis (secondary) of rheumatic fever and/or chorea **Rheumatic heart disease:** Prophylaxis (secondary) in patients with rheumatic heart disease **Syphilis and other venereal diseases:** Treatment of syphilis, yaws, bejel, and pinta
Dosage Regimen	**Adult Usual dosage range:** IM: 1.2 to 2.4 million units as a single dose • **Streptococcus (group A):** *Pharyngitis, acute treatment:* IM: 1.2 million units as a single dose *Secondary prophylaxis for rheumatic fever (prevention of recurrent attacks):* IM: 1.2 million units once every 21 to 28 days. Duration depends on risk factors and presence of valvular heart disease. IM: 600,000 units every 2 weeks *Secondary prophylaxis of glomerulonephritis:* IM: 1.2 million units every 4 weeks **or** 600,000 units twice monthly • **Syphilis (CDC):** *Primary, Secondary, Early Latent (<1-year duration):* IM: 2.4 million units as a single dose *Late Latent, Latent with unknown duration, or Tertiary Syphilis (with normal CSF examination):* IM: 2.4 million units once weekly for 3 doses *Neurosyphilis (including Ocular Syphilis):* Not indicated for initial treatment; aqueous penicillin G IV is preferred initial therapy. Following penicillin G IV initial treatment, may consider administration of penicillin G benzathine 2.4 million units IM once weekly for 3 weeks to provide a comparable total duration of therapy as for latent syphilis. **Dosing: Pediatric** • **Group A streptococcal (*Streptococcus pyogenes*) infection:** *Pharyngitis, treatment (primary prevention of rheumatic fever)*: **Note:** Empiric treatment is generally not recommended; treatment should be prescribed only when testing confirms presence of Group A *Streptococcus*. **Infants, Children, and Adolescents: IM:** ≤27 kg: 600,000 units as a single dose. >27 kg: 1.2 million units as a single dose.

	Rheumatic fever, secondary prevention: **Note:** Duration varies based on risk factors and presence of residual heart disease. Infants, Children, and Adolescents: IM: ≤27 kg: 600,000 units every 3 to 4 weeks. >27 kg: 1.2 million units every 3 to 4 weeks. **Note:** Every-4-week administration is recommended in the US where rheumatic fever incidence is low; every 3 weeks should be used to maintain desirable serum drug concentrations in patients who have had a breakthrough episode despite every-4-week dosing and in areas where incidence of acute rheumatic fever remains high. *Chronic carriers of Group A Streptococcus, treatment:* Limited data available: **Note:** Antibiotic therapy is generally not recommended for chronic *S. pyogenes* carriage; however, it may be considered in certain cases. Infants, Children, and Adolescents: IM: ≤27 kg: 600,000 units as a single dose in combination with oral rifampin for 4 days. >27 kg: 1.2 million units as a single dose in combination with oral rifampin for 4 days. • **Syphilis: Note:** Not recommended for the initial treatment of neurosyphilis (CDC). ***Congenital; patients with no clinical manifestations and normal cerebrospinal fluid (CSF):*** **Limited data available: Infants and Children: IM:** 50,000 units/kg/dose once weekly for up to 3 weeks; maximum dose: 2.4 million units/dose. ***Primary, secondary, or early latent (<1-year duration):*** **Infants, Children, and Adolescents**: IM: 50,000 units/kg once; maximum dose: 2.4 million units/dose. ***Re-treatment of primary, secondary, or early latent disease after failure of previous therapy:*** **Infants, Children, and Adolescents:** 50,000 units/kg/dose once weekly for 3 weeks; maximum dose: 2.4 million units/dose. **Note:** If CSF examination positive, treat as neurosyphilis. *Late latent (>1 year or unknown duration):* Infants, Children, and Adolescents: IM: 50,000 units/kg/dose once weekly for 3 weeks; maximum dose: 2.4 million units/dose (CDC).
Dosage adjustment	**Dosing: Renal Impairment:** Penicillin G is rapidly eliminated via renal tubular excretion and clearance is significantly delayed in patients with decreased renal function. Specific dosage adjustment recommendations are not available. **Dosing: Hepatic Impairment:** No dosage adjustment is needed in patients with hepatic impairment; patients with both hepatic and renal impairment may need dosage adjustment. **Geriatric Considerations** Not indicated as single drug therapy for neurosyphilis, but may be given 1 time/week for 3 weeks following IV treatment with Penicillin G (Parenteral/Aqueous). No adjustment for renal function or age is necessary.
Contra-indications	Hypersensitivity to penicillin(s) or any component of the formulation
Adverse Drug Reactions	**Cardiovascular**: Cerebrovascular accident, hypersensitivity angiitis, hypotension, palpitations, pulmonary embolism, syncope, tachycardia, vasodilation, vasospasm, vasodepressor syncope **Central nervous system**: Anxiety, coma, confusion, dizziness, drowsiness, euphoria, fatigue, headache, localized warm feeling, nervousness, neurologic abnormality (neurogenic bladder), numbness of extremities, pain, seizure, transverse myelitis **Dermatologic**: Diaphoresis, gangrene of skin and/or other subcutaneous tissues, pallor, pruritus, skin mottling, skin or other tissue necrosis (Nicolau syndrome), skin ulceration at injection site

	Gastrointestinal: Blood in stool, *Clostridioides difficile* associated diarrhea, intestinal necrosis, nausea, vomiting **Genitourinary**: Hematuria, impotence, priapism, proteinuria **Hematologic & oncologic**: Lymphadenopathy **Hepatic**: Increased serum aspartate aminotransferase Hypersensitivity: Anaphylaxis, hypersensitivity reaction **Immunologic**: Jarisch-Herxheimer reaction **Local**: Abscess at injection site, atrophy at injection site, bleeding at injection site, bruising at injection site, cellulitis at injection site, localized edema (at injection site), inflammation at injection site, injection site reaction (neurovascular damage), pain at injection site, residual mass at injection site, tissue necrosis at injection site **Neuromuscular & skeletal:** Arthropathy, asthenia, exacerbation of arthritis, periosteal disease, rhabdomyolysis, tremor Ophthalmic: Blindness, blurred vision **Renal:** Increased blood urea nitrogen, increased serum creatinine, myoglobinuria, renal failure syndrome **Respiratory:** Apnea, cyanotic extremities, dyspnea, hypoxia, pulmonary hypertension
Monitoring Parameters	Observe for signs and symptoms of anaphylaxis during first dose
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cholera Vaccine, ***Risk D: Consider therapy modification*** Bacillus clausii, Tolvaptan, Typhoid Vaccine, Sodium Picosulfate: ***Risk C: Monitor therapy*:** Acemetacin, Aminoglycosides, BCG Vaccine (Immunization), Dichlorphenamide, Lactobacillus and Estriol, Methotrexate, Mycophenolate, Probenecid, Sodium Benzoate,Teriflunomide, Tetracyclines, Vitamin K Antagonists
Pregnancy and Lactation	This drug should be used during pregnancy only if clearly needed Penicillin G is the drug of choice for treatment of syphilis during pregnancy Penicillin G benzathine is considered compatible with breastfeeding when used in usual recommended doses. Monitor infants for GI disturbances, such as thrush or diarrhea.
Administration	**Administration: IM only** Warm to room temperature before administration to lessen the pain associated with injection. Administer by deep IM injection at a slow, steady rate in the dorsogluteal region (upper outer quadrant of the buttock) or the ventrogluteal region. Do not inject near an artery or a nerve; permanent neurological damage or gangrene may result. When doses are repeated, rotate the injection site. **Do not administer IV, intra-arterially, or SubQ. inadvertent IV administration has resulted in thrombosis, severe neurovascular damage, cardiac arrest, and death.** **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy, especially with a history of beta-lactam hypersensitivity (including cephalosporins), history of sensitivity to multiple allergens, or previous IgE-mediated reactions (eg, anaphylaxis, angioedema, urticaria). Serious anaphylactic reactions require immediate emergency treatment with epinephrine, oxygen, intravenous steroids and airway management (including intubation) as indicated.

	• Severe cutaneous adverse reactions: Severe cutaneous adverse reactions (SCAR) (eg, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, acute generalized exanthematous pustulosis) have been reported; discontinue immediately if SCAR is suspected. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *Clostridioides* (formerly *Clostridium*) *difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment • Not for IV use; cardiopulmonary arrest and death have occurred from inadvertent IV administration. Administer by deep IM injection only. Quadriceps femoris fibrosis and atrophy have been reported after repeated IM injections of penicillin preparations into the anterolateral thigh. Injection into or near an artery or nerve could result in severe neurovascular damage or permanent neurological damage. • Prolonged use: Extended duration of therapy or use associated with high serum concentrations (eg, in renal insufficiency) may be associated with an increased risk for some adverse reactions (neutropenia, hemolytic anemia, serum sickness)
Storage	Store at 2°C to 8°C; do not freeze. Refer to manufacturer PIL if there are specific considerations.

9. Phenoxymethylpenicillin

Access Group

Generic Name	Phenoxymethylpenicillin
Dosage form/strengths	Tablets 1MU, 1.5MU
Route of administration	Oral
Pharmacologic category	Antibiotic, Penicillins (penicillin V) ATC: J01CE02
Indications	**Erysipelas:** Treatment of mild infection or step-down therapy after initial parenteral therapy. **Odontogenic infection (acute simple gingivitis):** Treatment of odontogenic infection, in conjunction with dental care for infections involving gum tissue. **Pneumococcal infections:** Treatment of mild to moderately severe pneumococcal respiratory tract infections, including otitis media. **Streptococcus, group A:** Secondary prophylaxis for rheumatic fever (prevention of secondary attacks). **Streptococcus, group A pharyngitis:** Initial treatment of pharyngitis caused by group A *Streptococcus*.
Dosage Regimen	**Adults** **Odontogenic infection: Acute simple gingivitis:** **Oral:** 500 mg every 6 to 8 hours for 5 to 7 days in combination with metronidazole **Skin and soft tissue infection:** **Erysipelas, treatment of mild infection or step-down therapy after initial parenteral therapy: Oral:** 500 mg every 6 hours; total duration is 5 days, with extension to 14 days for slow response, severe infection, or immunosuppression **Streptococcus, group A:** **Pharyngitis: Oral:** 500 mg 2 to 3 times daily for 10 days. **Secondary prophylaxis in patients with rheumatic fever (prevention of recurrent attacks) (alternative agent): Oral:** 250 mg twice daily. Duration depends on risk factors, age, and presence of valvular disease **Dosing: Pediatric** **General dosing: Infants, Children, and Adolescents:** **Mild to moderate infection: Oral:** 25 to 50 mg/kg/day in divided doses every 6 hours; maximum daily dose: 2,000 mg/day **Group A streptococcal infection:** ***Pharyngitis, acute treatment (primary prevention of rheumatic fever):*** **Children <27 kg: Oral:** 250 mg 2 to 3 times daily for 10 days. **Children ≥27 kg and Adolescents: Oral:** 500 mg 2 to 3 times daily for 10 days; in adolescents, 250 mg 4 times daily has also been suggested. **Pneumonia, community-acquired; Group A *Streptococcus*, mild infection or step-down therapy:** **Infants, Children, and Adolescents: Oral:** 50 to 75 mg/kg/day in divided doses 4 times daily
Dosage adjustment	**Dosing: Renal Impairment: Adult** Use with caution; excretion is prolonged in patients with renal impairment. No dosage

	adjustments needed. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments needed.
Contra-indications	Known hypersensitivity to any penicillin.
Adverse Drug Reactions	Adverse GI effects (e.g., nausea, vomiting, epigastric distress, diarrhea, black hairy tongue), hypersensitivity reactions (e.g., fever, eosinophilia, rash, urticaria, serum sickness-like reactions)
Monitoring Parameters	Periodic renal and hematologic function tests during prolonged therapy; monitor for signs of anaphylaxis during first dose
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical) Cholera Vaccine ***Risk D: Consider therapy modification*** Fexinidazole Sodium Picosulfate Typhoid Vaccine
Pregnancy and Lactation	**Pregnancy Category B** Penicillin V is considered compatible with breastfeeding when used in usual recommended doses.
Administration	Take on an empty stomach 1 hour before or 2 hours after meals, to enhance absorption. Do not use for initial treatment of severe infections. Should not be relied on in patients with nausea, vomiting, gastric dilatation, cardiospasm, or intestinal hypermotility. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Anaphylactic/hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy, especially with a history of beta-lactam hypersensitivity or history of sensitivity to multiple allergens.). Use with caution in asthmatic patients. If a serious reaction occurs, treatment with supportive care measures and airway protection should be instituted immediately. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. **Disease-related concerns:** • Renal impairment: Use with caution in patients with severe renal impairment. • Seizure disorders: Use with caution in patients with a history of seizure disorder; high levels, particularly in the presence of renal impairment, may increase risk of seizures.
Storage	Store at 20–25°C. Refer to manufacturer PIL if there are specific considerations.

10. Piperacillin and Tazobactam

Watch Group

Generic Name	Piperacillin and Tazobactam
Dosage form/strengths	Vial 4.5gm
Route of administration	Intravenous
Pharmacologic category	Antibiotic, Penicillin ATC: J01CR05
Indications	**Intra-abdominal infections:** Treatment of appendicitis complicated by rupture or abscess and peritonitis in adults and pediatric patients ≥2 months of age. **Pelvic infections:** Treatment of postpartum endometritis or pelvic inflammatory disease in adults. **Pneumonia, community-acquired:** Treatment of moderate severity community-acquired pneumonia in adults. **Pneumonia, hospital-acquired (nosocomial):** Treatment of moderate to severe hospital-acquired (nosocomial) pneumonia in adults and pediatric patients ≥2 months of age. **Skin and skin structure infections:** Treatment of skin and skin structure infections, including cellulitis, cutaneous abscesses, and ischemic/diabetic foot infections in adults
Dosage Regimen	**Dosing: Adult** **Note:** Adult doses are expressed as the combined amount of piperacillin and tazobactam. Infusion method: Dosing is presented based on the traditional infusion method over 30 minutes, unless otherwise specified **Usual dosage range:** *Traditional infusion method (over 30 minutes):* **IV:** Mild to moderate infections: 3.375 g every 6 hours. Severe infections: 4.5 g every 6 to 8 hours. For coverage of *Pseudomonas aeruginosa*: 4.5 g every 6 hours. Usual maximum dose: 18 g/day. **Dosing: Pediatric** **General dosing, susceptible infection:** Severe infection: *Traditional dosing:* • Neonates ≤30 weeks: 100 mg/kg (of piperacillin) every 8 hours. • Infants ≥2 months, Children, and Adolescents: IV: 240 to 300 mg piperacillin/kg/day divided in 3 to 4 doses; maximum daily dose: 16 g/day
Dosage adjustment	**Dosing: Renal Impairment: Adult**

CrCl (mL/minute)	If the usual recommended dose is 3.375 g every 6 hours	If the usual recommended dose is 4.5 g every 6 hours
100 to <130	Extended infusion preferred	Extended infusion preferred
40 to <100 (usual recommended dose)	3.375 g every 6 hours	4.5 g every 6 hours
20 to <40	2.25 g every 6 hours	4.5 g every 8 hours **or** 3.375 g every 6 hours
<20	2.25 g every 8 hours	4.5 g every 12 hours **or** 2.25 g every 6 hours

Dosing: Renal Impairment: Pediatric

	Note: Dosage recommendations are based on the piperacillin component. Dosing based on a usual dose of 200 to 300 mg piperacillin kg/day in divided doses every 6 hours. GFR >50 mL/minute/1.73 m^2: No adjustment required GFR 30 to 50 mL/minute/1.73 m^2: 35 to 50 mg piperacillin/kg/dose every 6 hours GFR <30 mL/minute/1.73 m^2: 35 to 50 mg piperacillin/kg/dose every 8 hours Intermittent hemodialysis (IHD): Hemodialysis removes 30% to 40% of a piperacillin/tazobactam dose: 50 to 75 mg piperacillin/kg/dose every 12 hours Peritoneal dialysis (PD): Peritoneal dialysis removes 21% of tazobactam and 6% of piperacillin: 50 to 75 mg piperacillin/kg/dose every 12 hours Continuous renal replacement therapy (CRRT): 35 to 50 mg piperacillin/kg/dose every 8 hours **Dosing: Hepatic Impairment:** No dosage adjustment necessary.
Contra-indications	Hypersensitivity to penicillins, cephalosporins, beta-lactamase inhibitors, or any component of the formulation
Adverse Drug Reactions	**>10%**: Gastrointestinal: Diarrhea (11%) **1% to 10%:** Dermatologic: Pruritus, skin rash Gastrointestinal: Abdominal pain, *Clostridioides difficile* colitis, constipation, dyspepsia, nausea, vomiting Infection: Candidiasis Nervous system: Headache, insomnia, rigors Miscellaneous: Fever
Monitoring Parameters	Creatinine, BUN, CBC with differential, PT, PTT, serum electrolytes, LFTs, urinalysis; signs of bleeding; monitor for signs of anaphylaxis during first dose
Drug Interactions	**Risk X: Avoid combination** BCG (Intravesical) Cholera Vaccine **Risk D: Consider therapy modification** Probenecid Sodium Picosulfate Typhoid Vaccine **Risk C: Monitor therapy** Acemetacin Aminoglycosides BCG Vaccine (Immunization) Dichlorphenamide Flucloxacillin Immune Checkpoint Inhibitors Lactobacillus and Estriol Methotrexate Mycophenolate Tetracyclines Vancomycin Vecuronium Vitamin K Antagonists (eg, warfarin)
Pregnancy and lactation	**pregnancy category B** Piperacillin/tazobactam is considered compatible with breastfeeding in women when used for the treatment of airway diseases
Administration	**Administration: IV** Administer by IV infusion over 30 minutes. **Preparation for Administration:** ***Single-dose vial:*** After initial reconstitution, further dilute in D5W or NS to a volume of 50 to 150 mL 4.5 g vial: Reconstitute 4.5 g vial with 20 mL of diluent (eg, D5W, NS, SWFI) to yield a final volume of 23.15 mL, resulting in a final concentration of piperacillin 172.8 mg/mL . **N.B**. Hypersensitivity test must be done before using injection form of this medicine. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Anaphylactoid/hypersensitivity reactions • CNS effects: May cause neuromuscular excitability and seizures. Risk is increased at higher

	doses, particularly in the presence of renal impairment and in patients with seizure disorders; monitor closely. • Dermatologic effects: Serious skin reactions have been reported. • Electrolyte abnormalities: Sodium content (2.84 mEq per gram of piperacillin) should be considered in patients requiring sodium restriction. Assess electrolytes periodically in patients with low potassium reserves, especially those receiving cytotoxic therapy or diuretics. • Hematologic effects: Prothrombin time, platelet aggregation, and clotting time abnormalities. Discontinue if thrombocytopenia or bleeding occurs. Leukopenia/neutropenia may occur; appears to be reversible. • Nephrotoxicity: especially when given in combination with vancomycin • Superinfection: in prolonged use ***Disease-related concerns:*** • Cystic fibrosis: An increased frequency of fever and rash has been reported in patients with cystic fibrosis receiving piperacillin. • Renal impairment: Use with caution in patients with renal impairment or in hemodialysis patients. Dosage adjustment recommended. ***Special populations:*** • Critically ill patients: may delay renal recovery as compared to other beta-lactam antibacterial drugs; consider alternative treatment options in critically ill patients. If alternative treatment options are inadequate or unavailable, closely monitor renal function. ***Concurrent drug therapy issues:*** • Drug-drug interactions: Potentially significant interactions may exist.
Storage	Vials: Store intact vials at 20°C to 25°C. after reconstitution: Use immediately Discard any unused portion after 24 hours if stored at 20°C to 25°C or after 48 hours if stored at 2°C to 8°C. Refer to manufacturer PIL if there are specific considerations.

11. Sultamicillin

Access Group

Generic Name	Sultamicillin
Dosage form/strengths	Tablets: 375 mg, 750 mg Oral Suspension: 250 mg/5ml
Route of administration	Oral
Pharmacologic category	Antibiotic, Penicillin ATC J01CR04
Indications	Treatment of susceptible bacterial infections including skin and skin structure infections, upper and lower respiratory tract infections, urinary tract infections, pyelonephritis, and gonococcal infections.
Dosage Regimen	– **Infants, Children, and Adolescents <30 kg**: 25 to 50 mg/kg/day in 2 divided doses – **Children ≥30 kg, Adolescents, and Adults**: Oral: Usual range: 375 to 750 mg every 12 hours; 2.25 g as a single dose in combination with probenecid has been reported for treatment of uncomplicated gonorrhea.
Dosage adjustment	**Renal impairment:** Severe impairment of renal function (creatinine clearance ≤30 ml/min): The dose of sultamicillin in such patients should be administered less frequently **Hepatic impairment**: No adjustments needed.
Contra-indications	The use of sultamicillin is contraindicated in individuals with a history of an allergic reaction to any of the penicillins.
Adverse Drug Reactions	**1-10%:** Headache, Diarrhea, Vomiting, Abdominal pain, Nausea, Rash, Pruritus.
Monitoring Parameters	monitor adverse effects or hypersensitivity reactions.
Drug Interactions	***Risk X: Avoid Combination*** Bacteriostatic drugs (chloramphenicol, erythromycin, sulfonamides and tetracyclines) ***Risk D: Consider Therapy Modification*** Anticoagulants Estrogen-containing oral contraceptives
Pregnancy and Lactation	safety for use in human pregnancy has not been established. Therefore, sultamicillin should be used during pregnancy only if the potential benefits outweigh the potential risk. The use of sultamicillin during lactation is not recommended
Administration	Oral without regards to food. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving therapy with betalactams. If an allergic reaction occurs, sultamicillin (sulbactam sodium/ampicillin sodium) must be discontinued immediately and appropriate alternative therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated. • Severe skin reactions, such as toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), dermatitis exfoliative, erythema multiforme, and acute generalized exanthematous

	pustulosis (AGEP) have been reported in patients on ampicillin/sulbactam therapy. If a severe skin reaction occurs, ampicillin/sulbactam should be discontinued and appropriate therapy should be initiated • Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including sultamicillin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon, leading to overgrowth of C. difficile. • Drug induced liver injury such as cholestatic hepatitis and jaundice have been associated with the use of ampicillin/sulbactam. Patients should be advised to contact their doctor if signs and symptoms of hepatic disease develop
Storage	Store below 30°C. The reconstituted oral suspension must be stored under refrigeration and discarded after 14 days. Refer to manufacturer PIL if there are specific considerations.

Quinolones

1. Ciprofloxacin

Watch Group

Generic Name	Ciprofloxacin
Dosage form/ strengths	**Tablets** 250mg, 500mg, 750mg **Extended Release Tablets**: 500 mg, 1g **Eye ointment** 0.3% **Ear or eye drops** 3mg/ml **Vial** 200mg, 400mg
Route of administration	*Oral, Opthalmic, IV*
Pharmacologic action	Antibiotic, Fluoroquinolone Systemic ATC: J01MA02 Ophthalmic ATC: S03AA07
Indications	*Systemic*: • **Children and Adolescents**: Treatment of complicated urinary tract infections and pyelonephritis due to E. coli. **Note**: Although effective, ciprofloxacin is not the drug of first choice in children. • **Infants, Children, Adolescents, and Adults**: Prophylaxis to reduce incidence or progression of disease following inhalation exposure to Bacillus anthracis; prophylaxis and treatment of plague (Yersinia pestis). • **Adults:** Treatment of the following infections when caused by susceptible bacteria: Urinary tract infections; acute uncomplicated cystitis in females, chronic bacterial prostatitis, bone and joint infections, complicated intra-abdominal infections (in combination with metronidazole), infectious diarrhea, typhoid fever (Salmonella typhi), hospital-acquired (nosocomial) pneumonia *Ophthalmic*: **Bacterial conjunctivitis**: Ointment or solution **Corneal ulcers:** Solution
Dosage Regimen	**Note:** Extended-release tablets and immediate-release formulations are not interchangeable. Unless otherwise specified, oral dosing reflects the use of immediate-release formulations. **Intra-abdominal infection (including perforated appendix, appendiceal abscess, acute diverticulitis, acute cholecystitis), community-acquired: Note:** For empiric therapy, usually administered in combination with metronidazole. Oral: 500 mg every 12 hours IV: 400 mg every 12 hours Duration: Duration of therapy is for 4 to 7 days following adequate source control **Osteomyelitis:** **Oral:** **Treatment**: 500 to 750 mg every 12 hours; when treating *P. aeruginosa*, 750 mg every 12 hours for ≥6 weeks **Chronic suppression in presence of retained infected orthopedic hardware:** 250 to 500 mg every 12 hours. IV: 400 mg every 12 hours; when treating *P. aeruginosa*, 400 mg every 8 hours for ≥6 weeks **Plague (*Yersinia pestis*) infection (alternative agent):** **Note:** Consult public health officials for event-specific recommendations: *Postexposure prophylaxis:* Oral: 500 mg twice daily for 7 days.

Treatment: **Note: Duration of therapy is 10 to 14 days.**
Oral: 500 to 750 mg every 12 hours
IV: 400 mg every 8 to 12 hours.
Pneumonia, as a component of empiric therapy or pathogen-specific therapy for *P. aeruginosa* in hospitalized patients: Note: For empiric therapy, must be used in combination with other appropriate agents.
Oral: 750 mg every 12 hours
IV: 400 mg every 8 hours.
Duration of therapy: 7 days; may be individualized based on patient-specific factors and response to therapy
***Salmonella* species, GI infection:**
Nontyphoidal, severe (nonbacteremic) illness or any severity in patients at high risk for invasive disease: Oral: 500 mg twice daily for 3 to 14 days (7 to 14 days in patients with HIV with a CD4 count ≥200 cells/mm^3). **Note:** Immunosuppressed patients (eg, patients with HIV and CD4 count <200 cells/mm^3) require a longer duration of treatment (eg, weeks to months) and may require a higher dose (eg, 750 mg twice daily).
Nontyphoidal bloodstream infection: IV: 400 mg twice daily for 14 days. **Note:** Immunosuppressed patients (eg, patients with HIV with CD4 count <200 cells/mm^3) and those with an extraintestinal focus of infection require a longer duration of treatment (eg, weeks or months).
Typhoid fever (Salmonella typhi and paratyphi): Severe disease or mild to moderate infection in patients at high risk of developing invasive disease. **Note:** Use only if MIC ≤0.06 mcg/mL as the incidence of fluoroquinolone-resistant strains is increasing (Humphries 2012).
Oral: 500 mg every 12 hours for 7 to 10 days.
IV: 400 mg every 12 hours for 7 to 10 days.
Septic arthritis (without prosthetic material) (alternative agent): Note: Use in combination with an aminoglycoside for initial treatment if *P. aeruginosa* suspected.
Oral: 500 to 750 mg twice daily.
IV: 400 mg every 12 hours.
Duration of therapy: 3 to 4 weeks (in the absence of osteomyelitis), including oral step-down therapy.
Urinary tract infection:
Acute uncomplicated or simple cystitis in females: **Note:** Use is discouraged due to safety concerns and significant *Escherichia coli* resistance; reserve for those who have no alternative treatment options.
Oral, immediate release: 250 mg every 12 hours for 3 days.
Oral, extended release: 500 mg every 24 hours for 3 days.
Acute pyelonephritis or other complicated UTI: **Note:** If the prevalence of fluoroquinolone resistance is >10%, an initial dose of a long-acting parenteral antimicrobial, such as ceftriaxone, ertapenem, or a consolidated 24-hour dose of an aminoglycoside is recommended for outpatients.
Oral, immediate release: 500 mg every 12 hours for 5 to 7 days.
Oral, extended release: 1 g every 24 hours for 5 to 7 days.
IV (inpatient): 400 mg every 12 hours for a total of 5 to 7 days.
Dosing: Pediatric
Note: In pediatric patients, ciprofloxacin is not routinely first-line therapy, but after assessment of risks and benefits, can be considered a reasonable alternative for some situations [eg, anthrax, resistance (cystic fibrosis)].
General dosing, susceptible infection: Infants, Children, and Adolescents:
Mild to moderate infections: Oral, immediate release: 10 mg/kg/dose twice daily; maximum

dose: 500 mg/dose.
Severe infections:
Oral, immediate release: 15 to 20 mg/kg/dose twice daily; maximum dose: 750 mg/dose.
IV: 10 mg/kg/dose every 8 to 12 hours; maximum dose: 400 mg/dose.

Ophthalmic:
Bacterial conjunctivitis: Ophthalmic:
Solution: Instill 1 to 2 drops into the conjunctival sac every 2 hours while awake for 2 days and then every 4 hours while awake for the next 5 days.
Ointment: Apply a $^1/_2$ inch ribbon into the conjunctival sac 3 times/day for the first 2 days, followed by a $^1/_2$ inch ribbon applied twice daily for the next 5 days.
Corneal ulcer

Corneal ulcer: Ophthalmic:
Solution: Instill 2 drops into affected eye:
every 15 minutes for the first 6 hours, then every 30 minutes for the remainder of the first day. On day 2, instill 2 drops every hour. On days 3 to 14, instill 2 drops every 4 hours. Treatment may continue after day 14 if re-epithelialization has not occurred.

Dosage adjustment

Renal impairment systemic dosing

CrCl (mL/minute)	Oral, immediate release	Oral, extended release	IV
CrCl >50 to <130	500-750/12hr	1 g every 24 hours	400 mg every 8 to 12 hours
CrCl 30 to 50	250 to 500 mg every 12 hours[b]	No adjustment needed	No adjustment needed
CrCl <30	500 mg every 24 hours[b]	500 mg every 24 hours	200[c] to 400 mg every 12 to 24 hours
Hemodialysis, intermittent (thrice weekly)[e]	250[d] to 500 mg every 24 hours[b]	500 mg every 24 hours	200[c] to 400 mg every 24 hours
Peritoneal dialysis	250[d] to 500 mg every 24 hours[b]	500 mg every 24 hours	200[c] to 400 mg every 24 hours

[b]For severe infections, 750 mg may be administered at the intervals noted above.

[c]Consider administering a loading dose of 400 mg × 1 if utilizing 200 mg every 24 hours.

[d]Consider administering a loading dose of 500 mg × 1 if utilizing 250 mg every 24 hours.

[e]Minimally dialyzable (<10%); when scheduled dose falls on a dialysis day, administer post dialysis.

Infants, Children, and Adolescents:
The following guidelines have been used by some clinicians for IV and oral immediate

	formulations on 10-15mg/kg/dose every 12 hours: GFR ≥30 mL/minute/1.73 m2: No dosage adjustment necessary GFR 10 to 29 mL/minute/1.73 m2: 10 to 15 mg/kg/dose every 18 hours GFR <10 mL/minute/1.73 m2: 10 to 15 mg/kg/dose every 24 hours Hemodialysis/peritoneal dialysis (PD) (after dialysis on dialysis days): Minimally dialyzable (<10%): 10 to 15 mg/kg/dose every 24 hours CRRT: 10 to 15 mg/kg/dose every 12 hours Oral, extended release: Adolescents ≥18 years: CrCl ≥30 mL/minute: No dosage adjustment necessary CrCl <30 mL/minute: 500 mg every 24 hours Hemodialysis/peritoneal dialysis (PD) (administer after dialysis on dialysis days): 500 mg every 24 hours **Dosing: Hepatic Impairment: Adult& Pediatrics** There are no dosage adjustments needed. Use with caution in severe impairment.
Contra-indications	Hypersensitivity to ciprofloxacin, any component of the formulation, or other quinolones; concurrent administration of tizanidine
Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** Aortic aneurysm/aortic dissection CNS effects/neuroexcitation Clostridioides (formerly Clostridium) difficile infection Glucose regulation/dysglycemia Hepatotoxicity Hypersensitivity reactions (immediate and delayed) Myasthenia gravis Peripheral neuropathy Phototoxicity/photoallergy QT prolongation Tendonitis/tendon rupture **>10%:** Neuromuscular & skeletal: Musculoskeletal signs and symptoms (children: 9% to 22%) **1% to 10%:** Dermatologic: Skin rash (1% to 2%) Gastrointestinal: Abdominal pain (children: 3%; adults: <1%), diarrhea (2% to 5%), dyspepsia (1% to 3%), nausea (3% to 4%), vomiting (1% to 5%) Genitourinary: Vulvovaginal candidiasis (2%) Local: Injection site reactions (IV: >1%) Nervous system: Dizziness (oral: 2%; IV: <1%), drowsiness, headache (oral: 1% to 3%; IV: >1%), insomnia, nervousness, neurological signs and symptoms (IV: children: 3%), restlessness (IV: >1%; oral: <1%) Respiratory: Asthma (children: 2%) Miscellaneous: Fever (children: 2%; adults: <1%)
Monitoring Parameters	**Monitoring Parameters** CBC, renal and hepatic function during prolonged therapy, altered mental status, signs and symptoms of tendonitis; signs and symptoms of disordered glucose regulation

Drug Interactions	***Risk X: Avoid combination*** Agomelatine, Aminolevulinic Acid, BCG (Intravesical), Cholera Vaccine, Lomitapide, Meptazinol, Nadifloxacin, Pimozide, Tizanidine ***Risk D: Consider therapy modification*** Clozapine, Erlotinib, some Iron Preparations, Lanthanum, Magnesium Salts, Multivitamins/Minerals (with ADEK, Folate, Iron), Pirfenidone, Rasagiline, Sevelamer, Sodium Picosulfate, Sucralfate, Theophylline Derivatives, Tolvaptan, Triazolam, Typhoid Vaccine, Zinc Salts Except: Zinc Chloride, Zolpidem
Pregnancy and Lactation	Use during pregnancy only if potential benefits justify potential risks to fetus and mother. Animal studies (rats and mice) using oral ciprofloxacin did not reveal evidence of harm to the fetus In general, quinolone antibiotics should be avoided in breastfeeding women if alternative agents are available. Based on adverse outcomes observed in animal studies, breastfeeding should be discontinued during therapy and for 2 days after the last ciprofloxacin dose if used for indications other than treating maternal *B. anthracis*. Mothers may express and discard milk during this time.
Administration	**Administration: IV** Administer by slow IV infusion over 60 minutes into a large vein (reduces risk of venous irritation) **Administration: Oral** • Administering 2 hours after meals is preferable. May administer with most foods to minimize GI upset; avoid antacid use; maintain proper hydration and urine output. • Administer orally at least 2 hours before or 6 hours after antacids or other products containing calcium, iron, or zinc. Separate oral administration from drugs that may impair absorption • May be administered with meals containing dairy products (calcium content <800 mg), but not with dairy products alone. • Extended release: Do not crush, split, or chew. **Preparation for Administration:** Injection, vial: May be diluted with NS, D5W, SWFI, D10W, D5$^1/_4$NS, D5$^1/_2$NS, LR to a final concentration not to exceed 2 mg/mL Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Fluoroquinolones, including ciprofloxacin, have been associated with disabling and potentially irreversible serious adverse reactions (e.g., tendinitis and tendon rupture, peripheral neuropathy, CNS effects) that have occurred together. Discontinue immediately and avoid use of fluoroquinolones, including ciprofloxacin, in patients who have experienced any of these serious adverse reactions • Fluoroquinolones, including ciprofloxacin, may exacerbate muscle weakness in patients with myasthenia gravis. Avoid in patients with known history of myasthenia gravis. • Because of risk of serious adverse reactions, use ciprofloxacin for treatment of acute bacterial sinusitis, acute bacterial exacerbations of chronic bronchitis, or uncomplicated urinary tract infections (UTIs) *only* when no other treatment options available •Altered cardiac conduction: Fluoroquinolones may prolong QTc interval; avoid use in patients with a history of or at risk for QTc prolongation, torsades de pointes, uncorrected electrolyte disorders (hypokalemia or hypomagnesemia), cardiac disease (heart failure, myocardial infarction, bradycardia) or concurrent administration of other medications known to prolong the QT interval (including Class Ia and Class III antiarrhythmics, cisapride, erythromycin, antipsychotics, and tricyclic antidepressants.

•Aortic aneurysm and dissection: Fluoroquinolones have been associated with aortic aneurysm ruptures or dissection within 2 months following use, particularly in elderly patients. Fluoroquinolones should not be used in patients with a known history of aortic aneurysm or those at increased risk, including patients with peripheral atherosclerotic vascular diseases, hypertension, genetic disorders involving blood vessel changes (eg, Marfan syndrome, Ehlers-Danlos syndrome), and elderly patients, unless no other treatment options are available. Longer treatment duration (eg, >14 days) may increase risk

•Crystalluria: Rarely, crystalluria has occurred; urine alkalinity may increase the risk. Ensure adequate hydration during therapy.

•Glucose regulation: Fluoroquinolones have been associated with disturbances in glucose regulation, including hyperglycemia and hypoglycemia. These events have occurred most often in patients receiving concomitant oral hypoglycemic agents or insulin. Severe cases of hypoglycemia, including coma and death, have been reported. Diabetic patients should be monitored closely for signs/symptoms of disordered glucose regulation. Discontinue if a hypoglycemic reaction occurs and immediately initiate appropriate therapy.

•Hepatotoxicity: Hepatocellular, cholestatic, or mixed liver injury has been reported, including hepatic necrosis, life-threatening hepatic events, and fatalities. Acute liver injury can be rapid onset (range: 1 to 39 days) and is often associated with hypersensitivity. The pattern of injury can be hepatocellular, cholestatic, or mixed. Most fatalities occurred in patients >55 years of age. Discontinue immediately if signs/symptoms of hepatitis (abdominal tenderness, dark urine, jaundice, pruritus) occur. Additionally, temporary increases in transaminases or alkaline phosphatase, or cholestatic jaundice may occur (highest risk in patients with previous liver damage.

•Hypersensitivity reactions: Severe hypersensitivity reactions, including anaphylaxis, have occurred with fluoroquinolone therapy. The spectrum of these reactions can vary widely; reactions may present as typical allergic symptoms (eg, itching, urticaria, rash, edema) after a single dose, or may manifest as severe idiosyncratic dermatologic (eg, Stevens-Johnson, toxic epidermal necrolysis), vascular (eg, vasculitis), pulmonary (eg, pneumonitis), renal (eg, nephritis), hepatic (eg, hepatitis, jaundice, hepatic failure or necrosis), and/or hematologic (eg, anemia, cytopenias) events, usually after multiple doses. Prompt discontinuation of drug should occur if skin rash or other symptoms arise.

•Photosensitivity/phototoxicity: Avoid excessive sunlight and take precautions to limit exposure (eg, loose fitting clothing, sunscreen); may cause moderate-to-severe phototoxicity reactions which may appear as exaggerated sunburn reactions. Discontinue use if phototoxicity occurs.

-Peripheral neuropathy: Fluoroquinolones have been associated with an increased risk of peripheral neuropathy; may occur soon after initiation of therapy and may be irreversible; discontinue immediately if symptoms of sensory or sensorimotor neuropathy occur. Avoid use in patients who have previously experienced peripheral neuropathy.

-Psychiatric reactions: Fluoroquinolones have been associated with an increased risk of psychiatric reactions, including toxic psychosis, hallucinations, or paranoia; may also cause nervousness, agitation, delirium, attention disturbances, insomnia, anxiety, nightmares, memory impairment, confusion, depression, and suicidal thoughts or actions. Use with caution in patients with a history of or risk factor for mental illness. Reactions may appear following the first dose; discontinue if reaction occurs and institute appropriate therapy.

• Superinfection: Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been

	observed >2 months postantibiotic treatment.
Storage	• Vial: Store between 5°C to 30°C; avoid freezing. Protect from light. Diluted solutions of 0.5 to 2 mg/mL are stable for up to 14 days refrigerated or at room temperature. • Tablet: Store between 20°C to 25°C; excursions are permitted between 15°C and 30°C. • Refer to manufacturer PIL if there are specific considerations.

2. Gatifloxacin

Watch Group

Generic Name	Gatifloxacin
Dosage form/strengths	Eye drops 0.3%, 0.5%
Route of administration	Ophthalmic
Pharmacologic action	Fluoroquinolone; Antibiotic, Ophthalmic ATC: S01AE06
Indications	**Conjunctivitis:** Treatment of bacterial conjunctivitis
Dosage Regimen	***Dosing: Adult,* Pediatric** ***Bacterial conjunctivitis:*** *Ophthalmic:* • *0.3% solution* Days 1 and 2: Instill 1 drop into affected eye(s) every 2 hours while awake (maximum: 8 times/day). Days 3 to 7: Instill 1 drop into affected eye(s) 4 times/day while awake. • 0.5% solution Day 1: Instill 1 drop into affected eye(s) every 2 hours while awake (maximum: 8 times/day) Days 2 to 7: Instill 1 drop into affected eye(s) 2 to 4 times/day while awake
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to gatifloxacin, other quinolones, or any component of the formulation
Adverse Drug Reactions	**1% to 10%:** Ophthalmic: Conjunctival hemorrhage, conjunctival irritation, conjunctivitis (worsening), decreased visual acuity, dry eye syndrome, eye discharge, eye irritation, eye pain, eye redness, eyelid edema, increased lacrimation, keratitis, papillary conjunctivitis
Monitoring Parameters	Assess for signs of bacterial superinfection. Educate patients to report immediately to prescriber vision changes, eye pain, severe eye irritation, signs of Stevens-Johnson syndrome/toxic epidermal necrolysis (red, swollen, blistered, or peeling skin [with or without fever]; red or irritated eyes; or sores in mouth, throat, nose, or eyes), or eye or eyelid edema. Educate patients about change in taste side effect.
Drug Interactions	Ophthalmic: There are no known significant interactions.
Pregnancy and Lactation	Systemic concentrations of gatifloxacin following ophthalmic administration are below the limit of quantification**. pregnancy category C.** It is not known if gatifloxacin is excreted in breast milk. The decision to continue or discontinue breast-feeding during therapy should take into account the risk of infant exposure, the benefits of breast-feeding to the infant, and benefits of treatment to the mother.

Administration	**Administration:** **Ophthalmic:** For topical ophthalmic use only. Avoid touching tip of applicator to eye, fingers, or other surfaces. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity reactions: Hypersensitivity reactions, including anaphylactic reactions, angioedema (including pharyngeal, laryngeal, or facial edema), dyspnea, urticaria, and itching, have been reported (even following a single dose) with topical ophthalmic gatifloxacin. Rare cases of Stevens-Johnson syndrome were also reported. If an allergic reaction occurs, discontinue use. • Superinfection: Prolonged use may result in fungal or bacterial superinfection. If superinfection is suspected, institute appropriate alternative therapy. • QTc Interval Prolongation • Disturbances in Blood Glucose • Tendon Effects • Peripheral neuropathy ***Special populations:*** • Contact lens wearers: Contact lenses should not be worn during treatment of ophthalmic infections. ***Dosage form specific issues:*** • Appropriate use: For topical ophthalmic use only. Do not inject ophthalmic solution subconjunctivally or introduce directly into the anterior chamber of the eye (may cause corneal endothelial cell injury).
Storage	Store between 15°C to 25°C; protect from freezing. Refer to manufacturer PIL if there are specific considerations.

3. Levofloxacin

Watch Group

Generic Name	Levofloxacin
Dosage form/strengths	**Vial** 500mg, 750mg **Tablets** 250mg, 500mg, 750mg **Eye drops** 0.5% (5mg/ml)
Route of administration	*IV, Oral, Ophthalmic solution*
Pharmacological action	Antibiotic, Fluoroquinolone Systemic ATC: J01MA12 Ophthalmic ATC: S01AE05
Indications	Treatment of community-acquired pneumonia, including multidrug-resistant strains of Streptococcus pneumoniae (MDRSP); nosocomial pneumonia; chronic obstructive pulmonary disease, acute exacerbation; rhinosinusitis, acute bacterial (ABRS); prostatitis (chronic bacterial); urinary tract infection (uncomplicated or complicated); acute pyelonephritis; skin or skin structure infections (uncomplicated or complicated); inhalational anthrax (postexposure) to reduce incidence or disease progression; prophylaxis and treatment of plague (pneumonic and septicemic) due to Yersinia pestis Limitations of use: Because fluoroquinolones have been associated with disabling and potentially irreversible serious adverse reactions (eg, tendinopathy and tendon rupture, peripheral neuropathy, CNS effects), reserve levofloxacin for use in patients who have no alternative treatment options for acute exacerbation of chronic bronchitis, acute bacterial sinusitis, and uncomplicated urinary tract infections.
Dosage Regimen	**Conventional dosing:** **Adult**: **Oral/IV** :500-750 mg once daily **Pediatric**: Note: In pediatric patients, fluoroquinolones are not routinely first-line therapy, but after assessment of risks and benefits, can be considered a reasonable alternative for situations where no safe and effective substitute is available (eg, multidrug resistance) or in situations where the only alternative is parenteral therapy and levofloxacin offers an oral therapy option. **Oral, IV** 6 months to <5 years**:** 8 to 10 mg/kg/dose twice daily ≥5 years: 10 mg/kg/dose once daily; maximum dose: 750 mg/day **Bacterial conjunctivitis:** Ophthalmic: Adult, pediatric Treatment day 1 and day 2: Instill 1 to 2 drops into affected eye(s) every 2 hours while awake, up to 8 times daily Treatment day 3 through day 7: Instill 1 to 2 drops into affected eye(s) every 4 hours while awake, up to 4 times daily **Note:** Dosages of oral and IV levofloxacin are identical. Safety of levofloxacin given for >28 days in adults and >14 days in pediatric patients not studied,

Dosage adjustment

Renal impairment: Adult

Usual Daily Dosage for Normal Renal Function (Cl_{cr} ≥ 50 mL/min)	Cl_{cr} (mL/min)	Dosage for Renal Impairment
250 mg	20–49	Dosage adjustment not required
	10–19	Uncomplicated UTIs: Dosage adjustment not required. Other infections: 250 mg once every 48 hours
	Hemodialysis or CAPD patients	Information not available
500 mg	20–49	Initial 500-mg dose, then 250 mg once every 24 hours
	10–19	Initial 500-mg dose, then 250 mg once every 48 hours
	Hemodialysis or CAPD patients	Initial 500-mg dose, then 250 mg once every 48 hours; supplemental doses not required after dialysis
750 mg	20–49	750 mg once every 48 hours
	10–19	Initial 750-mg dose, then 500 mg once every 48 hours
	Hemodialysis or CAPD patients	Initial 750-mg dose, then 500 mg once every 48 hours; supplemental doses not required after dialysis

Dosing: Renal Impairment: Pediatric

Infants, Children, and Adolescents: IV, Oral: The following adjustments have been recommended. Note: Renally adjusted dose recommendations are based on doses of 5 to 10 mg/kg/dose every 12 hours in ages ≤5 years and 5 to 10 mg/kg/dose every 24 hours in ages >5 years.

GFR ≥30 mL/minute/1.73 m^2: No adjustment necessary

GFR 10 to 29 mL/minute/1.73 m^2: 5 to 10 mg/kg/dose every 24 hours

GFR <10 mL/minute/1.73 m^2: 5 to 10 mg/kg/dose every 48 hours

Intermittent hemodialysis: 5 to 10 mg/kg/dose every 48 hours; not removed by hemodialysis; supplemental levofloxacin doses are not required

Peritoneal dialysis (PD): 5 to 10 mg/kg/dose every 48 hours; not removed by peritoneal dialysis; supplemental levofloxacin doses are not required

Continuous renal replacement therapy (CRRT): 10 mg/kg/dose every 24 hours

- **No dosage adjustment for hepatic impairment.**

Contra-indications

Hypersensitivity to levofloxacin, any component of the formulation, or other quinolones

Adverse Drug Reactions

Adverse Reactions (Significant): Considerations

Aortic aneurysm/aortic dissection

CNS effects/neuroexcitation

	Clostridioides difficile infection Glucose regulation/dysglycemia Hepatotoxicity Hypersensitivity reactions (immediate and delayed) Myasthenia gravis Peripheral neuropathy Phototoxicity/photoallergy QT prolongation **1% to 10%:** Cardiovascular: Chest pain (1%), edema (1%) Dermatologic: Pruritus (1%), skin rash (2%) Gastrointestinal: Abdominal pain (2%), constipation (3%), diarrhea (5%), dyspepsia (2%), nausea (7%), vomiting (2%) Genitourinary: Vaginitis (1%) Infection: Candidiasis (1%) Local: Injection site reaction (1%) Nervous system: Dizziness (3%), headache (6%), insomnia (4%) Respiratory: Dyspnea (1%)
Monitoring Parameters	Evaluation of organ system functions (renal, hepatic, and hematopoietic) is recommended periodically during therapy; the possibility of crystalluria should be assessed; WBC and signs of infection, altered mental status, signs and symptoms of tendonitis; signs and symptoms of disordered glucose regulation
Drug Interactions	***Risk X: Avoid combination*** Aminolevulinic Acid Amiodarone BCG (Intravesical) Antacids Cholera Vaccine Fexinidazole Nadifloxacin Pimozide QT-prolonging Class IA Antiarrhythmics QT-prolonging Class III Antiarrhythmics Strontium Ranelate ***Risk D: Consider therapy modification*** Antacids: Exception: Sodium Bicarbonate Calcium Salts Delamanid Didanosine Domperidone Iron Preparations Lanthanum Methadone Magnesium Salts Multivitamins/Minerals (with ADEK, Folate, Iron) Multivitamins/Minerals (with AE, No Iron) QT-prolonging Kinase Inhibitors QT-prolonging Miscellaneous Agents Quinapril Sevelamer Sodium Picosulfate Sucralfate Typhoid Vaccine Zinc Salts
Pregnancy and Lactation	**Pregnancy risk factor C** When administered orally or IV, levofloxacin enters breast milk. The amount of levofloxacin available systemically following topical application of the ophthalmic drops is significantly less in comparison to oral or IV doses. Caution be exercised when administering levofloxacin ophthalmic drops to nursing women.
Administration	**Administration: IV** Infuse 250 to 500 mg IV solution over 60 minutes; infuse 750 mg IV solution over 90 minutes. Too rapid of infusion can lead to hypotension. Avoid administration through an intravenous line with a solution containing multivalent cations (eg, magnesium, calcium). Maintain adequate hydration of patient to prevent crystalluria or cylindruria. **Administration: Oral** Tablets may be administered without regard to meals. Maintain adequate hydration of patient to prevent crystalluria. Administer at least 2 hours before or 2 hours after antacids containing magnesium or aluminum, sucralfate, metal cations (eg, iron), multivitamin preparations with zinc, or didanosine chewable/buffered tablets or the pediatric powder for solution. **Preparation for Administration:**

	Solution for injection: Single-use vials must be further diluted in compatible solution (eg, D5W, NS) to a final concentration of 5 mg/mL prior to infusion. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • **Altered cardiac conduction** • **Aortic aneurysm and dissection**: Fluoroquinolones have been associated with aortic aneurysm ruptures or dissection within 2 months following use, particularly in elderly patients. • **Glucose regulation**: including hyperglycemia and hypoglycemia. Diabetic patients should be monitored closely. • **Hepatotoxicity**: Unrelated to hypersensitivity, severe hepatotoxicity (including acute hepatitis and fatalities) has been reported. Elderly patients may be at greater risk. • **Hypersensitivity reactions**: Severe hypersensitivity reactions, including anaphylaxis, have occurred with quinolone therapy. • **Phototoxicity**: Avoid excessive sunlight and take precautions to limit exposure (eg, loose-fitting clothing, sunscreen) • Serious adverse reactions: [US Boxed Warning]: Fluoroquinolones are associated with disabling and potentially irreversible serious adverse reactions that may occur together, including tendinitis and tendon rupture, peripheral neuropathy, and CNS effects. Discontinue levofloxacin immediately and avoid use of fluoroquinolones in patients who experience any of these serious adverse reactions. Patients of any age or without preexisting risk factors have experienced these reactions; may occur within hours to weeks after initiation. - **CNS effects**: May occur following the first dose; discontinue immediately and avoid further use of fluoroquinolones in patients who experience these reactions. Avoid use in patients who have previously experienced peripheral neuropathy. - **Psychiatric reactions**: Use with caution in patients with a history of or risk factor for depression. Reactions may occur following the first dose; discontinue if reaction occurs and institute appropriate therapy. - **Tendinitis/tendon rupture**: risk may be increased with concurrent corticosteroids, solid organ transplant recipients, and in patients >60 years of age, but has also occurred in patients without these risk factors. Discontinue at first sign of tendon pain, swelling, inflammation or rupture. • **Superinfection**: Prolonged use ***Disease-related concerns:*** • Myasthenia gravis: [US Boxed Warning]: May exacerbate muscle weakness related to myasthenia gravis; avoid use in patients with known history of myasthenia gravis. • Renal impairment: dosage adjustment required. May increase risk of tendon rupture. • Rheumatoid arthritis: Use with caution. may increase risk of tendon rupture. ***Special populations:*** • Elderly: Adverse effects (eg, hepatotoxicity, tendon rupture, QT changes, aortic dissection) may be increased in the elderly. • G6PD deficiency: Hemolytic reactions may (rarely) occur with quinolone use in patients with latent or actual G6PD deficiency. • Pediatric: Safety of use in pediatric patients for >14 days of therapy has not been studied; increased incidence of musculoskeletal disorders (eg, arthralgia, tendon rupture) has been observed in children. ***Other warnings/precautions:*** • Appropriate use: [US Boxed Warning]: Reserve use of levofloxacin for treatment of acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, or uncomplicated urinary tract infection for patients who have no alternative treatment options because of the risk of disabling and potentially serious adverse reactions (eg, tendinitis and tendon rupture,

	peripheral neuropathy, CNS effects).
Storage	• Vial: Store at room temperature. Protect from light. • Diluted solution (5 mg/mL) is stable in NS, D_5W, D_5NS, D_5LR or sodium lactate for 72 hours when stored at room temperature; stable for 14 days when stored under refrigeration. • Premixed: Store at ≤25°C; do not freeze. Brief exposure to 40°C does not adversely affect the product. Protect from light. • Tablet, oral solution: Store at 25°C; excursions permitted to 15- 30°C. • Refer to manufacturer PIL if there are specific considerations.

4. Lomefloxacin

Watch Group

Generic Name	Lomefloxacin
Dosage form/strengths	-Ophthalmic Solution, eye drops: 3 mg/ml -Film coated tablets : 400 mg
Route of administration	Oral ,Ophthalmic
Pharmacologic category	Antibiotic, Quinolone Systemic ATC: J01MA07 Opthalmic ATC: S01AE04
Indications	**-Tablets:** **1-Treatment of adults with mild to moderate infections caused by susceptible strains of the designated microorganisms in the following conditions:** **a-Lower respiratory tract:** -Acute Bacterial Exacerbation of Chronic Bronchitis caused by Haemophilus, influenzae or Moraxella catarrhalis **b-Urinary tract:** -Uncomplicated Urinary Tract Infections (cystitis) caused by Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, or Staphylococcus saprophyticus -Complicated Urinary Tract Infections caused by Escherichia coli, Klebsiellapneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Citrobacter diversus, or Enterobacter cloacae **2-Prevention of infection in the following situations:** -Transrectal prostate biopsy -Transurethral surgical procedures **-Ophthalmic Solution:** -Bacterial infections, including conjunctivitis, blepharitis, blepharoconjunctivitis which are due to Lomefloxacin susceptible germs and Staphylococcus aureus- induced corneal ulcers.
Dosage Regimen	**-Oral Dosing Adults:** **-Treatment:** 1-Acute bacterial exacerbation of chronic bronchitis: 400 mg once daily for 10 days 2-Uncomplicated cystitis in females caused by E coli: 400 mg once daily for 3 days 3-Uncomplicated cystitis caused by K pneumoniae, P mirabilis, or S Saprophyticus: 400 mg once daily for 10 days 4-Complicated UTI: 400 mg once daily for 14 days -Prevention: -Transrectal prostate biopsy: 400 mg single dose 1–6 hours prior to procedure -Transurethral surgical procedures: 400 mg single dose 2–6 hours prior to procedure **-Ophthalmic solution:** -Adults and children (above 1 year of age): -Initial:5 drops within 20 minutes or 1 drop every hour during 6-10 hours. -Maintenance: 1 drop to be instilled 2-3 times daily into the lower conjunctival sac. Duration of the treatment: 7 to 9 days.
Dosage adjustment	-Oral: **-Renal impairment:** -Creatinine clearance > 10 mL/min/1.73 m2 but < 40 mL/min/1.73 m2: initial loading dose of 400 mg followed by daily maintenance doses of 200 mg once daily for the duration of treatment. **-Hepatic impairment:**

	-No dosage adjustment needed.
Contra-indications	-History of hypersensitivity to lomefloxacin or any member of the quinolone group
Adverse Drug Reactions	-Headache (3.6%), nausea (3.5%), photosensitivity (2.3%), dizziness (2.1%), diarrhea (1.4%), and abdominal pain (1.2%)
Monitoring Parameters	No needed data
Drug Interactions	-Tablets: Antacids and sucralfate, Probenecid -Opthalamic: Preparations containing heavy metals, such as zinc , Bacteriostatic ophthalmic antibiotics
Pregnancy and Lactation	**pregnancy category C** Contraindicated (Use only if no other alternatives) Lactation: No Human Data—Probably Compatible
Administration	**-Tablets:** Administered orally without regard to meals. Sucralfate and antacids containing magnesium or aluminum should not be taken within 4 hours before or 2 hours after taking lomefloxacin. **-Ophthalamic:** -Administered without regard to meals. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	**Tablets:** -Drug should be administered 12 hours before exposure to direct or indirect sunlight (including exposure through glass and exposure through sunscreens and sunblocks) and artificial ultraviolet light (eg, sunlamps) -Drug should be discontinued l at the first signs or symptoms of phototoxicity reaction such as a sensation of skin burning, redness, swelling, blisters, rash, itching, or dermatitis patient who has experienced a phototoxic reaction should avoid re-exposure to sunlight and artificial ultraviolet light until he has completely recovered from the reaction. -Patient should drink fluids liberally. -Caution before operating an automobile or machinery or engaging in activities requiring mental alertness and coordination as drug causes dizziness and lightheadedness - Treatment should be discontinued and physician informed if patient experience pain, inflammation, or rupture of a tendon, and to rest and refrain from exercise until diagnosis of tendinitis or tendon rupture has been confidently excluded -Caution in patients with history of convulsion - Should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, and patients receiving class IA (quinidine, procainamide), or class III (amiodarone, sotalol) antiarrhythmic agents. **-Ophthalmic:** -Intensive exposure to sunlight or UV radiation should be avoided
Storage	Store at (15° to 25°C). Refer to manufacturer PIL if there are specific considerations.

Watch Group

5. Moxifloxacin

Generic Name	Moxifloxacin
Dosage form/strengths	Tablets 400mg, Ophthalmic solution 0.5% Vial 400mg
Route of administration	Oral, ophthalmic, IV
Pharmacologic action	Antibiotic, Fluoroquinolone; Systemic ATC: J01MA14 Ophthalmic ATC: S01AE07
Indications	**Treatment of** mild to moderate community-acquired pneumonia, including multidrug-resistant *Streptococcus pneumoniae* (MDRSP); acute bacterial exacerbation of chronic bronchitis; acute bacterial rhinosinusitis; complicated and uncomplicated skin and skin structure infections; complicated intra-abdominal infections; prophylaxis and treatment of plague, including pneumonic and septicemic plague, due to *Yersinia pestis*. **Limitations of use**: Because fluoroquinolones have been associated with disabling and potentially irreversible serious adverse reactions (eg, tendinopathy and tendon rupture, peripheral neuropathy, CNS effects), reserve use of moxifloxacin for acute exacerbation of chronic bronchitis or acute sinusitis for patients who have no alternative treatment options. **Bacterial conjunctivitis:** Treatment of bacterial conjunctivitis caused by susceptible organisms
Dosage Regimen	**Dosing: Adult** **Oral, IV:** 400 mg once daily **Duration:** Individualize based on rapidity of culture conversion, extent of disease, and patient-specific factors, including clinical response and toxicity **Bacterial conjunctivitis:** Ophthalmic: Instill 1 drop into affected eye(s) 2-3 times daily for 7 days. **Dosing: Pediatric** **Note:** In pediatric patients, fluoroquinolones are not routinely first-line therapy, but after assessment of risks and benefits, can be considered a reasonable alternative for situations where no safe and effective substitute is available (eg, multidrug resistance), limited data available about dosing.
Dosage adjustment	**Dosing: Renal Impairment: Adult** No dosage adjustment necessary. **Dosing: Hepatic Impairment:** No dosage adjustment necessary; however, use with caution in this patient population secondary to the risk of QT prolongation.
Contra-indications	Hypersensitivity to moxifloxacin, other quinolone antibiotics, or any component of the formulation
Adverse Drug Reactions	**1% to 10%:** Central nervous system: Headache (4%), dizziness (3%), insomnia (2%)

	Endocrine & metabolic: Decreased serum glucose (≥2%), hyperchloremia (≥2%), increased serum albumin (≥2%), hypokalemia (1%) Gastrointestinal: Nausea (7%), diarrhea (6%), decreased amylase (≥2%), constipation (2%), vomiting (2%), abdominal pain (1% to 2%), dyspepsia Hematologic & oncologic: Decreased basophils (≥2%), decreased red blood cells (≥2%), eosinopenia (≥2%), increased MCH (≥2%), increased neutrophils (≥2%), leukocytosis (≥2%), prolonged prothrombin time (≥2%), anemia (1%) Hepatic: Decreased serum bilirubin (≥2%), increased serum bilirubin (≥2%), increased serum alanine aminotransferase (1%) Immunologic: Increased serum globulins (≥2%) Renal: Increased ionized serum calcium (≥2%) Respiratory: Hypoxia (≥2%) Miscellaneous: Fever (1%)
Monitoring Parameters	WBC, signs of infection, signs/symptoms of disordered glucose regulation, ECG in patients with liver cirrhosis
Drug Interactions	• ***Risk X: Avoid combination*** Aminolevulinic Acid BCG (Intravesical) Cholera Vaccine Nadifloxacin Pimozide QT-prolonging Agents Strontium Ranelate • ***Risk D: Consider therapy modification*** Delamanid Didanosine Iron Preparations Lanthanum Magnesium Salts Multivitamins/Minerals (with ADEK, Folate, Iron) Quinapril Sevelamer Sodium Picosulfate Sucralfate Typhoid Vaccine Zinc Salts • ***Risk C: Monitor therapy*** Agents with Blood Glucose Lowering Effects Amisulpride Amphetamines BCG Vaccine (Immunization Corticosteroids Haloperidol Heroin Hydroxychloroquine Lactobacillus and Estriol: Methylphenidate Mycophenolate Nonsteroidal Anti-Inflammatory Agents Ondansetron Pentamidine Porfimer QT-prolonging Agents Varenicline Verteporfin Vitamin K Antagonists
Pregnancy and Lactation	**Pregnancy Category C** It is not known if moxifloxacin is present in breast milk. According to the manufacturer, the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of treatment to the mother. Use of fluoroquinolone antibiotics should be avoided if alternative agents are available
Administration	**IV**: Infuse over 60 minutes; do not infuse by rapid or bolus intravenous infusion. **Oral**: Administer without regard to meals. Administer at least 4 hours before or 8 hours after products containing magnesium, aluminum, iron, or zinc, including antacids, sucralfate, multivitamins, and didanosine (buffered tablets for oral suspension or the pediatric powder for oral solution). Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Altered cardiac conduction: Fluoroquinolones may prolong QTc interval; avoid use in patients with known QTc prolongation, ventricular arrhythmias including torsades de pointes, proarrhythmic conditions (eg, clinically significant bradycardia, acute myocardial ischemia), uncorrected hypokalemia, hypomagnesemia, or concurrent administration of

other medications known to prolong the QT interval (including Class Ia and Class III antiarrhythmics, cisapride, erythromycin, antipsychotics, and tricyclic antidepressants).
• Aortic aneurysm and dissection: Fluoroquinolones have been associated with aortic aneurysm ruptures or dissection within 2 months following use, particularly in elderly patients.
• Glucose regulation: Fluoroquinolones have been associated with disturbances in glucose regulation, including hyperglycemia and hypoglycemia.
• Hepatotoxicity: Fulminant hepatitis potentially leading to liver failure (including fatalities) has been reported with use; patients should be advised to discontinue treatment and promptly report signs/ symptoms of hepatitis (eg, abdominal pain, jaundice, dark urine, pale stools).
• Hypersensitivity reactions: Severe hypersensitivity reactions, including anaphylaxis, have occurred with quinolone therapy. The spectrum of these reactions can vary widely; reactions may present as typical allergic symptoms (eg, itching, urticaria, rash, edema) after a single dose, or may manifest as severe idiosyncratic dermatologic (eg, Stevens-Johnson, toxic epidermal necrolysis), vascular (eg, vasculitis), pulmonary (eg, pneumonitis), renal (eg, nephritis), hepatic (eg, hepatic failure or necrosis), and/or hematologic (eg, anemia, cytopenias) events, usually after multiple doses. Prompt discontinuation of drug should occur if skin rash or other symptoms arise.
• Photosensitivity: Avoid excessive sunlight and take precautions to limit exposure (eg, loose fitting clothing, sunscreen); may rarely cause moderate to severe phototoxicity reactions. Discontinue use if phototoxicity occurs.
• Serious adverse reactions: [US Boxed Warning]: Fluoroquinolones are associated with disabling and potentially irreversible serious adverse reactions that may occur together, including tendinitis and tendon rupture, peripheral neuropathy, and CNS effects. Discontinue moxifloxacin immediately and avoid use of fluoroquinolones in patients who experience any of these serious adverse reactions. Patients of any age or without pre-existing risk factors have experienced these reactions; may occur within hours to weeks after initiation.
- CNS effects: Fluoroquinolones have been associated with an increased risk of CNS effects including seizures, increased intracranial pressure (including pseudotumor cerebri), lightheadedness, dizziness, and tremors.
- Peripheral neuropathy
- Psychiatric reactions: Fluoroquinolones have been associated with an increased risk of psychiatric reactions, including toxic psychosis, hallucinations, or paranoia; may also cause nervousness, agitation, delirium, attention disturbances, insomnia, anxiety, nightmares, memory impairment, confusion, depression, and suicidal thoughts or actions.
- Tendinitis/tendon rupture: Fluoroquinolones have been associated with an increased risk of tendonitis and tendon rupture in all ages
• Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment.

Disease-related concerns:

• Cardiovascular disease: Use with caution in patients with significant bradycardia or acute myocardial ischemia.
• Diabetes: Use with caution in patients with diabetes mellitus; glucose regulation may be altered.
• Hepatic impairment: Use with caution in patients with mild, moderate, or severe hepatic impairment or liver cirrhosis; may increase the risk of QT prolongation.
• Myasthenia gravis: [US Boxed Warning]: May exacerbate muscle weakness related to myasthenia gravis; avoid use in patients with known history of myasthenia gravis. Cases of

	severe exacerbations, including the need for ventilatory support, and deaths have been reported. • Rheumatoid arthritis: Use with caution in patients with rheumatoid arthritis; may increase risk of tendon rupture. *Special populations:* • Elderly: Adverse effects (eg, tendon rupture, QT changes) may be increased in elderly patients. • G6PD deficiency: Hemolytic reactions may (rarely) occur with quinolone use in patients with latent or actual G6PD deficiency. • Pediatric: Efficacy of systemically administered moxifloxacin (oral, intravenous) have not been established in pediatric patients. *Other warnings/precautions:* • Appropriate use: [US Boxed Warning]: Reserve use of moxifloxacin for treatment of acute bacterial sinusitis or acute bacterial exacerbation of chronic bronchitis for patients who have no alternative treatment options because of the risk of disabling and potentially serious adverse reactions (eg, tendinitis and tendon rupture, peripheral neuropathy, CNS effects).
Storage	Store at 25°C; excursions are permitted between 15°C and 30°C. Avoid high humidity. Do not refrigerate infusion solution; discard unused portion. Opthalmic: Store at 2°C to 25°C Refer to manufacturer PIL if there are specific considerations.

6. Norfloxacin

Watch Group

Generic Name	Norfloxacin
Dosage form/strengths	-Tablets: 400 mg -Ophthalmic solution: 15 mg/5ml
Route of administration	Oral, Ophthalmic
Pharmacologic category	Antibiotic, Fluoroquinolone ATC systemic: J01MA06 ATC: Ophthalmic: S01AE02
Indications	-Tablets: Uncomplicated and complicated urinary tract infections caused by susceptible gram-negative and gram-positive bacteria -Opthalmic solution: Treatment of conjunctivitis caused by susceptible strains
Dosage Regimen	**-Tablets: Adult dosing** **-Prostatitis:** Oral: 400 mg every 12 hours for 4 to 6 weeks -Urinary tract infection: **-Cystitis, acute uncomplicated or acute simple cystitis:** Oral: 400 mg twice daily for 3 days (females) or 5 days (males) **-Complicated (including pyelonephritis):** Oral: 400 mg twice daily for 5 to 7 days **-Ophthalmic solution:** -Adults and pediatric ≥1 year : one or two drops to be instilled in each eye 4 times/day for 7 days
Dosage adjustment	**-Oral:** **-Renal Impairment**: CrCl ≤30 mL/minute/1.73 m2: 400 mg once daily **-Hepatic Impairment:** - Norfloxacin is eliminated primarily through biliary and renal excretion and is only moderately metabolized in the liver. Cases of hepatitis have been reported with norfloxacin. Specific dosage adjustment are not available
Contra-indications	**-Tablets & Ophthalmic solution:** -Hypersensitivity to norfloxacin, quinolones, or any component of the formulation **-Tablets only:** - History of tendonitis or tendon rupture associated with quinolone use
Adverse Drug Reactions	**-Oral:** **1 – 10%:** -Gastrointestinal: Nausea (2%) -Nervous system: Dizziness (1%), headache (2%) **-Ophthalmic:** -Local burning ,discomfort ,bitter taste following instillation ,conjunctival hyperemia , photophobia,corneal deposits , chemosis
Monitoring Parameters	**-Tablets:** -CBC, Renal and hepatic function **-Ophthalmic solution:** Response of bacteria to drug

Drug Interactions	**-Tablets:** ***Risk X: Avoid combination*** Aminolevulinic Acid, BCG (Intravesical), Cholera Vaccine, Nadifloxacin, Nitrofurantoin, Strontium Ranelate ***Risk D: Consider therapy modification*** Antacids, Calcium Salts, Delamanid, Didanosine, Iron Preparations, Lanthanum, Magnesium Salts, Multivitamins/Minerals, Sevelamer, Sodium Picosulfate, Sucralfat, Typhoid Vaccine, Zinc.
Pregnancy and Lactation	Pregnancy Category C It is not known if concentrations would be detectable after a higher dose than 200 mg or multiple doses. Due to the potential for serious adverse reactions in the nursing infant, the manufacturer recommends a decision be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of treatment to the mother.
Administration	**-Tablets:** - Administer on an empty stomach with water (at least 1 hour before or 2 hours after meals, milk, or other dairy products). -Hold antacids, sucralfate, or multivitamins/supplements containing iron, zinc, magnesium, or aluminum for at least 2 hours before or after giving norfloxacin; do not administer together Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	**-Tablets:** -Avoid use in patients with a history of QTc prolongation, uncorrected hypokalemia, hypomagnesemia, or concurrent administration of other medications known to prolong the QT interval (including Class Ia and Class III antiarrhythmics, cisapride, erythromycin, antipsychotics, and tricyclic antidepressants). -Should not be used in patients with a known history of aortic aneurysm or those at increased risk, including patients with peripheral atherosclerotic vascular diseases, hypertension, genetic disorders involving blood vessel changes (eg, Marfan syndrome, Ehlers-Danlos syndrome), and elderly patients, unless no other treatment options are available -Patients should be monitored closely for signs/symptoms of disordered glucose regulation. -Avoid excessive sunlight and take precautions to limit exposure (eg, loose fitting clothing, sunscreen); may cause moderate-to-severe phototoxicity reactions. Discontinue use if photosensitivity occurs. -Use with caution in patients with known or suspected CNS disorder, or risk factors that may predispose to seizures or lower the seizure threshold. -Avoid use in patients who have previously experienced peripheral neuropathy -Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. -avoid use in patients with known history of myasthenia gravis -use with caution in patients with renal or hepatic impairment -Hemolytic reactions may (rarely) occur with fluoroquinolone use in patients with G6PD deficiency -Fluoroquinolones have been associated with an increased risk of tendonitis and tendon rupture in all ages; risk may be increased with concurrent corticosteroids, solid organ transplant recipients, and in patients >60 years of age, but has also occurred in patients without risk factors
Storage	**-Tablets:** Store at 25°C; excursions permitted to 15°C to 30°C. **-Ophthalmic:** Store at 15-30°C. Protect from light Refer to manufacturer PIL if there are specific considerations.

Watch Group

7. Ofloxacin

Generic Name	Ofloxacin
Dosage form/strengths	Tablets: 200mg, 300mg, 400mg Ophthalmic solution 3mg/ml
Route of administration	Oral, Ophthalmic
Pharmacologic action	Antibiotic, Fluoroquinolone Systemic ATC: J01MA01 Opthalmic ATC: S01AE01
Indications	**Treatment of:** **Community-acquired pneumonia,** **Skin and soft tissue infections (uncomplicated),** **Urethritis and cervicitis (nongonococcal)** due to *Chlamydia trachomatis* infection, **Pelvic inflammatory disease (acute),** **Cystitis (uncomplicated),** **Urinary tract infections (complicated),** **Prostatitis** **Opthalmic:** Treatment of Bacterial conjunctivitis and Corneal ulcer
Dosage Regimen	**Dosing: Adult** **usual adult dose:** 200 to 400 mg every 12 hours **Cervicitis/urethritis:** Oral: *Nongonococcal (due to Chlamydia trachomatis) (alternative agent):* 300 mg every 12 hours for 7 days *Pelvic inflammatory disease, outpatient therapy, mild to moderate disease (alternative agent):* **Oral:** 400 mg every 12 hours for 10 to 14 days. Guidelines recommend use of a fluoroquinolone in combination with metronidazole **Skin and soft tissue infection, uncomplicated: Oral:** 400 mg every 12 hours. Treat for 5 to 14 days depending on severity and clinical response. **Urinary tract infection:** ○ *Cystitis, acute uncomplicated or acute simple cystitis (infection limited to the bladder without signs/symptoms of upper tract, prostate, or systemic infection) (alternative agent):* **Note:** Use is discouraged due to safety concerns and increasing resistance; reserve for those who have no alternative treatment options. **Oral:** 200 mg every 12 hours for 3 days (females) or 5 days (males). ○ *Urinary tract infection, complicated (including pyelonephritis):* **Note:** If the prevalence of fluoroquinolone resistance is >10%, an initial dose of a long-acting parenteral antimicrobial (eg, ceftriaxone) followed by oral therapy is recommended for outpatients. **Oral:** 200 mg every 12 hours for 5 to 7 days **Dosing: Pediatric** **Susceptible infection:** Limited data available: Children: Oral: 15 mg/kg/day divided every 12 hours Children weighing ≥45 kg and Adolescents: Oral: 300-400 mg twice daily

	Opthalmic Adult, Pediatric **Bacterial conjunctivitis:** Ophthalmic: Initial: Instill 1 to 2 drops in affected eye(s) every 2 to 4 hours for the first 2 days (Days 1 and 2); then instill 1 to 2 drops 4 times daily for an additional 5 days (Days 3 through 7) **Corneal ulcer**: Ophthalmic: Initial: Instill 1 to 2 drops in affected eye(s) every 30 minutes while awake and every 4 to 6 hours at night for the first 2 days (Days 1 and 2); then instill 1 to 2 drops every hour while awake for 4 to 6 additional days (Days 3 through 7 to 9); thereafter, 1 to 2 drops 4 times daily until clinical cure is achieved
Dosage adjustment	**Dosing: Renal Impairment: Adult** Oral: After a normal initial dose, adjust as follows: CrCl >50 mL/minute: No dosage adjustment necessary. CrCl 20 to 50 mL/minute: Administer usual recommended dose every 24 hours. CrCl <20 mL/minute: Administer half the usual recommended dose every 24 hours. Intermittent hemodialysis (IHD): 100 to 200 mg after dialysis Peritoneal dialysis: 200 mg every 24 hours Continuous renal replacement therapy (CRRT): 300 mg every 24 hours **Dosing: Hepatic Impairment: Adult** Use with caution. Severe impairment (eg, cirrhosis with or without ascites): Maximum dose: 400 mg/day **Dosing: Renal Impairment: Pediatric** There are no specific pediatric recommendations; based on experience in adult patients, dosing adjustment is suggested. **Dosing: Hepatic Impairment: Pediatric** There are no specific pediatric recommendations; based on experience in adult patients, dosing adjustment is suggested.
Contra-indications	Hypersensitivity to ofloxacin, other quinolones, or any component of the formulation
Adverse Drug Reactions	Oral: **1% to 10%:** Cardiovascular: Chest pain (1% to 3%) Central nervous system: Headache (1% to 9%), insomnia (3% to 7%), dizziness (1% to 5%), fatigue (1% to 3%), drowsiness (1% to 3%), sleep disorder (1% to 3%), nervousness (1% to 3%), pain (trunk) Dermatologic: Pruritus (≤3%), skin rash (≤3%), genital pruritus (women: 1% to 3%) Gastrointestinal: Nausea (3% to 10%), diarrhea (1% to 4%), vomiting (1% to 4%), abdominal cramps (1% to 3%), constipation (1% to 3%), decreased appetite (1% to 3%), dysgeusia (1% to 3%), flatulence (1% to 3%), gastrointestinal distress (1% to 3%), xerostomia (1% to 3%) Genitourinary: Vaginitis (1% to 5%) Ophthalmic: Visual disturbance (1% to 3%) Respiratory: Pharyngitis (1% to 3%) Miscellaneous: Fever (1% to 3%) **Ophthalmic**: Blurred vision, burning sensation of eyes, conjunctivitis (chemical), eye discomfort, eye pain, eye pruritus, eye redness, keratitis (chemical), lacrimation, photophobia, stinging of eyes, swelling of eye, xerophthalmia
Monitoring Parameters	Monitor CBC, renal and hepatic function periodically if therapy is prolonged; signs and symptoms of disordered glucose regulation.

Drug Interactions	***Oral:*** ***Risk X: Avoid combination*** Aminolevulinic Acid BCG (Intravesical) Cholera Vaccine Fexinidazole Nadifloxacin Strontium Ranelate ***Risk D: Consider therapy modification*** Antacids Calcium Salts Delamanid Didanosine Iron Preparation Lanthanum Magnesium Salts ***Risk C: Monitor therapy*** Agents with Blood Glucose Lowering Effects: Amphetamines BCG Vaccine Corticosteroids Haloperidol Lactobacillus and Estriol Methylphenidate Mycophenolate Nonsteroidal Anti-Inflammatory Agents Probenecid QT-prolonging Agents Theophylline Derivatives Varenicline Verteporfin Vitamin K Antagonists
Pregnancy and Lactation	**Pregnancy Risk Factor C** Ofloxacin is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, the manufacturer recommends a decision be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of treatment to the mother.
Administration	**Oral:** Administer with or without food. Do not take within 2 hours of sucralfate, didanosine, iron, zinc, or antacids containing magnesium, calcium, or aluminum. drink plenty of fluids to maintain proper hydration and urine output **Ophthalmic** For ophthalmic use only; not for injection. Avoid touching tip of applicator to eye, fingers, or other surfaces. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Altered cardiac conduction: Fluoroquinolones may prolong QTc interval; avoid use in patients with a history of QTc prolongation, uncorrected hypokalemia, hypomagnesemia, or concurrent administration of other medications known to prolong the QT interval (including Class Ia and Class III antiarrhythmics, cisapride, erythromycin, antipsychotics, and tricyclic antidepressants). • Aortic aneurysm and dissection: Fluoroquinolones have been associated with aortic aneurysm ruptures or dissection within 2 months following use, particularly in elderly patients. Fluoroquinolones should not be used in patients with a known history of aortic aneurysm or those at increased risk, including patients with peripheral atherosclerotic vascular diseases, hypertension, genetic disorders involving blood vessel changes (eg, Marfan syndrome, Ehlers-Danlos syndrome), and elderly patients, unless no other treatment options are available. Longer treatment duration (eg, >14 days) may increase risk. • CNS effects: Fluoroquinolones have been associated with an increased risk of CNS effects including seizures, increased intracranial pressure (including pseudotumor cerebri), dizziness, lightheadedness, and tremors. Use with caution in patients with known or suspected CNS disorders (eg, severe cerebral arteriosclerosis, epilepsy) or other risk factors that may predispose to seizures or lower the seizure threshold. • Glucose regulation: Fluoroquinolones have been associated with disturbances in glucose regulation, including hyperglycemia and hypoglycemia. These events have occurred most often in patients receiving concomitant oral hypoglycemic agents or insulin. Severe cases of hypoglycemia, including coma and death, have been reported. Diabetic patients should be monitored closely for signs/symptoms of disordered glucose regulation. Discontinue if a hypoglycemic reaction occurs and immediately initiate appropriate therapy. • Hypersensitivity reactions: Severe, sometimes fatal, hypersensitivity reactions, including

anaphylaxis, have occurred with quinolone therapy. The spectrum of these reactions can vary widely; reactions may present as typical allergic symptoms (eg, itching, urticaria, rash, edema) after a single dose, or may manifest as severe idiosyncratic dermatologic (eg, Stevens-Johnson, toxic epidermal necrolysis), vascular (eg, vasculitis), pulmonary (eg, pneumonitis), renal (eg, nephritis), hepatic (eg, hepatic failure or necrosis), and/or hematologic (eg, anemia, cytopenias) events, usually after multiple doses. Prompt discontinuation of drug should occur if skin rash or other symptoms arise.

• Peripheral neuropathy: Peripheral neuropathy has been reported (rare); may occur soon after initiation of therapy and may be irreversible; discontinue if symptoms of sensory or sensorimotor neuropathy occur.

• Phototoxicity: Avoid excessive sunlight and take precautions to limit exposure (eg, loose fitting clothing, sunscreen); may cause moderate to severe phototoxicity reactions. Discontinue use if photosensitivity occurs.

• Psychiatric reactions: Fluoroquinolones have been associated with an increased risk of psychiatric reactions, including toxic psychosis or hallucinations; may also cause nervousness, agitation, confusion, disorientation, delirium, attention disturbances, and memory impairment. Use with caution in patients with a history of or risk factor for depression; discontinue if reaction occurs and institute appropriate therapy.

• Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment.

• Tendon inflammation/rupture: [US Boxed Warning]: There have been reports of tendon inflammation and/or rupture with quinolone antibiotics; risk may be increased with concurrent corticosteroids, organ transplant recipients, and in patients >60 years of age. Discontinue at first sign of tendon inflammation or pain. May occur even after discontinuation of therapy.

Disease-related concerns:

• Hepatic impairment: Use with caution in patients with hepatic impairment.

• Myasthenia gravis: [US Boxed Warning]: May exacerbate muscle weakness related to myasthenia gravis. Cases of severe exacerbations, including the need for ventilatory support and deaths have been reported; avoid use in patients with myasthenia gravis.

• Renal impairment: Use with caution in patients with renal impairment; dosage adjustment required. May increase risk of tendon rupture.

• Rheumatoid arthritis: Use with caution in patients with rheumatoid arthritis; may increase risk of tendon rupture.

• Seizures: Use with caution in individuals at risk of seizures (CNS disorders or concurrent therapy with medications which may lower seizure threshold). Potential for seizures, although very rare, may be increased with concomitant NSAID therapy.

• Syphilis: Since ofloxacin is ineffective in the treatment of syphilis and may mask symptoms, all patients should be tested for syphilis at the time of gonorrheal diagnosis and 3 months later. **Note:** As of April 2007, the CDC no longer recommends the use of fluoroquinolones for the treatment of uncomplicated gonococcal disease.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special populations:

• Elderly: Adverse effects (eg, tendon rupture, QT changes) may be increased in the elderly.

• G6PD deficiency: Hemolytic reactions may (rarely) occur with quinolone use in patients with latent or actual G6PD deficiency

	• Contact lens wearers: Contact lenses should not be worn during treatment of ophthalmic infections.
Storage	Oral: Store at 20°C to 25°C Ophthalmic: Store 15°C to 25°C Refer to manufacturer PIL if there are specific considerations.

Topical

1. Benzyl Benzoate

Generic Name	Benzyl Benzoate
Dosage form/strengths	Topical cream: 20 gm/100ml Topical Lotion: 25 ml/100ml
Route of administration	Topical
Pharmacologic category	Antiparasitic Agent, Topical; Pediculocide; Scabicidal Agent ATC: P03AX01
Indications	**Pediculosis (lice):** Treatment of pediculosis (lice) **Scabies:** Treatment of scabies.
Dosage Regimen	**Dosing: Adult, Pediatric:** **Note:** Dosing recommendations may vary per country (consult product labeling). **Pediculosis (lice):** Topical: After washing hair, apply sufficient amount to moisten hair. After 3 to 5 minutes, rinse hair thoroughly and comb with a fine-tooth comb to remove nits. May repeat application if necessary. **Note:** Refer to dilution instructions for use in children **Scabies:** Topical: After bathing, apply to moist skin and allow to dry, then reapply. Apply at night; bathe and remove the drug the next morning. May repeat application in 24 hours if necessary. **Note:** Refer to dilution instructions for use in children
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to benzyl benzoate or any component of the formulation; application to skin areas that may have greater absorption (eg, wounds, burns)
Adverse Drug Reactions	Central nervous system: Burning sensation Dermatologic: Contact dermatitis, erythematous rash, skin rash Local: Application site irritation Hypersensitivity: Hypersensitivity reaction Ophthalmic: Eye irritation Respiratory: Nasal mucosa irritation
Monitoring Parameters	No monitoring data needed.
Drug Interactions	There are no known significant interactions.
Pregnancy	**Category C.** Topical medications have little systemic absorption. When treatment is needed, benzyl benzoate may be used in pregnant females
Administration	**Administration: Topical** For topical use only. Do not swallow. Avoid contact with eyes, face, mucous membranes, or broken skin. Shake well prior to application. Apply to a small test area prior to full application

	to assess hypersensitivity reaction. Dilution is recommended in elderly patients. Wash all bedding and clothing in between and after applications. Pediculosis (lice) treatment: Apply only enough solution to moisten the affected area. A towel may be wrapped around the hair when treating head lice. Use a fine-tooth comb to remove dead lice and nits. Scabies treatment: Apply preferably at night after evening bath to moist skin; application should include intertriginous areas of the body (armpits, abdomen, and buttocks). Allow to dry, then reapply. Dress or lie down without wiping. Take a bath the following morning to remove. **Preparation for Administration: Adult** Dilution is not required for adults. Dilution is recommended prior to application in elderly patients. Mix 1 part solution with 3 parts water. **Preparation for Administration: Pediatric** Dilution is recommended prior to application in infants and children. Dilution instructions may vary; consult specific product labeling. Infants: Mix 1 part solution with 3 parts water. Children: Mix 1 part solution with 1 to 3 parts water Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity: Use with caution in patients with a history of allergic reaction to other topical products. ***Other warnings/precautions:*** • Appropriate use: For topical use only; do not ingest solution. Do not apply to face, eyes, lips, or mucous membranes. Application is contraindicated on skin areas that may have greater absorption (eg, wounds, burns).
Storage	Store at room temperature; protect from light and moisture. Refer to manufacturer PIL if there are specific considerations.

2. Clotrimazole

Generic Name	Clotrimazole
Dosage form/strengths	Aerosol 1% Solution 1% Topical powder 1% Topical cream 1% Topical spray 10mg/ml Vaginal tablets 100mg, 200mg, 500mg Vaginal cream 2%, 10gm/100gm
Route of administration	*Topical, inhalation, intravaginal*
Pharmacologic category	Antifungal Agent, Imidazole Derivative ATC (Topical): D01AC01 ATC (Vaginal): G01AF02
Indications	**Topical cream and solution:** Topical treatment of candidiasis due to *Candida albicans* and tinea versicolor caused by *Malassezia furfur* **Topical ointment:** Topical treatment of tinea cruris, *C. albicans*, tinea corporis, and tinea pedis **Vaginal cream:** Treatment of vaginal yeast infections and relief of associated external vulvar itching and irritation **Vaginal tablet:** Treatment of vaginal candidiasis
Dosage Regimen	**Dosing: Adult** **Cutaneous candidiasis:** Topical: Cream, solution: Apply to affected area twice daily; if no improvement occurs after 4 weeks of therapy, re-evaluate diagnosis. **vulvovaginal candidiasis:** Intravaginal: **Note:** A longer duration may be necessary in patients with complicated infection (ie, recurrent or severe infection, infection with non-*albicans Candida*, or infection in an immunocompromised host) (CDC). Cream (1%): Insert 1 applicatorful of 1% vaginal cream daily (at bedtime) for 7 consecutive days. May also apply externally twice daily for 7 days as needed for itching and irritation. Cream 2%: Intravaginal**:** Insert 1 applicatorful (~5 g) once daily (at bedtime) for 3 days. May also apply externally twice daily for 7 days, as needed, for itching and irritation. Vaginal Tablet: 500 mg tablet: Insert 1 vaginal tablet as a single dose (preferably at bedtime) 200 mg tablet: Insert 1 vaginal tablet once daily for 3 consecutive days (preferably at bedtime) **Note:** When tablets are used in conjunction with an external cream, apply cream over the irritated area 1 to 2 times/day as needed for up to 7 consecutive days **Tinea infections:** *Tinea corporis/tinea cruris:* **Topical:** Cream 1%, solution 1%: Apply to affected and surrounding area(s) twice daily until clinical resolution, typically 1 to 4 weeks. *Tinea versicolor:* **Topical:** Cream 1%, solution 1%: Apply to affected area(s) and immediate surrounding skin twice daily for 2 weeks. **Dosing: Pediatric** **Cutaneous candidiasis:** Topical ointment: Children ≥2 years and Adolescents: Topical: Apply

	twice daily (morning and night) for 2 weeks. **Tinea corporis, tinea cruris, and tinea pedis**: Children ≥2 years and Adolescents: Topical: Apply twice daily (morning and night). Duration: 2 weeks for tinea cruris; 4 weeks for tinea corporis and tinea pedis **Vulvovaginal candidiasis:** Children ≥12 years and Adolescents: Intravaginal: Cream (1%): Insert 1 applicatorful of 1% vaginal cream daily (preferably at bedtime) for 7 consecutive days; some patients may require 14 days (CDC). May also apply externally twice daily for 7 days as needed for itching and irritation. Cream (2%): Insert 1 applicatorful of 2% vaginal cream daily (preferably at bedtime) for 3 consecutive days. May also apply externally twice daily for 7 days as needed for itching and irritation.
Dosage adjustment	**Dosing: Renal Impairment: Adult** There are no dosage adjustments needed. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to clotrimazole or any component of the formulation. Documentation of allergenic cross-reactivity for imidazole antifungals is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty.
Adverse Drug Reactions	**Topical, Vaginal**: 1% to 10%: Genitourinary: Vulvovaginal burning
Monitoring Parameters	Assess for effectiveness of treatment. Assess for severe skin irritation.
Drug Interactions	**Progesterone**: Antifungal Agents (Vaginal) may diminish the therapeutic effect of Progesterone. *Risk X: Avoid combination* **Sirolimus**: Clotrimazole (Topical) may increase the serum concentration of Sirolimus. *Risk C: Monitor therapy* **Tacrolimus** (Systemic): Clotrimazole (Topical) may increase the serum concentration of Tacrolimus (Systemic). *Risk C: Monitor therapy*
Pregnancy and Lactation	**Pregnancy category B** It is not known if clotrimazole is present in breast milk following oral administration. Because clotrimazole has poor oral bioavailability, it is unlikely to adversely affect the breastfed infant.
Administration	**Administration: Topical** For external use only. Avoid contact with eyes and application to severely cracked or irritated areas. Cleanse and thoroughly dry area prior to application. Apply a thin layer to affected area. For treatment of athlete's foot, pay special attention to spaces between the toes; wear well-fitting, ventilated shoes and change shoes and socks at least once a day. **Administration: Intravaginal** For vaginal use only. Cream may also be applied externally for itching and irritation of surrounding areas. Do not use tampons, douches, spermicides, or other vaginal products or have vaginal intercourse during treatment. Vaginal tablet [Canadian product]: Should be inserted deep into the vagina to ensure tablet dissolves completely. If tablet does not dissolve completely within one night, consider use of a

	vaginal cream. **Administration: Pediatric** Topical: For external use only. Apply sparingly and rub gently into the cleansed, affected area; do not apply to the eye. For tinea pedis, also apply to spaces between the toes. Children under 12 years should be supervised during use. Vaginal: Wash hands before using. Insert full applicator into vagina gently and expel cream into vagina. Wash applicator with soap and water following use. Remain lying down for 30 minutes following administration. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Local irritation: If irritation/sensitivity develops, discontinue therapy and institute appropriate alternative therapy. ***Other warnings/precautions:*** • Appropriate use: Topical: For external use only; avoid contact with the eyes. Not effective for treatment of scalp or nails. When used for self-medication, discontinue use and contact a healthcare provider if there is no improvement in 2 weeks (jock itch) or 4 weeks (athlete's foot, ringworm). • Self-medication: Vaginal: When used for self-medication (OTC), consult a health care provider before use if experiencing vaginal itching and discomfort for the first time, frequent vaginal yeast infections (eg, monthly, 3 in 6 months), or exposure to HIV. A mild increase in vaginal itching, burning, or irritation may occur with use; a health care provider should be consulted before switching to another agent if patient does not experience complete relief. Discontinue use and contact a health care provider if symptoms do not improve in 3 days or last more than 7 days, or if symptoms of a more serious condition occur (eg, abdominal pain, back/shoulder pain, fever, chills, nausea, vomiting, foul-smelling vaginal discharge). For vaginal use only; do not use tampons, douches, spermicides, or other vaginal products or have vaginal intercourse during treatment.
Storage	Recommendations vary. Refer to manufacturer PIL if there are specific considerations.

3. Econazole

Generic Name	Econazole
Dosage form/strengths	Topical Cream, Lotion or spray: 1 % Vaginal Pessary/ovules: 150 mg Vaginal Cream: 1 gm/100g
Route of administration	Topical, vaginal
Pharmacologic category	Antifungal Agent, Imidazole Derivative ATC (Topical): D01AC03 ATC (Gynecological): G01AF05
Indications	**Fungal infection:** Cream: Treatment of tinea pedis, tinea cruris, and tinea corporis and in the treatment of cutaneous candidiasis, and in treatment of tinea versicolor. Vaginal cream: Treatment of mycotic vulvovaginitis and mycotic balanitis Vaginal suppository: Treatment of vaginitis due to *Candida albicans* and other yeasts
Dosage Regimen	**Dosing: Adult** **Cutaneous candidiasis:** Topical: Cream: Apply sufficient quantity twice daily (morning and evening) for 2 weeks **Tinea versicolor:** Topical: Cream: Apply sufficient amount to cover affected areas once daily for 2 weeks **Tinea cruris, tinea corporis: Topical:** Cream 1%: Apply to affected and surrounding area(s) once daily until clinical resolution, typically 1 to 3 weeks **Tinea and fungal skin infections:** Topical: Apply once daily in the evening for 3 consecutive days. May repeat 3-day treatment course after 2 weeks if infection not resolved. For prevention of relapse, may repeat 3-day treatment course at 1 month and 3 months after initial treatment. **Vulvovaginitis: Vaginal:** Cream: Insert 1 applicator full (5 g) and apply topically to affected areas once daily in the evening for at least 14 days. Suppository: Insert 1 suppository (150 mg) once daily in the evening for 3 days. **Dosing: Pediatric** **Candidiasis cutaneous (including diaper dermatitis):** Limited data available: Infants, Children, and Adolescents: Topical: Cream: Apply sufficient amount to cover affected area twice daily **Tinea corporis, tinea cruris, and tinea versicolor (smaller lesions):** Children and Adolescents: Limited data available: Topical: Cream: Apply sufficient amount to cover affected area once daily for 4 weeks **Tinea pedis:** Cream: Children and Adolescents: Limited data available: Topical: Apply sufficient amount to cover affected area once daily for 4 weeks **Vulvovaginitis:** Adolescents ≥16 years: Vaginal: Cream or suppository: Refer to adult dosing.
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.

Contra-indications	Cream, vaginal cream/suppository: Hypersensitivity to econazole, other imidazoles, or any component of the formulation
Adverse Drug Reactions	**1% to 10%:** Dermatologic: Burning sensation of skin, erythema, pruritus, stinging of the skin
Monitoring Parameters	Reassess diagnosis if no clinical improvement after completion of treatment course.
Drug Interactions	Vitamin K Antagonists (eg, warfarin): Econazole may increase the serum concentration of Vitamin K Antagonists. *Risk C: Monitor therapy*
Pregnancy and Lactation	**Pregnancy Category C.** avoid use in the first trimester and apply sparingly during the second and third trimesters if needed for topical fungal infections It is not known if econazole is present in breast milk. Consider benefits and risks.
Administration	**Administration: Topical** For external use only. Not for oral, ophthalmic, or vaginal use. Avoid contact with the eyes. Cream: For treatment of balanitis, apply to penis, including under the foreskin if applicable. Avoid contact with latex condoms and diaphragms. **Administration: Intravaginal** Administer in the evening. Wash hands prior to administration. Cream: Insert into vagina using a vaginal applicator (avoid use of applicator in pregnant women). Apply additional thin layer of cream to the vulva. Suppository: Insert high into the vagina Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** • Irritation: Discontinue if sensitivity or irritation occurs. ***Other warnings/precautions:*** • Appropriate use: For topical use only; avoid contact with eyes, mouth, nose, or other mucous membranes
Storage	Store below 30°C. Refer to manufacturer PIL if there are specific considerations.

4. Erythromycin and Zinc Acetate

Generic Name	Erythromycin and Zinc Acetate
Dosage form/strengths	Paint: Erythromycin - Zinc Acetate: 4 gm/100g-1.2 gm/100g Topical Lotion: 4 gm/100ml-1.2 gm/100ml
Route of administration	*Topical*
Pharmacologic category	Acne Products; Antibiotic, Macrolide ATC: D10AF52
Indications	**Acne:** Treatment of acne vulgaris
Dosage Regimen	**Dosing: Adult** **Acne:** Topical: Apply to affected area twice daily; usual treatment duration is 10 - 12 weeks. **Dosing: Pediatric** **Acne:** Children ≥12 years and Adolescents: Topical: Apply to affected area twice daily; usual treatment duration is 10 to 12 weeks.
Dosage adjustment	**Dosing: Renal Impairment: Adult** There are no dosage adjustments available **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments available.
Contra-indications	Hypersensitivity to erythromycin, other macrolide antibiotics, zinc acetate, or any component of the formulation
Adverse Drug Reactions	Frequency not defined: Dermatologic: Acute generalized exanthematous pustulosis
Monitoring Parameters	No monitoring data needed.
Drug Interactions	***Risk X: Avoid combination*** Clindamycin (Topical)
Pregnancy and Latcation	**Pregnancy category** B. There are no data on the excretion of Zinc acetate topical into human milk. Elemental zinc is known to be excreted into human milk and may lead to copper deficiency in the nursing infant.
Administration	**Administration: Topical** Prior to treatment, thoroughly wash affected area. Unscrew the protective cap, hold the bottle upside down, and place the pad against the affected area. Spread solution over affected area and surrounding skin. The amount of solution dispensed may be increased by pressing the pad of the bottle more firmly against the skin. Blot any excess solution off with tissues. Make-up may be applied after medication has dried. Avoid contact with the eyes, nose, mouth, and other mucous membranes. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects:*** Allergic reactions: Allergic reactions, including acute generalized exanthematous pustulosis (AGEP), may occur. Discontinue therapy if an allergic reaction occurs. ***Other warnings/precautions:*** Appropriate use: For topical use only; not for ophthalmic use. Avoid contact with eyes, nose, mouth, mucous membranes, or broken skin. Consider alternate therapy in patients with poor tolerance to macrolide or lincosamide antibiotics.
Storage	Store at ≤25°C. Refer to manufacturer PIL if there are specific considerations.

5. Isoconazole

Generic Name	Isoconazole
Dosage form/strengths	Vaginal ovules 300, 600mg Topical cream 1%
Route of administration	Topical, intravaginal
Pharmacologic category	Imidazole antifungal ATC (Topical): D01AC05 ATC (Vaginal): G01AF07
Indications	**Vaginal: Fungal infections of the vagina**: Treatment of fungal vaginal infections, including mixed infections with gram-positive bacteria **Topical: Superficial fungal infections:** Treatment of superficial fungal infections caused by dermatophytes, yeasts and yeast-like fungi, and molds, including infections on or near the hands, the interdigital spaces of the feet, and in the inguinal and genital regions
Dosage Regimen	**Vaginal** infections it is usually given as a pessary (600 mg) once as a single dose. **Topical:** Superficial fungal infections**:** Apply to the affected areas once or twice daily for 1-3 weeks
Dosage adjustment	No adjustments needed
Contra-indications	Tuberculous and syphilitic infections in the area to be treated, viral infections (herpes simplex, vaccinia, varicella and smallpox). Pregnancy. Not recommended for use in infants and children
Adverse Drug Reactions	1-10%: Local reactions including burning or itching may occur after application of isoconazole. Intravaginal preparations of azole antifungals may damage latex contraceptives and additional contraceptive measures are therefore necessary during local application.
Monitoring Parameters	Not data needed
Drug Interactions	Warfarin: concomitant use may increase use of plasma levels of warfarin.
Pregnancy and Lactation	Isoconazole is poorly absorbed following application to mucous membranes or intact skin. Use during pregnancy and breastfeeding would not be expected to result in significant exposure or harm. Application to the nipples should be avoided in women who are nursing.
Administration	Topical for external use only, vaginal: Avoid administration during menstruation. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Not to be used on skin creases due to presence of potent corticosteroid. • Prolonged use may lead to skin thinning, loss of elasticity, dilatation of superficial blood vessels, telangiectasiae and ecchymoses especially when used on face or with occlusive dressings. • Excessive use on damaged skin may lead to substantial systemic absorption resulting in depression of the hypothalmus-pituitary adrenal axis especially in children. • Caution when used near the eye.
Storage	Store below 30°C. Refer to manufacturer PIL if there are specific considerations.

6. Miconazole

Generic Name	Miconazole
Dosage form/strengths	Oral gel 2% Vaginal ovules 400mg, 1200 Vaginal Cream 2% Vaginal suppository 200mg, 400mg Topical Cream, gel, powder 2% Powder or liquid spray Tincture 2%
Route of administration	Topical , Intravaginal, oral
Pharmacologic category	Antifungal Agent, Imidazole Derivative; ATC (Topical): D01AC02 ATC (Gynecological): G01AF04
Indications	Treatment of vulvovaginal candidiasis and a variety of skin and mucous membrane fungal infections Treatment of oropharyngeal candidiasis
Dosage Regimen	**Adult Dosing:** ***Tinea corporis/tinea cruris:*** Topical: Aerosol powder (tinea corporis only), cream, ointment, powder, solution: Apply to affected and surrounding area(s) twice daily until clinical resolution, typically 1 to 4 weeks **Vulvovaginal candidiasis:** Intravaginal: **Note:** A longer duration may be necessary in patients with complicated infection (ie, recurrent or severe infection, infection with non-*albicans Candida*, infection in an immunocompromised host) *Cream, 2%:* Insert 1 applicatorful at bedtime for 7 days Suppository 200 mg: **Intravaginal:** Insert 1 suppository once daily (at bedtime) for 3 days **Pediatric dosing:** **Tinea cruris:** Children ≥2 years and Adolescents: Topical cream, spray, powder, aerosol powder or solution: Topical: Apply twice daily for 2-4 weeks
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to miconazole or any component of the formulation
Adverse Drug Reactions	**Topical:** Dermatologic: Allergic contact dermatitis, burning sensation of skin, maceration of skin **Vaginal:** Gastrointestinal: Abdominal cramps Genitourinary: Vulvovaginal burning, vulvovaginal irritation, vulvovaginal pruritus **Oral**: >10%: Local: Application site reaction (10% to 12%; including glossalgia, local discomfort, local pain, local pruritus, localized burning, localized edema, oral mucosa ulcer, toothache)
Monitoring Parameters	Caution patients with diabetes to test serum glucose regularly; may inhibit the metabolism of oral sulfonylureas. Teach patient bleeding precautions.
Drug Interactions	***Risk X: Avoid combination*** Progesterone ***Risk D: Consider therapy modification***

	Vitamin K Antagonists
Pregnancy and Lactation	**pregnancy risk category C** Following vaginal administration, small amounts are absorbed systemically. Based on available data, vaginal use of miconazole is not associated with an increased risk of adverse pregnancy outcomes. Avoid prolonged use while breastfeeding. use of the gel is not recommended. There is minimal systemic absorption following buccal application. Consider benefits and risk.
Administration	Oral Gel: Apply after meals. Gel should not be swallowed immediately but allowed to linger in the mouth for as long as possible. Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity reactions: Hypersensitivity reactions (including anaphylactic reactions) have been reported. Monitor patients with a history of azole hypersensitivity. • Skin reactions: Gel: Serious dermatologic reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TENs) have been reported with oral gel products. Discontinue use at the first appearance of skin rash. ***Disease-related concerns:*** • Hepatic impairment: Although systemic absorption is typically minimal, use with caution in patients with hepatic impairment. The gel formulation is contraindicated with liver dysfunction. ***Special populations:*** • Pediatric: Gel: Use with caution in pediatric patients to ensure the gel does not obstruct the throat. Do not apply to the back of the throat. Divide the dose into smaller portions and observe the patient for possible choking. Consider the swallowing function of all pediatric patients prior to use, especially in infants aged 4 to 6 months. Increase lower age limit to 5 to 6 months in preterm infants or infants exhibiting slow neuromuscular development. Do not apply gel to the nipple of a breastfeeding woman for administration to an infant.
Storage	Store at room temperature. Refer to manufacturer PIL if there are specific considerations

7. Mupirocin

Generic Name	Mupirocin
Dosage form/strengths	Topical Cream: 20 mg/gm, 2 gm/100g Topical Ointment: 20 mg/gm 2 gm/100g
Route of administration	Topical
Pharmacologic category	Antibiotic, Topical ATC: D06AX09
Indications	**Impetigo:** Treatment of impetigo due to *Staphylococcus aureus* and *Streptococcus pyogenes* (topical ointment). **Secondary skin infection:** Treatment of secondarily infected traumatic skin lesions (up to 10 cm in length or 100 cm^2 in area) due to susceptible isolates of *S. aureus* and *S. pyogenes* (topical cream).
Dosage Regimen	**Dosing: Adult** **Superficial skin infection:** ***Impetigo (limited number of lesions):*** Topical: Ointment: Apply to affected area 2 to 3 times daily for 5 days. ***Secondary skin infection (localized infection of wounds, burns, dermatitis, or other lesions):*** Topical: Cream, Ointment: Apply to affected area 2 to 3 times daily, typically for 7 to 14 days depending on severity and clinical response; if no response after 3 to 5 days, re-evaluate treatment. **Dosing: Pediatric** **MRSA or impetigo, treatment; minor skin infection or a limited number of infected lesions:** Infants, Children, and Adolescents: Topical: Cream, Ointment: Apply small amount 3 times daily for 5 to 10 days; patients not showing clinical response after 5 days should be reevaluated
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to mupirocin or any component of the formulation
Adverse Drug Reactions	**1% to 10%:** Central nervous system: Headache, localized burning, stinging sensation Dermatologic: Pruritus, skin rash Gastrointestinal: Nausea, dysgeusia Local: Local pain Respiratory: Rhinitis, respiratory congestion, pharyngitis, cough
Monitoring Parameters	No monitoring necessary.
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	**Pregnancy Category** B It is not known if mupirocin is present in breast milk. Systemic absorption following topical application is minimal and significant exposure to a breastfeeding infant is not expected.
Administration	**Administration: Topical** Topical cream, ointment: For external use only; not for use in eyes or on mucous

	membranes (components may be absorbed systemically and cause drying and irritation). Apply small amount to affected area using gauze pad or cotton swab; area may be covered with a gauze dressing if desired. In case of accidental contact in or near eyes, rinse well with water. Wash hands before and after application. Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Concerns related to adverse effects:*** • Hypersensitivity: May be associated with systemic allergic reactions, including anaphylaxis, urticaria, angioedema, and generalized rash. If a systemic reaction occurs, discontinue use. • Irritation: If sensitization or local irritation occurs, discontinue use. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. ***Disease-related concerns:*** • Renal impairment: Topical ointment and intranasal: Use with caution in patients with renal impairment (has not been studied). ***Dosage form specific issues:*** • Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling. • Polyethylene glycol: Potentially toxic amounts of polyethylene glycol contained in some topical products may be absorbed percutaneously in patients with extensive burns or open wounds. Do not use polyethylene glycol-based ointments in conditions where absorption of large quantities of polyethylene glycol is possible, especially in the presence of moderate or severe renal impairment. ***Other warnings/precautions:*** • Appropriate use: For external use only. Avoid contact with eyes; in case of accidental contact in or near eyes, rinse well with water. - Topical cream and ointment: Not for ophthalmic or nasal use or use on mucosal surfaces. May cover treated areas with gauze dressing. • Limitations of use: - Topical ointment: Should not be used with intravenous (IV) cannulae or at central IV sites because of the potential to promote fungal infections and antimicrobial resistance.
Storage	Topical cream, ointment: Store at or below 25°C. Do not freeze. Refer to manufacturer PIL if there are specific considerations

8. Neomycin, Polymyxin B, and Dexamethasone

Generic Name	Neomycin, Polymyxin B, and Dexamethasone
Dosage form/strengths	**Ophthalmic Suspension:** Dexamethasone 1 mg/ml; Neomycin Sulphate 3.5 mg/ml; Polymyxin B Sulphate 6000 I.U./ml **Eye ointment**: Dexamethasone 1 mg ; Neomycin Sulphate 5mg ; Polymyxin B Sulphate 6000 I.U.
Route of administration	*ophthalmic*
Pharmacologic category	Antibiotic/Corticosteroid, Ophthalmic ATC: A07AA51
Indications	**Inflammatory ocular conditions:** Management of corticosteroid-responsive inflammatory ocular conditions where bacterial infection or a risk of bacterial infection exists
Dosage Regimen	**Dosing: Adult** **Inflammatory ocular conditions:** Ophthalmic: Suspension: Instill 1 to 2 drops into the conjunctival sac of the affected eye(s) 4 to 6 times daily. In severe disease, drops may be used hourly; frequency should decrease as signs and symptoms improve. Ointment: Place 1.25 cm in the conjunctival sac of the affected eye(s) 3 to 4 times daily **Note:** If signs and symptoms do not improve after 2 days of treatment, the patient should be reevaluated. **Dosing: Pediatric** **Inflammatory ocular conditions:** Ophthalmic: Suspension: Children ≥2 years and Adolescents: Instill 1 to 2 drops into the conjunctival sac of the affected eye(s) 4 to 6 times daily; in severe disease, drops may be used hourly and tapered to discontinuation
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to neomycin, polymyxin B, dexamethasone, or any component of the formulation; viral disease of the cornea and conjunctiva (including epithelial herpes simplex keratitis [dendritic keratitis], vaccinia, varicella); mycobacterial ophthalmic infection; fungal diseases of ocular structures *Canadian labeling:* Additional contraindications (not in US labeling): Untreated parasitic ophthalmic infection
Adverse Drug Reactions	**Frequency not defined:** **Hypersensitivity**: Hypersensitivity reaction **Infection**: Secondary infection **Ophthalmic**: Glaucoma, increased intraocular pressure, optic nerve damage (infrequent), subcapsular posterior cataract **Miscellaneous**: Wound healing impairment
Monitoring Parameters	Monitor intraocular pressure with use >10 days and in patients with glaucoma; reevaluate if signs and symptoms persist beyond 2 days.
Drug Interactions	**CYP3A4 Inhibitors (Strong):** May increase the serum concentration of Dexamethasone (Ophthalmic). ***Risk C: Monitor therapy*** **Nonsteroidal Anti-Inflammatory Agents (Ophthalmic):** May enhance the adverse/toxic effect of

	Corticosteroids (Ophthalmic). Healing of ophthalmic tissue during concomitant administration of ophthalmic products may be delayed. ***Risk C: Monitor therapy***
Pregnancy and Lactation	Adverse events have been observed with topical corticosteroids in animal reproduction studies. If ophthalmic agents are needed during pregnancy, the minimum effective dose should be used in combination with punctal occlusion to decrease potential exposure to the fetus. Refer to individual agents. It is not known if systemic absorption following topical administration results in detectable quantities in human milk. caution should be exercised when administering neomycin/polymyxin B/dexamethasone to breastfeeding women. Refer to individual agents.
Administration	**Administration: Ophthalmic** **Note:** Contact lenses should not be worn during therapy. **Ointment**: Apply into pocket between eyeball and lower lid; patient should look downward before closing eye. To avoid contamination, do not touch tip of tube to eye or any other surface. **Suspension**: Shake well before using. Tilt head back, instill suspension into the conjunctival sac, and close eye(s). Apply light finger pressure on lacrimal sac for 1 minute following instillation. To avoid contamination, do not touch dropper to eye or any other surface. Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Concerns related to adverse effects:*** • Immunosuppression: Prolonged use of corticosteroids (including ophthalmic preparations) may increase the incidence of secondary ocular infections (including fungal infections). Acute purulent ocular infections may be masked or exacerbated with use. Fungal infection should be suspected in any patient with persistent corneal ulceration who has received corticosteroids. • Neomycin sensitization: Neomycin may cause cutaneous sensitization. Discontinue use if hypersensitivity occurs. Cross-sensitivity to other topical or systemic aminoglycosides may occur. • Ocular effects: Prolonged use of corticosteroids may result in glaucoma; damage to the optic nerve, defects in visual acuity and fields of vision, corneal and scleral thinning (leading to perforation), and posterior subcapsular cataract formation may occur. Use following cataract surgery may delay healing or increase the incidence of bleb formation. ***Disease-related concerns:*** • Glaucoma: Use with caution in patients with glaucoma. • Ocular herpes simplex: Use with extreme caution in patients with a history of ocular herpes simplex; frequent slit lamp microscopy is recommended. ***Dosage-forms specific issues:*** • Ophthalmic suspension: May contain benzalkonium chloride, which may be absorbed by soft contact lenses; contact lenses should not be worn during treatment of ophthalmologic infections. ***Other warnings/precautions:*** • Appropriate use: Never directly introduce (eg, inject) into the anterior chamber. A maximum of 8 g of ointment or 20 mL of suspension should be prescribed initially; reevaluate patients (eg, intraocular pressure and exams using magnification and fluorescein staining, where appropriate) prior to additional refills. Use >10 days should include routine monitoring of intraocular pressure. Inadvertent contamination of multiple-dose ophthalmic bottle dropper and tips has caused bacterial keratitis.
Storage	Store at a temperature ≤ 25°C Refer to manufacturer PIL if there are specific considerations

9. Natamycin

Generic Name	Natamycin
Dosage form/strengths	Sterile ophthalmic suspension: 50mg/ml
Route of administration	Ophthalmic
Pharmacologic category	Antifungal Agent, Ophthalmic ATC: S01AA10
Indications	**Ocular fungal infections:** Treatment of fungal blepharitis, conjunctivitis, and keratitis caused by susceptible organisms, including *Fusarium solani* keratitis.
Dosage Regimen	**Ophthalmic Dosing: Adult** **Fungal blepharitis or conjunctivitis:** Instill 1 drop in conjunctival sac 4-6 times daily. **Fungal keratitis:** Instill 1 drop in conjunctival sac every 1-2 hours, after 3-4 days reduce to one drop 6 - 8 times daily; usual course is 2 - 3 weeks or until resolution of active fungal keratitis.
Dosage adjustment	**Dosing: Altered Kidney or Hepatic Functions:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to natamycin or any component of the formulation
Adverse Drug Reactions	Allergic reaction, chest pain, corneal opacity, dyspnea, eye discomfort, edema, hyperemia, irritation and/or pain, foreign body sensation, parasthesia, tearing, vision changes
Monitoring Parameters	No monitoring data needed.
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	**pregnancy category C**. Animal reproduction studies have not been conducted. It is not known if natamycin is excreted in breast milk. Caution should be exercised when administering natamycin to nursing women.
Administration	**Administration: Adult** Ophthalmic: For topical ophthalmic use only. Shake well before using. Wash hands before and after use. Do not touch tip of applicator to eye or other surfaces. Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Disease-related concerns:*** • Epithelial ulceration: Suspension may adhere to epithelial ulcers; retention of the suspension in the fornices occurs regularly. ***Special populations:*** • Contact lens wearers: Contains benzalkonium chloride, which may be absorbed by soft contact lenses; remove lenses prior to administration. Contact lenses should not be worn during treatment of ophthalmologic infections (fungal blepharitis, conjunctivitis, and keratitis). ***Other warnings/precautions:*** • Appropriate use: For topical ophthalmic use only. Failure to improve (keratitis) after 7 to 10 days of administration suggests infection caused by a microorganism not susceptible to natamycin; efficacy as a single agent in fungal endophthalmitis has not been established.
Storage	Store at 2°C to 24°C; do not freeze. Protect from excessive heat and light. Refer to manufacturer PIL if there are specific considerations

10. Terbinafine

Generic Name	Terbinafine
Dosage form/strengths	Topical gel, cream or solution: 10 mg/gm Topical Spray: 1 %, 0.888 gm/100g Topical Aerosol Powder: 1% Tablets: 250mg
Route of administration	*Topical, Oral*
Pharmacologic category	Antifungal Agent ATC (Topical): D01AE15 ATC (systemic): D01BA02
Indications	**Topical: Dermatologic fungal infections:** Treatment of tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm). **Systemic use: Onychomycosis:** Treatment of onychomycosis of the toenail or fingernail caused by dermatophytes (tinea unguium).
Dosage Regimen	***Dosing: Adult*** **Onychomycosis:** **Oral:** 250 mg once daily for 6 weeks (fingernail) or 12 weeks (toenail). **Tinea pedis:** Topical: Cream 1%, gel 1%: Apply to affected and surrounding area(s) once or twice daily (cream) or once daily (gel or spray) until 1 week after clinical resolution, typically for 2 weeks total **Tinea corporis, Tinea cruris:** Topical: Cream, gel, solution (spray): Apply to affected area once daily for 1 week ***Dosing: Pediatric*** **Tinea corporis (ringworm)**: Children ≥12 years and Adolescents: Topical: Cream, gel: Apply to affected area once daily for at least 1 week **Tinea cruris (jock itch):** Children ≥12 years and Adolescents: Topical: Cream, gel, solution (spray): Apply to affected area once daily for at least 1 week **Tinea pedis (athlete's foot):** Children ≥12 years and Adolescents: Topical: Cream: Apply between the toes to affected area twice daily for at least 1 week; apply on the bottom or sides of feet twice daily for 2 weeks Gel: Apply to affected area once daily at bedtime for at least 1 week
Dosage adjustment	CrCl 20 to 50 mL/minute: Administer 50% of the usual dose. CrCl <20 mL/minute: Use of alternative agent may be preferred **Dosing: Hepatic Impairment:** use is contraindicated in adults with chronic or active hepatic disease.
Contra-indications	Hypersensitivity to terbinafine or any component of the formulation.
Adverse Drug Reactions	**Topical: 1% to 10%:** Dermatologic: Burning sensation of skin, contact dermatitis, exfoliation of skin, pruritus, skin irritation, skin rash, stinging of the skin, xeroderma Local: Local irritation **Sysytemic:** **Adverse Reactions (Significant): Considerations** Hepatotoxicity

	Hypersensitivity reactions (delayed) Taste & smell disturbances Thrombotic microangiopathy >10%: Nervous system: Headache (13%) 1% to 10%: Dermatologic: Pruritus (3%), skin rash (6%), urticaria (1%) Gastrointestinal: Diarrhea (6%), dysgeusia (3%; may be severe and result in weight loss, anxiety, and depression) (See Table 1), dyspepsia (4%) Hepatic: Increased serum transaminases (3%)
Monitoring Parameters	Liver function tests at baseline and periodically during treatment; signs/symptoms of liver injury; CBC (if used >6 weeks in immunodeficient patients or if clinical signs or symptoms of secondary infection occur); taste and/or smell disturbances; skin rash, signs/symptoms of hypersensitivity reaction.
Drug Interactions	Systemic: ***Risk X: Avoid combination*:** Doxorubicin Mequitazine Saccharomyces boulardii ***Risk D: Consider therapy modification*** Eliglustat Tamoxifen
Pregnancy and Lactation	**Pregnancy Category** B Systemic therapy is not recommended during pregnancy Breastfeeding during systemic therapy is not recommended. Systemic absorption is limited following topical application. Breastfeeding mothers should not apply topical formulations to the breast and infants should avoid contact with treated skin
Administration	**Oral: Administer without regard to meals.** **Topical: Administration:** For external use only; avoid contact with eyes or mouth. Do not use on nails, scalp, or for vaginal yeast infections. Wash affected area with soap and water prior to use and dry completely; wash hands after use. Apply in sufficient quantity. Spray: Hold 4 to 6 inches from skin during application. Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Concerns related to adverse events:*** • Local irritation: If irritation/sensitivity develops, discontinue therapy and institute appropriate alternative therapy. ***Dosage form specific issues:*** • Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; the "gasping syndrome" consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension, and cardiovascular collapse; avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling. ***Other warnings/precautions:*** • Appropriate use: For topical use only. Not intended for ophthalmologic, oral, or vaginal administration. Do not use on nails or scalp. **Systemic**: • Hepatic impairment: Use is contraindicated in patients with active or chronic hepatic disease; clearance is reduced by ~50% in hepatic cirrhosis. • Renal impairment: Use with caution in patients with renal dysfunction (CrCl ≤50 mL/minute); clearance is reduced by ~50%. • Appropriate use: Due to potential toxicity, confirmation of diagnostic testing of nail or skin

	specimens prior to treatment of onychomycosis or dermatomycosis is recommended.
Storage	Store at <30°C. Refer to manufacturer PIL if there are specific considerations

11. Selenium Sulfide

Generic Name	Selenium Sulfide
Dosage form/strengths	Shampoo 0.025 gm (2.5%) Topical Cream/lotion: 2.5 gm
Route of administration	Topical
Pharmacologic category	Antiseborrheic Agent, Topical ATC: D01AE13
Indications	**Dandruff, scalp seborrhea:** Treatment of dandruff and seborrheic dermatitis of the scalp **Tinea versicolor:** Treatment of tinea versicolor
Dosage Regimen	**Dandruff, scalp seborrhea:** Topical: Lotion, shampoo (2.25%): Massage ~5 to 10 mL into wet scalp; leave on scalp for 2 to 3 minutes, then rinse scalp thoroughly. Usually 2 applications each week for 2 weeks will be effective. After this, may repeat at less frequent intervals (eg, once weekly, every 2 to 4 weeks). **Tinea versicolor:** Topical: Apply to affected area with small amounts of water; leave on skin for 10 minutes, then rinse thoroughly; repeat once every day for 7 days.
Dosage adjustment	No dosage adjustments needed
Contra-indications	Hypersensitivity to selenium sulfide or any component of the formulation.
Adverse Drug Reactions	Central nervous system: Lethargy Dermatologic: Alopecia or hair discoloration, unusual dryness or oiliness of scalp Gastrointestinal: Vomiting following long-term use on damaged skin, abdominal pain, garlic breath Local: Burning, itching, irritation, stinging (transient) Neuromuscular & skeletal: Tremor Miscellaneous: Diaphoresis
Monitoring Parameters	Assess for any broken or irritated skin that may signal that this medication should not be taken at this time. Assess for effectiveness of therapy.
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	**pregnancy** category C Animal reproduction studies have not been conducted. Not recommended for use in pregnant women. **Breastfeeding Considerations** It is not known if selenium sulfide is present in breast milk following topical application. Caution should be exercised when administering selenium sulfide to breastfeeding women.
Administration	**Administration: Topical** Shake well before using. For external use only; not for ophthalmic, oral, anal or intravaginal use. Do not use when acute inflammation or exudation is present or on damaged skin or mucous membranes. May damage jewelry; remove before treatment.

	Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Concerns related to adverse effects:*** • Local effects: Skin irritation or sensitization may occur; discontinue use if irritation or sensitivity occurs. ***Other warnings/precautions:*** • Appropriate use: For external use only; not for ophthalmic, oral, anal or intravaginal use. Due to the risk of systemic toxicity, do not use when acute inflammation or exudation is present or on damaged skin or mucous membranes.
Storage	Store at 20°C to 25°C; excursions permitted between 15°C to 30°C. Protect from heat and freezing. Refer to manufacturer PIL if there are specific considerations

12. Silver Sulfadiazine

Access Group

Generic Name	Silver Sulfadiazine
Dosage form/strengths	Topical Cream: 1 gm/100g, 10mg/gm Dressing: 1% Topical Aerosol 1%
Route of administration	Topical
Pharmacologic category	Antibiotic, Topical ATC: D06BA01
Indications	**Burn treatment:** As an adjunct for the prevention and treatment of wound sepsis in patients with second- and third-degree burns.
Dosage Regimen	**Dosing: Adult** **Burn treatment:** Topical: Apply once or twice daily; reapply as needed to areas where the cream is removed by patient activity as the burned area should be covered with cream at all times. Continue use until healing has occurred or the burn site is ready for grafting. Do not discontinue therapy if the possibility of infection exists unless a significant adverse reaction has occurred. **Dosing: Pediatric** **Note:** Continue use until healing has occurred or the burn site is ready for grafting. Do not discontinue therapy if the possibility of infection exists unless a significant adverse reaction has occurred. **Burn, treatment:** Infants >2 months, Children, and Adolescents: Limited data available in infants and children: Topical: Apply once or twice daily; reapply as needed; burned area should be covered with cream at all times
Dosage adjustment	**Dosing: Renal Impairment:** Sulfadiazine may accumulate with renal impairment. Accumulation will depend on the body surface area involved and the extent of tissue damage. **Dosing: Hepatic Impairment:** Sulfonamides may cause hepatic impairment; use with caution in hepatic disease. Discontinuation of treatment may be needed if hepatic impairment occurs with treatment
Contra-indications	Hypersensitivity to silver sulfadiazine or any component of the formulation; pregnant women approaching or at term; premature infants or neonates ≤2 months of age.
Adverse Drug Reactions	Dermatologic: Erythema multiforme, pruritus, skin discoloration, skin photosensitivity, skin rash Hematologic & oncologic: Agranulocytosis, aplastic anemia, hemolytic anemia, leukopenia Hepatic: Hepatitis Hypersensitivity: Hypersensitivity reaction (may be related to sulfa component) Renal: Interstitial nephritis
Monitoring Parameters	Serum electrolytes, urinalysis, renal function tests, CBC in patients with extensive burns on long-term treatment. Serum sulfa concentrations, if clinically indicated.

Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	**Pregnancy** Category B Use is not recommended unless clearly needed, especially in pregnant women approaching or at term. Sulfonamides are known to be excreted in human milk and all sulfonamide derivatives are known to increase the possibility of kernicterus. There is a possibility for serious adverse reactions in nursing infants from sulfonamides. A decision should be made to discontinue breastfeeding or discontinue the drug, taking into account the importance of the drug to the mother.
Administration	**Administration: Topical** For topical use only; avoid contact with eyes. Apply with a sterile-gloved hand. Burned area should be covered with cream at all times; reapply to areas where cream has been removed by patient activity. Dressings may be used if necessary. Reapply immediately after hydrotherapy. Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Concerns related to adverse effects:*** • Sulfonamide allergy: Chemical similarities are present among sulfonamides, sulfonylureas, carbonic anhydrase inhibitors, thiazides, and loop diuretics (except ethacrynic acid). Use in patients with sulfonamide allergy is specifically contraindicated in product labeling, however, a risk of cross-reaction exists in patients with allergy to any of these compounds; avoid use when previous reaction has been severe. • Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. Fungal proliferation may rarely occur in and below the eschar. • Systemic effects: Systemic absorption may be significant and adverse reactions may occur. ***Disease-related concerns:*** • G6PD deficiency: Use with caution in patients with G6PD deficiency; hemolysis may occur. • Hepatic impairment: Use with caution in patients with hepatic impairment; sulfadiazine may accumulate. • Renal impairment: Use with caution in patients with renal impairment; sulfadiazine may accumulate. ***Dosage form specific issues:*** • Propylene glycol: Some dosage forms may contain propylene glycol; large amounts are potentially toxic and have been associated hyperosmolality, lactic acidosis, seizures, and respiratory depression; use caution. ***Other warnings/precautions:*** • Appropriate use: For topical use only. Avoid contact with eyes.
Storage	Store at 20°C to 25°C. Refer to manufacturer PIL if there are specific considerations

13. Sodium Fusidate/ Fusidic acid

Generic Name	Sodium Fusidate/ Fusidic acid
Dosage form/strengths	Tablets 250mg Ointment, cream 2% Dressing 2% 20mg/gm eye drops 1mg/gm Oral Suspension 250 mg/5ml
Route of administration	Oral, topical, Opthalmic
Pharmacologic category	Antibiotic, Miscellaneous; Antibiotic, Topical ATC (Topical): D06AX01 ATC (Dressing): D09AA02 ATC (Systemic): J01XC01 ATC (Ophthalmic): S01AA13
Indications	***Topical*: Skin infections:** Treatment of primary (eg, impetigo contagiosa, erythrasma) and secondary (eg, infected wounds, infected burns) skin infections caused by susceptible *Staphylococcus aureus*, *Streptococcus* spp., *Corynebacterium minutissimum* ***Systemic use*:** For the treatment of susceptible staphylococcal infections, including cutaneous infections, osteomyelitis, pneumonia, septicemia, wound infections, endocarditis, and superinfected cystic fibrosis
Dosage Regimen	**Topical Dosing: Adult, Pediatric** **Skin infections:** Topical: Apply small amount to affected area 2 to 3 times daily for 7 to 14 days. If a gauze dressing is used, frequency of application may be reduced to once or twice daily **Oral adult dose** Oral: Adolescents and Adults: Suspension: 750 to 1,500 mg 3 times daily. Tablets: 250 mg twice daily or 500 to 1,000 mg 3 times daily. **Ophthalmic infections/conjunctivitis:** Ophthalmic: Instill 1 drop into the conjunctival sac of each eye every 12 hours for 7 days; reassess if infection has not resolved after 7 days **Dosing in pediatrics:** Children <1 year: Suspension: 50 mg/kg/day administered in 3 divided doses. Children 1 to 5 years: Suspension: 250 mg 3 times daily. Children >5 to 12 years: Suspension: 500 to 1,000 mg 3 times daily. Tablets: 250 to 500 mg 3 times daily. **Ophthalmic infections/conjunctivitis:** Children ≥2 years and Adolescents: Refer to adult dosing.
Dosage adjustment	**Renal impairment:** No dosage adjustment is needed **Hepatic impairment:** Fusidates should be given with caution to patients with hepatic impairment
Contra-indications	Hypersensitivity to fusidic acid or any component of the formulation
Adverse Drug Reactions	**Frequency not defined:**

	Central nervous system: Pain (with treatment of deep leg ulcers) GIT: jaundice and changes in liver function Blood: There have been occasional reports of granulocytopenia and thrombocytopenia after the use of fusidic acid systemically. Sideroblastic anaemia has also been reported.UK licensed product information also states that there have been isolated cases of neutropenia, agranulocytosis, and pancytopenia
Monitoring Parameters	periodic monitoring of hepatic function is recommended in patients with hepatic impairment and in those receiving high or prolonged oral doses
Drug Interactions	There are no known significant interactions. interaction has been suspected with drugs metabolised by the hepatic cytochrome P450 isoenzyme CYP3A4
Pregnancy and Lactation	Adverse effects were not observed in animal reproduction studies. Fusidic acid crosses the placenta following systemic administration. Systemic absorption following topical application is minimal. Fusidic acid is present in breast milk following systemic administration; however, systemic absorption following topical application is minimal
Administration	For topical use only; do not use near the eyes. Crust of impetigo contagiosa does not need to be removed prior to application of cream or ointment. When indicated, incision and drainage of infected lesions should precede application of the cream or ointment. Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Concerns related to adverse effects:*** • Skin reactions: Excipients in the topical cream and ointment may cause local skin reaction (eg, contact dermatitis); discontinue use if irritation or sensitization develops. • Superinfection: Prolonged use may result in superinfection (including fungal infections). Discontinue use if superinfection occurs; evaluate and treat appropriately. • Hypersensitivity reactions in the form of rashes and irritation may occur with topical fusidates; rash is rare after systemic use. • Fusidic acid competes with bilirubin for binding to albuminin vitro and caution has been advised if it is given to premature, jaundiced, acidotic, or seriously-ill neonates because of the risk of kernicterus. ***Other warnings/precautions:*** • Appropriate use: Do not use topical cream or ointment near the eye; conjunctival irritation may occur. Supplemental systemic therapy may be necessary for severe or refractory lesions. • Neonates: Not indicated for use in neonatal conjunctivitis.
Storage	Cream, ointment: Store below 30°C. Use ointment within 3 months of first opening the tube Ophthalmic solution: Store at 2°C to 25°C. Discard each multi-dose tube 28 days after opening. Refer to manufacturer PIL if there are specific considerations

14. Permethrin

Generic Name	Permethrin
Dosage form/strengths	Topical Cream, Lotion, Ointment, Emulsion: 2.5%, 5% Shampoo 1%
Route of administration	Topical
Pharmacologic category	Antiparasitic Agent, Pediculocide; Scabicidal Agent ATC: P03AC04
Indications	**Head lice (lotion/cream rinse):** Treatment of head lice (*Pediculus humanus capitis*) and its nits (eggs). **Scabies (cream):** Treatment of scabies (*Sarcoptes scabiei*) infestation
Dosage Regimen	**Dosing: Adult** **Head lice:** Topical: Cream rinse/lotion 1%: Prior to application, wash hair with conditioner-free shampoo; rinse with water and towel dry. Apply a sufficient amount of lotion or cream rinse to saturate the hair and scalp (especially behind the ears and nape of neck). Leave on hair for 10 minutes (but no longer), then rinse off with warm water; remove remaining nits with a nit comb. A single application is generally sufficient; however, may repeat 7 days after first treatment if lice or nits are still present. **Scabies:** Topical: Cream 5%: Thoroughly massage cream (30 g for an average adult) from head to soles of feet; leave on for 8 to 14 hours before removing (shower or bath); for infants and the elderly, also apply on the hairline, neck, scalp, temple, and forehead; may repeat if living mites are observed 14 days after first treatment; one application is generally curative. **Dosing: Pediatric** **Head lice: Note:** Usual first-line treatment (or pyrethrins) if community resistance is not an issue; Infants ≥2 months, Children, and Adolescents: Topical: Solution/rinse 1%: After hair has been washed with shampoo (nonconditioning), rinsed with water, and towel dried, apply a sufficient volume of permethrin solution/rinse to saturate the hair and scalp; also apply behind the ears and at the base of the neck; leave on hair for 10 minutes before rinsing off with water; remove remaining nits. May repeat in 7 to 10 days if live lice or nits observed; optimal time to repeat is at day 9 based on the life cycle of lice. **Pubic lice:** Limited data available: Adolescents: Topical: Solution/rinse 1%: Apply to affected area, leave on for 10 minutes, then wash off **Scabies:** Infants ≥2 months, Children, and Adolescents: Topical: Cream 5%: Apply and massage in cream from head to toe (average adult requires 30 g); leave on for 8 to 14 hours before washing off with water; for infants, also apply on the hairline, neck, scalp, temple, and forehead; may reapply in 14 days if live mites appear.
Dosage adjustment	**Dosing: Renal Impairment:** There are no dosage adjustments needed. **Dosing: Hepatic Impairment:** There are no dosage adjustments needed.
Contra-indications	Hypersensitivity to any pyrethroid or pyrethrin, or to any component of the formulation. OTC labeling (cream rinse/lotion): When used for self-medication, do not use on infants <2 months of age; near the eyes; inside the nose, ear, mouth, or vagina. Consult health care provider for use on eyebrows or eyelashes.

Adverse Drug Reactions	**1% to 10%:** Central nervous system: Local discomfort (scalp), localized burning, localized numbness, tingling of skin Dermatologic: Pruritus, erythema, skin rash (scalp), stinging of the skin Local: Localized edema
Monitoring Parameters	Assess head, hair, and skin surfaces for presence of lice and nits. Teach patient appropriate application
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	**Pregnancy Risk Factor B** The amount of permethrin available systemically following topical application is ≤2%. The CDC considers permethrin as one of the drugs of choice for the treatment of pubic lice during pregnancy; permethrin is the preferred treatment of scabies during pregnancy and during breastfeeding. breastfeeding is not expected to result in significant exposure to a breastfed child.
Administration	**Administration: Topical** Avoid contact with eyes and mucous membranes during application. Because scabies and lice are so contagious, use caution to avoid spreading or infecting oneself; wear gloves when applying. For the treatment of head lice, use as a portion of a whole lice removal program, which includes washing or dry cleaning all clothing, hats, bedding, and towels recently worn or used by the patient and washing combs, brushes, and hair accessories in hot water; items that cannot be washed should be sealed in a plastic bag for ≥4 weeks. Refer to manufacturer's labeling for additional information. **Cream 5%:** Apply to skin from head to soles of feet. Remove cream after 8 to 14 hours (shower or bath). **Rinse** 1%: Shake well before using. Apply immediately after hair is shampooed (without conditioner), rinsed, and towel-dried. Apply enough product to saturate hair and scalp (especially behind ears and on nape of neck). Leave on hair for 10 minutes (but no longer) before rinsing with warm water. Remove nits with fine-tooth comb. Protect eyes with a washcloth or towel Refer to manufacturer PIL if there are specific considerations
Warnings/ Precautions	***Concerns related to adverse effects:*** • Skin irritation: Treatment may temporarily exacerbate the symptoms of itching, redness, and swelling. Discontinue use if hypersensitivity occurs. ***Other warnings/precautions:*** • Appropriate use: For external use only. Avoid contact with eyes. • Ragweed allergy (cream rinse/lotion): May cause difficulty in breathing or an asthmatic attack.
Storage	Store at 20°C to 25°C Refer to manufacturer PIL if there are specific considerations

List of Antibiotics in Formulary according to WHO AWaRe list

Acess	Watch	Reserve
Amikacin	Azithromycin	Aztreonam
Amoxicillin	Cefaclor	Ceftaroline fosamil
Amoxicillin and Clavulanate	Cefdinir	Ceftazidime and Avibactam
Ampicillin	Cefepime	Ceftolozane and Tazobactam
Ampicillin and Sulbactam	Cefixime	Colistimethate
Benzylpenicillin [Penicillin G]	Cefoperazone	Linezolid
Cefadroxil	Cefotaxime	Tedizolid
Cefazolin	Cefoxitin	Tigecycline
Cephalexin	Cefpodoxime	
Cephradine	Cefprozil	
Chloramphenicol	Ceftazidime	
Clindamycin	Ceftriaxone	
Cloxacillin	Cefuroxime	
Doxycycline	Ciprofloxacin	
Flucloxacillin	Clarithromycin	
Gentamicin	Ertapenem	
Metronidazole	Erythromycin	
Nitrofurantoin	Fosfomycin	
Penicillin G Benzathine	Gatifloxacin	
Phenoxymethylpenicillin	Imipenem and Cilastatin	
Secnidazole	Levofloxacin	
Silver Sulfadiazine (topical)	Lincomycin	
Sulfamethoxazole and Trimethoprim	Lomefloxacin	
Sultamicillin	Meropenem	
Tetracycline	Moxifloxacin	
Thiamphenicol	Neomycin	
	Norfloxacin	
	Ofloxacin	
	Oxytetracycline	
	Piperacillin and Tazobactam	
	Rifampicin	
	Rifaximin	
	Roxithromycin	
	Spiramycin	
	Streptomycin	
	Teicoplanin	
	Tobramycin	
	Vancomycin	

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Uptodate

BNF

WHO aware list

www.whocc.no/atc_ddd_index/