Central Administration of Pharmaceutical Care
General Administration of Drug Utilization and Pharmacy Practice

Egyptian National Endocrine System Formulary

2024

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Preface

The Egyptian Drug Formulary is published by the Egyptian Drug Authority, the Central Administration of Pharmaceutical Care, by the General Administration of Drug Utilization and Pharmacy Practice. It has been discussed within the Committee for Pharmacy Practice Guidelines and National Drug Lists.

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

The Egyptian Drug Formulary is a guide that should be interpreted in light of professional clinical 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 for the work team for errors or omissions.

Egyptian Drug Formulary Manual

(Endocrine System Drugs)

The Egyptian Drug Formulary (Endocrine System Drugs) contains a list of medicines registered in the Egyptian drug database included in the essential medicines list or widely used on the Egyptian pharmaceutical market. 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.

The Egyptian Drug Formulary (Endocrine system drugs) presents detailed practical information for healthcare 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. Dosage regimens for adults and children.
7. Dosage adjustments if needed.
8. Contraindications.
9. Adverse drug reaction.
10. Monitoring parameters.
11. Drug Interactions: that imply avoidance or considering modifications.
12. Pregnancy and lactation.

13. 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 Leaflet if there are other specific considerations.

14. Warnings/Precautions.
15. Storage

- For reconstituted vials, apply mentioned storage conditions only if prepared in aseptic techniques and ISO-controlled conditions according to USP 797 standards, otherwise discard immediately if not used.
- USP develops standards for compounding medications to help ensure 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.

Endocrine System Formulary

This document includes medications that contribute in management of disorders that involve glands, hormones or reproductive system. It also includes medications that affect Endocrine system (including contraceptives).

Therapeutic classes include: 5 Alpha-Reductase Inhibitor, Androgens, Antidiabetic Agent (Alpha-Glucosidase Inhibitor, Biguanides, Dipeptidyl peptidase 4 (DPP-4) inhibitors,

Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist, Meglitinide, Sulfonylureas, Sodium-glucose Cotransporter 2 (SGLT2) Inhibitors, Thiazolidinedione), Insulins, Antithyroid Agents (Sulfur - containing Imidazoles, Thiouracil), Contraceptives, (Combined hormonal, Devices, Emergency, Progestogen), Corticosteroids, Dopamine-receptor agonists, Estrogens, Glycogenolytic hormones, Ovulation Stimulant, Oxytocics, Posterior pituitary hormone Analogue, Thyroid Hormones.

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Disclaimer

Any information about drugs mentioned inside this formulary is general, and does not cover all data of the medications included. The content is not intended for use as medical advice for individual problems or for evaluating the risks and benefits of taking a particular drug. Generally, all knowledge and best practices are subject to frequent changes and updates.

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List of Abbreviations

5-ARIs	5-alpha-reductase inhibitors
ACE	Angiotensin Converting Enzyme
ACTH	AdrenoCorticoTropic Hormone
ALT	Alanine Transaminase
ART	Assisted Reproductive Technology
AST	Aspartate Aminotransferase
ATC	The Anatomical Therapeutic Chemical code
ATE	Arterial thromboembolism
Beta-hCG	Beta Human Chorionic Gonadotropin
BMD	Bone Mass Density
BMI	Body Mass Index
BP	Blood Pressure
BPH	Benign Prostatic Hyperplasia
bpm	beats per minute
CNS	Central Nervous System
COC	Combined Oral Contraceptive
CrCl	Creatinine Clearance
CSCR	Central Serous Chorioretinopathy
CYP	Cytochrome P450
D5W	Dextrose 5% in Water
DITP	Drug-Induced Thrombocytopenia
DPP-4 inhibitors	Dipeptidyl peptidase 4 inhibitors
ER	Extended Release
ESRD	End-Stage Renal Disease
GI	Gastrointestinal
HPA	Hypothalamic-Pituitary-Adrenal Axis
HRT	Hormone Replacement Therapy
IM	Intramuscular
IOP	Increased Intraocular Pressure
IR	Immediate Release
Iud	IntraUterine Device
IUS	intrauterine system
MACE	Major Adverse Cardiovascular Events
MI	Myocardial Infarction
MRI	Magnetic Resonance Imaging
MTC	Medullary Thyroid Carcinoma
NME	Necrolytic Migratory Erythema
NS	Normal Saline

OHSS	Ovarian Hyperstimulation Syndrome
PCOS	Polycystic Ovarian Syndrome
PID	Pelvic Inflammatory Disease
PIL	Patient Information Leaflet
POME	Serious Pulmonary Oil Microembolism
PSA	Prostate-Specific Antigen
PUD	Peptic Ulcer Disease
SC	Subcutaneous
SERM	Selective Estrogen Receptor Modulator
SGLT2	Sodium-Glucose Cotransporter 2
SIADH	Inappropriate Antidiuretic Hormone
SLE	Systemic Lupus Erythematosus
STD	Sexually Transmitted Disease
STI	Sexually Transmitted Infection
TFT	Thyroid Function Test
TSH	Thyroid-Stimulating Hormone
ULN	Upper Limit Normal
VTE	Venous Thromboembolic Event

5 Alpha-Reductase Inhibitor

Finasteride

Generic Name	Finasteride
Dosage form/strengths	Tablets 1mg, 5mg Capsules 1mg, 5mg
Route of Administration	Oral
Pharmacologic Category	5 Alpha-Reductase Inhibitor ATC: G04CB01
Indications	**Androgenetic alopecia:** Treatment of male pattern hair loss in men. **Benign prostatic hyperplasia:** Treatment of symptomatic benign prostatic hyperplasia (BPH) to improve symptoms, induce regression of the enlarged prostate, improve urinary flow, and reduce the of need for BPH-related surgery; May be used alone or in combination with an alpha-1 blocker. **N.B.** Not approved for the prevention of prostate cancer.
Dosage Regimen	**Androgenetic alopecia (male pattern hair loss)** Oral: 1 mg once daily. Continue for 3-6 months to assess full effect; Continuous use is recommended to sustain benefit. If treatment is stopped, the beneficial effects reverse by 6-12 months. **Benign prostatic hyperplasia (alternative agent)** **Oral:** 5 mg once daily (either as a single agent or in combination with an alpha-1 blocker); 6 to 12 months of treatment is usually needed to improve symptoms. **N.B.** Not indicated for use in women or children.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** No dosage adjustment is necessary. **Dosing: Hepatic Impairment: Adult** No dosage adjustment available data. Use caution.
Contra-indications	• Hypersensitivity to Finasteride or any component of the formulation. • Pregnancy or patients who may potentially be pregnant.
Adverse Drug Reactions	**Sexual dysfunction:** which may persist after discontinuation. Delayed Onset; may begin after 6 months of therapy. Appear mostly with higher doses (5mg/day). Sexual disorders may diminish by time e.g. 2-4 years. **Adverse Reactions** **>10**%: Genitourinary: Impotence • **1% to 10%**Endocrine & metabolic: Decreased libido, gynecomastia. • Genitourinary: Breast tenderness, decreased ejaculate volume, ejaculatory disorder, sexual disorder. • Respiratory: Rhinitis.
Monitoring Parameters	**Notes** • After 6 months of treatment, 50% decrease in serum Prostate-specific antigen (PSA) concentrations can be expected. • Establish a new PSA baseline ≥ 6 months after treatment initiation and monitor PSA periodically thereafter. Any increase from baseline, may signal the presence of prostate cancer.

	• Any sustained increase in PSA levels of patients treated with Finasteride 5mg should be carefully evaluated, including consideration of non-compliance to Finasteride therapy.
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	**Pregnancy**: Use is contraindicated during pregnancy due to potential risk to a male fetus. Not indicated for use in women. **Lactation**: Not indicated for use in women. It is not known if finasteride is present in breast milk.
Administration	**Oral:** This may be administered with or without meals. N.B. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Hazardous agent (NIOSH 2016 [group 3]): Women should not handle crushed or broken finasteride tablets when they are pregnant or may potentially be pregnant, due to potential risk to a male fetus; Pregnancy Category X. • Diminished urinary flow: Carefully monitor patients with a large residual urinary volume or severely diminished urinary flow for obstructive uropathy; these patients may not be candidates for finasteride therapy. • Hepatic impairment: The effect of hepatic insufficiency on the pharmacokinetics of finasteride has not been studied. • Breast cancer: reported at post marketing period. Instruct patients to report any changes in their breast tissue such as lumps, pain, gynecomastia, or nipple discharge. • Prostate cancer: When compared to placebo, 5-alpha-reductase inhibitors (5-ARIs) have been associated with an increase in the incidence of high-grade prostate cancers. • Mood alterations and depression Mood alterations including depressed mood, depression, and, less frequently, suicidal ideation has been reported. Monitor carefully. • Appropriate use: Not indicated for use in pediatric patients or women.
Storage	Store between 15°C to 30°C. Keep the container tightly closed and protect it from moisture. **N.B** Refer to manufacturer PIL if there are specific considerations.

Androgens

Danazol

Generic Name	Danazol
Dosage form/strengths	Capsule: 100mg, 200mg
Route of Administration	Oral
Pharmacologic Category	Androgen ATC: G03XA01
Indications	• **Endometriosis**. To control pain, pelvic tenderness and other associated symptoms and to resolve or reduce the extent of endometriotic foci. Danazol capsules may be used as sole therapy, in preparation for or following surgery or in patients not responding to other treatments. • **Dysfunctional uterine bleeding** presenting as menorrhagia. • **Treatment of severe cyclical mastalgia** with or without nodularity (fibrocystic disease) unresponsive to counselling or simple analgesics. To reduce pain, tenderness and nodularity. Malignancy should be ruled out prior to therapy. • **Control of benign, multiple or recurrent breast cysts** in conjunction with aspiration. Severe symptomatic gynecomastia, both idiopathic as well as drug induced, to reduce the size of the breast and to control associated pain and tenderness. • **Pre-operative thinning of the endometrium** prior to hysteroscopic endometrial ablation. • **Prophylaxis of hereditary angioedema attacks:** Prevention of attacks of angioedema of all types (cutaneous, abdominal, laryngeal) in males and females.
Dosage Regimen	**Endometriosis** **Initial** • Individualize dosage carefully according to individual requirements and responses. • Administer the lowest effective dosage to minimize risk and occurrence of adverse effects. - *Mild disease:* **Oral:** 200 to 400 mg/day in 2 divided doses. - *Moderate to severe disease or infertility due to endometriosis:* **Oral:** 800 mg/day in 2 divided doses. Gradually reduce dosage, depending on the therapeutic response, to a level sufficient to maintain amenorrhea. - Duration of therapy**:** Continue therapy uninterrupted for 3 to 6 months; may extend up to 9 months, if needed. If symptoms recur following discontinuation, may reinitiate treatment. **Dysfunctional uterine bleeding:** 200 mg daily, normally for 3 months. **Severe cyclical mastalgia**: Initial dose of 200-300 mg daily, according to severity, for 3-6 months. **Benign breast fibrocystic disease**: Initial dose 300 mg daily, for 3 to 6 months. **Gynecomastia:** 200 mg daily in adolescents which may be increased to 400 mg

	daily if no response is obtained after two months. Adults may be given 400 mg daily for a 6-month course. **Pre-operative thinning of the endometrium**: the usual dose is 400-800 mg daily given normally for 3-6 weeks. **Prophylaxis of hereditary angioedema attacks**: Long-term prophylaxis: **Oral:** Initial: 100 to 200 mg once daily. After a favorable initial response, decrease the dosage by 50% or less at intervals of 1 to 3 months; if an attack occurs, increase the daily dosage by up to 200 mg/day. Usual dosage range: 100 mg every other day to 200 mg 3 times daily **N.B.** Danazol is not recommended for the treatment of acute attacks. **Pediatric or elderly dosing:** Not recommended.
Dosage Adjustment	**Hepatic Impairment** No specific dosage recommendations; contraindicated in patients with markedly impaired hepatic function. **Renal Impairment** No specific dosage recommendations; contraindicated in patients with markedly impaired renal function.
Contra-indications	• Hypersensitivity to danazol or any component of the formulation. • Undiagnosed abnormal genital bleeding. • Pregnancy; breastfeeding. • Porphyria. • Markedly impaired hepatic, renal, or cardiac function. • Androgen-dependent tumor. • Active or history of thrombosis or thromboembolic disease.
Adverse Drug Reactions	• **Cardiovascular**: Acute myocardial infarction, edema, flushing, increased blood pressure, palpitations, syncope, tachycardia, thrombosis (including thromboembolic complications and thromboembolism. • **Dermatologic**: Acne vulgaris, alopecia, diaphoresis, erythema multiforme, maculopapular rash, Papular rash, pruritus, purpuric rash, seborrhea, skin photosensitivity, Stevens-Johnson syndrome, urticaria, vesicular eruption. • **Endocrine & metabolic**: Altered serum glucose, change in libido, changes in serum lipids, decreased sex hormone binding globulin, decreased thyroxine-binding globulin, exacerbation of porphyria, fluid retention, hirsutism, increased sex hormone-binding globulin, increased thyroxine-binding globulin, menstrual disease, weight gain. • **Gastrointestinal**: Change in appetite, constipation, gastroenteritis, gingival hemorrhage, nausea, pancreatitis, vomiting. • **Genitourinary**: Breast atrophy, hematuria, inhibition of spermatogenesis, nipple discharge, pelvic pain, spermatozoa disorder, vaginal dryness, vaginal irritation. • **Hematologic & oncologic**: Abnormal blood cell levels, change in serum protein, petechial rash, polycythemia, purpuric disease. • **Hepatic**: Hepatic adenoma, hepatic failure, hepatic neoplasm, hepatotoxicity (idiosyncratic), peliosis hepatitis.

	• **Nervous system**: Anxiety, asthenia, chills, depression, dizziness, emotional lability, fatigue, Guillain-Barre syndrome, headache, intracranial hypertension, nervousness, paresthesia, seizure, sleep disorder, voice disorder, tremor. • **Neuromuscular & skeletal**: Arthralgia, back pain, increased creatine phosphokinase in blood specimen, joint swelling, limb pain, muscle cramps, muscle spasm, myalgia, neck pain. • **Ophthalmic**: Cataract, visual disturbance. • **Respiratory**: Interstitial pneumonitis, nasal congestion. • **Miscellaneous**: Fever.
Monitoring Parameters	• Pregnancy status before use in patients who may become pregnant. • Liver and renal function tests (periodically) • CBC • Lipid Profile (baseline, every 6 months while on therapy and 6 months after discontinuation). • Signs of intracranial hypertension (papilledema, headache, nausea, vomiting), androgenic changes, and/or fluid retention. • Liver ultrasound (baseline and biannually) in case of Hereditary angioedema, long-term prophylaxis.
Drug Interactions	***Risk X: Avoid combination*** Pimozide, Simvastatin. ***Risk D: Consider therapy modification*** Cyclosporine, Lemborexant, Lomitapide, Lonafarnib, Lovastatin, Sirolimus, Ubrogepant, Vitamin K Antagonists (e.g. warfarin).
Pregnancy and Lactation	**Pregnancy**: Contraindicated. Evidence of hazard in human pregnancy. Evaluate pregnancy status before use in patients who may become pregnant. A non-hormonal method of contraception should also be used during therapy. **Lactation:** The use of Danazol is contraindicated in breastfeeding patients due to potential risk.
Administration	**Oral**: Administer consistently about food. **N.B**. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	**Caution in patients with** hepatic or renal disease, hypertension or other cardiovascular diseases, diabetes mellitus, polycythemia, epilepsy, lipoprotein disorder, androgenic reaction to previous gonadal steroid therapy. **Adjustments in concomitant therapy:** may be needed in patients with hypertension, diabetes mellitus or epilepsy. **Danazol should be stopped immediately if:** Clinically significant adverse event occurred, and particularly if there is evidence of papilledema, headache, visual disturbances or other signs of raised intracranial pressure, jaundice or other significant hepatic disturbance, thrombosis or thromboembolism. **Initiation** should be during menstruation. An effective, non-hormonal method of contraception should be used. **Danazol may cause** Intracranial hypertension, Thromboembolic events, fluid retention, nonreversible androgenic effects and blood lipid changes with increased risk of arteriosclerosis and coronary artery disease.

	Other disease-related concerns• Cyclic breast pain (mastalgia) associated with benign breast disorders: Use is reserved for severe and refractory cases that have not responded to conservative measures and analgesics. Malignancy should be ruled out before therapy. • Diabetes: Insulin requirements may be increased; monitor carefully. • Porphyria: May cause exacerbations of acute intermittent porphyria; use is contraindicated in patients with porphyria. • Endometriosis: Danazol is generally reserved for the treatment of pain associated with endometriosis when other agents are not available, due to its high incidence of adverse events.
Storage	Store between 15°C to 30°C. Protect from light. **N.B** Refer to manufacturer PIL if there are specific considerations.

Testosterone

Generic Name	Testosterone
Dosage form/strengths	**Solution for I.M Injection** - Testosterone enanthate: 250mg/ml (corresponding to 180mg testosterone). - Testosterone undecanoate: 1000 mg/4ml (corresponding to 631.5 testosterone), 750mg /3ml (corresponding to 473.6 testosterone).
Route of Administration	IM
Pharmacologic Category	Androgen ATC: G03BA03
Indications	Hypogonadism due to androgen deficiency in men. **N.B**. Not for men with hypogonadal conditions that are not associated with structural or genetic etiologies (e.g. age-related hypogonadism)
Dosage Regimen	**Adult dosing** **Hypogonadism, in men:** Initial dosage and usual dosage range are based on dosage form as follows **IM** - **Solution (Testosterone Enanthate)** Initial: 250mg every 2 to 3 weeks. Usual dosage range**:** 250mg every 3-6 weeks, according to individual requirement. - **Solution (Testosterone Undecanoate):** 1000 mg; repeat dose after 6 weeks, and then every 10-14 weeks thereafter. ***Dosage adjustment:*** Adjust therapy within the usual dosage range every 3 to 12 months if needed based on symptoms and testosterone levels.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** There are no dosage adjustments available. Caution. May enhance edema formation. Contraindicated in serious renal disease. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments needed. May enhance edema formation. Contraindicated in serious hepatic disease
Contra-indications	• Hypersensitivity to any component of the formulation. • Androgen-dependent carcinoma. • Marked cardiac, hepatic, or renal disease. • Liver tumors. • Thrombophilia. • Pregnancy; breastfeeding; not indicated for use in women.
Adverse Drug Reactions	**>10%** • Cardiovascular: Hypertension (including exacerbation of hypertension: ≤13%).

	• Dermatologic: Skin blister (application site: 12%). • Genitourinary: Prostate-specific antigen increase (1% to 18%). • Hematologic & oncologic: Increased hematocrit (1% to 14%). • Local: Application-site pruritus (37%). **1% to 10%** • Cardiovascular: Peripheral edema, peripheral vascular disease. • Dermatologic: Acne vulgaris, alopecia, bulla (application site), contact dermatitis, crusted skin, erythema of skin, excoriation of skin (nasal; intranasal), hyperhidrosis, pruritus, skin rash, xeroderma. • Endocrine & metabolic: Decreased HDL cholesterol, decreased libido, gynecomastia, hot flash, increased plasma estradiol concentration, increased serum prolactin, increased thyroid stimulating hormone level, weight gain. • Gastrointestinal: Abdominal pain, ageusia, bitter taste, decreased appetite, diarrhea, dysgeusia, dyspepsia, eructation, gastric ulcer with hemorrhage, gastroesophageal reflux disease, gastrointestinal hemorrhage, gingival pain, gingival swelling, gingivitis, increased appetite, nausea, oral irritation, oral mucosa changes, toothache, vomiting • Genitourinary: Benign prostatic hypertrophy, breast hypertrophy, difficulty in micturition, dysuria, ejaculatory disorder, hematuria, impotence, mastalgia, pelvic pain, prostate carcinoma, prostate induration, prostatic disease, prostatitis, spontaneous erections, testicular atrophy, testicular disease, urinary frequency, urinary incontinence, urinary tract infection. • Hematologic & oncologic: Anemia, increased hemoglobin, polycythemia. • Hepatic: Abnormal hepatic function tests, increased serum bilirubin. • Local: Application-site burning, application-site edema, application-site erythema, application-site induration, application-site irritation, application-site rash, application-site vesicles, bleeding at injection site, bruising at injection site, erythema at injection site, local skin exfoliation (application site), pain at injection site. • Nervous system: Abnormal dreams, abnormality in thinking, aggressive behavior, altered sense of smell, anosmia, anxiety, asthenia, body pain, chills, confusion, depression, emotional lability, fatigue, headache, insomnia, irritability, nervousness, outbursts of anger, paresthesia, stinging sensation, vertigo. • Neuromuscular & skeletal: Abnormal bone growth, arthralgia, back pain, hemarthrosis, increased creatine phosphokinase in blood specimen, limb pain, musculoskeletal pain • Renal: Polyuria. • Respiratory: Bronchitis, cough, dry nose, epistaxis, nasal congestion, nasal discomfort, nasal mucosa swelling, nasopharyngitis, rhinorrhea, sinusitis, sleep apnea, upper respiratory tract infection.
Monitoring Parameters	**Before treatment initiation**

	• Serum testosterone levels • Liver function test, lipid profile. • Hemoglobin and hematocrit: Baseline hematocrit value >50% is a contraindication • Evaluate cardiovascular risk factors. • PSA and prostate exam **During treatment** • Serum testosterone levels occasionally during treatment and at the end of an injection interval. • Blood pressure. • Liver function test, lipid profile. • Blood glucose • Hematocrit and hemoglobin regularly to detect increased red blood cell mass and polycythemia. Discontinue therapy if hematocrit exceeds 50%. • PSA • Monitor patients with benign prostatic hyperplasia for worsening signs. • Monitor for symptoms of pain, edema, and erythema in the lower extremity (evaluate for deep vein thrombosis) and acute shortness of breath (evaluate for pulmonary embolism). • Monitor serum calcium concentrations regularly. • More frequent monitoring of international normalized ratio (INR) and prothrombin time are recommended in patients taking warfarin.
Drug Interactions	***Risk X: Avoid combination*** Dehydroepiandrosterone. ***Risk D: Consider therapy modification*** Cyclosporine (Systemic), Vitamin K Antagonists (e.g., warfarin). ***Notes*** - Change in insulin sensitivity or glycemic control. - Changes in anticoagulant activity. - Concomitant use with corticosteroids may result in increased fluid retention and requires careful monitoring, particularly in patients with cardiac, renal or hepatic disease. - Concomitant administration of cold medications may lead to additional increases in blood pressure.
Pregnancy and Lactation	Testosterone is contraindicated in cases of pregnancy or breastfeeding.
Administration	**Administration: IM** Administer very slowly (over two minutes) by deep IM injection into the gluteal muscle. Warming the injection to room temperature and shaking the vial will help re-dissolve crystals that have formed after storage. **Hazardous agent (NIOSH 2016 [group 3]):** Use appropriate precautions for receiving, handling, administration, and disposal. **N.B** Refer to manufacturer PIL if there are specific considerations.

Warnings/ Precautions	• **Cardiovascular events**: Testosterone can cause blood pressure increases that can increase the risk of major adverse cardiovascular events (MACE). • **In patients suffering from severe cardiac, hepatic, or renal insufficiency or ischemic heart disease**: Testosterone may cause severe complications characterized by edema with or without congestive cardiac failure. In such cases, discontinue immediately. • **Clotting disorders**: there have been reports of thrombotic events (e.g. deep-vein thrombosis, pulmonary embolism, ocular thrombosis) in patients with risk factors for venous thromboembolism (VTE) during testosterone therapy. In thrombophilic patients, VTE cases have been reported even under anticoagulation treatment. • **Serious Pulmonary Oil Microembolism (POME) reactions**, involving urge to cough, dyspnea, chest pain, dizziness, and syncope occurred rarely. These reactions are reversible and can occur after any injection of testosterone during the course of therapy, including after the first dose. Observe closely after each injection. Treatment is usually supportive, e.g. by administration of supplemental oxygen. • **Hypercalcemia**: May cause hypercalcemia in patients with prolonged immobilization or cancer. • **Carcinogenicity**: Cases of benign and malignant liver tumors or prostate hyperplasia have been observed after the use of Testosterone. Observe carefully. • **Caution in epilepsy and migraine:** may be aggravated**.** • **Abuse and dependence:** Particularly by using doses that are higher than recommended. Abuse of testosterone and other anabolic androgenic steroids can lead to serious adverse reactions which may be fatal including: cardiovascular, hepatic and psychiatric events. Testosterone abuse may result in dependence and withdrawal symptoms upon significant dose reduction or abrupt discontinuation of use. May potentiate sleep apnea. May induce depression, mood changes and anxiety. • **Older adults**: Patients >65 years of age may be at greater risk for prostatic hyperplasia, prostate cancer, fluid retention, and transaminase elevations.
Storage	**Injection**: Protect from light. Inspect visually for particles before administration. Only clear solutions free from particles should be used. **N.B** Refer to manufacturer PIL if there are specific considerations.

Antidiabetic Agent, Alpha-Glucosidase Inhibitor

Acarbose

Generic Name	Acarbose
Dosage form/strengths	Tablets: 25mg, 50mg, 100mg
Route of Administration	Oral
Pharmacologic Category	Antidiabetic Agent, Alpha-Glucosidase Inhibitor. ATC: A10BF01
Indications	**Treatment of type 2 diabetes mellitus** in combination or as monotherapy, Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Dosage Regimen	**Note:** Used for patients with metformin contraindications or intolerance. **Adult dosing:** **Oral** **Initial**: 25 mg 3 times daily with the start of each main meal (may start once daily). **Maintenance dose**: 50 to 100 mg 3 times daily is reached after 4–8-week interval to achieve the desired 1-hour postprandial glucose concentration (i.e. <180 mg/dL) and tolerance. **Maximum dose** for patients ≤60 kg: 50 mg 3 times daily; for patients >60 kg: 100 mg 3 times daily). Not recommended in pediatrics.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** • CrCl ≥25 mL/ minute/1.73 m ^{2}: There are no dosage adjustments available • CrCl <25 ml/minute/1.73 m ^{2}: Use is not recommended as systemic exposure increase 6-fold. **Dosage: Hepatic Impairment: Adult** There are no dosage adjustments available; Not recommended.
Contra-indications	• Hypersensitivity to Acarbose or any component of the formulation. • Diabetic ketoacidosis. • Cirrhosis. • Hepatic or renal severe impairment. • Inflammatory bowel disease, colonic ulceration, partial intestinal obstruction, patients predisposed to intestinal obstruction; chronic intestinal diseases associated with marked disorders of digestion or absorption; conditions that may deteriorate as a result of increased gas formation in the intestine.
Adverse Drug Reactions	**>10%:** Gastrointestinal: Frequency and intensity of flatulence (74%) tend to abate with time; diarrhea (31%) and abdominal pain (19%) tend to return to pretreatment levels over time. **1% to 10%:** Hepatic: Increased serum transaminases (≤4%).
Monitoring Parameters	• Glycosylated hemoglobin levels *HbA_{1c}*. • Liver and kidney function every 3 months during the first year of treatment and periodically thereafter.

Drug Interactions	***Risk D: Consider therapy modification*** Insulin, Sulfonylureas. **Notes** - Acarbose may affect Digoxin bioavailability and may require dose adjustment. Monitor. - Charcoal and digestive enzyme preparations containing carbohydrate splitting enzymes (e.g. amylase, Pancreatin) may reduce the effect of Acarbose and should not therefore be taken concomitantly. - Concomitant administration of cholestyramine may enhance the effects of Acarbose. Avoid.
Pregnancy and Lactation	**Pregnancy**: Not recommended due to lack of data. Agents other than acarbose are currently recommended to treat diabetes mellitus in pregnancy. Breastfeeding is not recommended by the manufacturer. **Lactation**: Not recommended due to lack of data.
Administration	**Administration: Oral** Administer with the first bite of each main meal. **N.B**. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Elevated serum transaminases**: If elevations are observed, a reduction in dosage or withdrawal of therapy may be indicated, particularly if the elevations persist. Fulminant hepatitis (which may be fatal) has been reported. • **Hypoglycemia**: Acarbose has an antihyperglycemic effect, but does not itself induce hypoglycemia. Hypoglycemia may occur with combination therapy. In patients taking Acarbose, oral glucose (dextrose) should be used instead of sucrose (cane sugar) in the treatment of mild-to-moderate hypoglycemia since the hydrolysis of sucrose to glucose and fructose is inhibited by Acarbose. • **Hepatic impairment**: Use with caution in patients with hepatic impairment. • **Renal impairment**: Not recommended in patients with significant impairment (serum creatinine >2 mg/dL or CrCl <25 mL/minute/1.73 m ^{2}). • **Appropriate use**: Diet: Increased intake of sucrose (cane sugar) and food that contains sucrose during treatment can lead to GI symptoms (eg, flatulence and bloating), loose stools, and occasionally diarrhea. If a diabetic diet is not followed, the GI side effects may be intensified. If severe symptoms develop in spite of adherence to a diabetic diet, temporarily or permanently reduce dose. • **Gastrointestinal side effects** usually develop during the first few weeks of therapy. They are most commonly mild-to-moderate gastrointestinal effects, such as flatulence, diarrhea, or abdominal discomfort, and generally diminish in frequency and intensity with time.
Storage	Store between 15-30°C. Protect from moisture. **N.B** Refer to manufacturer PIL if there are specific considerations.

Antidiabetic Agent, Biguanides

Metformin

Generic Name	Metformin
Dosage form/strengths	Tablets: 500mg, 850mg, 1000mg Oral Solution: 500 mg/5ml Modified Release Tablet: 500mg, 850mg, 1000mg And in combinations.
Route of Administration	Oral
Pharmacologic Category	Antidiabetic Agent, Biguanide ATC: A10BA02
Indications	**Diabetes mellitus, type 2, treatment:** Management of type 2 diabetes mellitus when hyperglycemia cannot be managed with diet and exercise alone.
Dosage Regimen	**Adult dosing** **Immediate release** ***Initial:*** Oral**:** 500 mg once or twice daily **or** 850 mg once daily Dose adjustments: may increase gradually by 500mg increments every 7 days. Usually done in 500 mg or 850 mg increments every 7 days (range: 5 days to 1 month). ***Usual maintenance dosage:*** Oral**:** 1 g twice daily **or** 850 mg twice daily ***Maximum:*** Oral**:** 2.55 g/day. If doses >2 g/day are needed, consider administering in 3 divided doses to minimize GI adverse effects. **Extended-release** ***Initial:*** Oral**:** 500 mg to 1 g once daily. Dose adjustments: may increase gradually by 500mg increments every 10-15 days. ***Maximum:*** Oral**:** 2 g/day. If glycemic control is not achieved at the maximum dose given once daily, may divide the maximum dose and administer it twice daily. **Pediatric dosing** **Immediate-*release tablet or solution*:** **Children ≥10 years and Adolescents**: ***Initial***: 500 once daily or 850mg once daily. Increase dose every 1 to 2 weeks as tolerated; maximum dose: 1,000 mg twice daily **or** 850 mg 3 times daily.
Dosage Adjustment	**Dosing: Renal Impairment: Adult** **eGFR ≥60 mL/min.:** No dose adjustments are needed. **eGFR between 45-60 mL/min** maximum dose 2g divided by 2-3 times. Start at 1gm daily. Monitor every 3 to 6 months. **eGFR between 30-45 mL/min:** 1gm daily divided 2-3 times. Start at 500mg daily**.** Initiation of metformin in those patients is not recommended. However, if the patient was on metformin before the deterioration of kidney function,

	metformin might be continued with close monitoring **eGFR <30 mL/minute/1.73 m^2:** Use is contraindicated**.** **Dosing: Hepatic Impairment: Adult** Use with caution because patients with liver impairment are at higher risk for developing lactic acidosis. Avoid in severe cases.
Contra-indications	• Hypersensitivity. • Acute metabolic acidosis including (Lactic acidosis and Diabetic ketoacidosis). • Severe renal failure or hepatic dysfunction.
Adverse Drug Reactions	**>10%** • Gastrointestinal: Diarrhea (IR tablet: 53%; ER tablet: 10%), flatulence (12%), nausea and vomiting (IR tablet: 26%; ER tablet: 7%) **1% to 10%** • Cardiovascular: Chest discomfort, flushing, palpitations. • Dermatologic: Diaphoresis. • Endocrine & metabolic: Hypoglycemia, vitamin B12 deficiency (7%). • Gastrointestinal: Abdominal distention, abdominal distress (6%), abdominal pain, abnormal stools, dyspepsia (7%), heartburn. • Nervous system: Chills, dizziness, headache (6%). • Neuromuscular & skeletal: Asthenia (9%), myalgia. • Respiratory: Dyspnea, flu-like symptoms, upper respiratory tract infection.
Monitoring Parameters	• Blood glucose. • Hematologic parameters (e.g., hemoglobin/hematocrit and red blood cell indices) Initial and annually. • Glycosylated hemoglobin A1c (HbA1c). • Liver function test. • Renal function initially and annually. • Monitor vitamin B12 serum concentrations in patient at risk.
Drug Interactions	***Risk X: Avoid combination*** Alcohol (Ethyl), Pacritinib. ***Risk D: Consider therapy modification*** Cimetidine, Dolutegravir, Erdafitinib, Fexinidazole, Fludeoxyglucose, Iodinated Contrast Agents, Patiromer, Ranolazine, Risdiplam, Tafenoquine.
Pregnancy and Lactation	**Pregnancy**: Human Data Suggest Low Risk. Metformin is a preferred second-line choice for women who decline insulin therapy or are unable to safely administer insulin. While no teratogenic effects have been associated with metformin, no long-term safety data are available. **Lactation**: Not recommended due to the potential for hypoglycemia in nursing infants.
Administration	**Oral**: Administer with a meal (to decrease GI upset). Administer solution or suspension with the supplied dosing cup.

	Extended-release tablets: Swallow whole; do not crush, cut, or chew. Administer once-daily doses with the evening meal. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Lactic acidosis**: A very rare, but serious metabolic complication, most often occurs due to accumulation of Metformin at acute worsening of renal function or cardio-respiratory illness or sepsis. Other risk factors for lactic acidosis are excessive alcohol intake, hepatic insufficiency, inadequately controlled diabetes, ketosis, prolonged fasting and any conditions associated with hypoxia, as well as concomitant use of medicinal products that may cause lactic acidosis. • Lactic acidosis is characterized by abdominal pain, muscle cramps, asthenia and hypothermia followed by coma. In case of suspected symptoms, the patient should stop taking metformin and seek immediate medical attention. Diagnostic laboratory findings are decreased blood pH (< 7.35), increased plasma lactate levels (>5 mmol/L) and an increased anion gap and lactate/pyruvate ratio. • **Renal impairment**: Metformin is substantially excreted by the kidney; dosing adjustments may be required. Metformin is contraindicated in patients with GFR <30ml/min and should be temporarily discontinued in the presence of conditions that alter renal functions. • **Cardiac function**: Patients with heart failure are more at risk of hypoxia and renal insufficiency. In patients with stable chronic heart failure, metformin may be used with a regular monitoring of cardiac and renal function. • **Surgical procedures:** Metformin-containing products should be withheld the day of surgery; restart after renal function is stable**.** • **Metformin may reduce vitamin B12 serum levels**. The risk of low vitamin B12 levels increases with increasing metformin dose, treatment duration, and/or in patients with risk factors known to cause vitamin B12 deficiency. Monitor. • **Hepatic impairment**: Use cautiously in patients due to risk for lactic acidosis. An increased risk of mortality has been observed with higher metformin doses (e.g., >1 g) and more severe liver dysfunction. Cases of metformin-induced hepatotoxicity have also been reported. • **Iodinated contrast**: Administration of iodinated contrast agents has been associated with contrast-induced nephropathy resulting in an increased risk of lactic acidosis due to reduced metformin excretion. Temporarily withhold Metformin prior to or at the time of iodinated contrast administration. Reassess kidney function ≥48 hours after contrast administration and resume therapy if kidney function is acceptable.
Storage	Store between 15°C to 30°C N.B Refer to manufacturer PIL if there are specific considerations.

Antidiabetic Agent, Dipeptidyl Peptidase 4 (DPP-4) Inhibitor

Alogliptin

Generic Name	Alogliptin
Dosage Form/Strengths	Tablets: 6.25 mg, 12.5 mg, 25 mg.
Route of Administration	*Oral*
Pharmacologic Category	Antidiabetic Agent, Dipeptidyl Peptidase 4 (DPP-4) Inhibitor. ATC: A10BH04
Indications	Improve glycemic control in adults with type 2 diabetes mellitus in adjunct to diet and exercise.
Dosage Regimen	**Adult dosing** Oral: 25mg once daily. **Pediatrics** The safety and efficacy of alogliptin in children and adolescents < 18 years old have not been established.
Dosage Adjustment	**Renal impairment** • Moderate (CrCl ≥ 30 to ≤ 50 mL/min): 12.5mg once daily. • Severe (CrCl < 30 mL/min): 6.25 mg once daily. • Renal dialysis or peritoneal dialysis: Not studied. **Hepatic impairment** • Mild to moderate hepatic impairment: No dose adjustment is necessary. • Severe hepatic impairment: Not studied.
Contra-Indications	History of serious hypersensitivity to alogliptin or any of the excipients.
Adverse Drug Reactions	**1% to 10%** • **Endocrine & metabolic**: Hypoglycemia (2% to 5%). • **Nervous system**: Headache (4%). • **Renal**: Decreased creatinine clearance (2%), renal function abnormality (3%). • **Respiratory**: Nasopharyngitis (5%), upper respiratory tract infection (5%).
Monitoring Parameters	• Bloos glucose and glycosylated hemoglobin. • Renal function prior to therapy and periodically thereafter. • Hepatic function if clinically indicated.
Drug Interactions	***Risk D: Consider therapy modification*** Insulins, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy**: Limited data. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. **Lactation**: No data. Asses benefit to potential risk.
Administration	**Oral administration** Can be taken with or without food. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/	• **Pancreatitis**: There have been postmarketing reports of acute

Precautions	pancreatitis. Patients should be informed about symptom of acute pancreatitis which is persistent, severe abdominal pain, which may radiate to the back. If pancreatitis is suspected, alogliptin should be discontinued and do not restart if pancreatitis is confirmed. Caution should be exercised in patients with a history of pancreatitis. • **Heart failure**: Consider the risks and benefits of alogliptin prior to initiating treatment in patients at risk for heart failure such as those with a prior history of heart failure and a history of renal impairment. • **Hypersensitivity reaction:** Serious reactions have been spontaneously reported including anaphylactic reactions, angioedema and exfoliative skin conditions including Stevens-Johnson syndrome and erythema multiforme. • **Hepatic effects**: Postmarketing reports of hepatic failure, sometimes fatal. Causality cannot be excluded. If liver injury is detected, alogliptin should be interrupted and assess patient forcauses. Do not restart I liver injury is confirmed with no other etiology. • **Bullous pemphigoid:** There have been post-marketing reports of bullous pemphigoid in patients taking DPP-4 inhibitors. Tell patients to report development of blisters or erosions. If bullous pemphigoid is suspected, alogliptin should be discontinued. • **Hypoglycemia:** A lower dose of insulin or other antidiabetic products (such as metformin or thiazolidinedione) may be considered to reduce the risk of hypoglycaemia when used in combination with alogliptin. Alogliptin has not been studied in combination with sodium glucose cotransporter 2 (SGLT-2) inhibitors or glucagon like peptide 1 (GLP-1) analogues. • **Arthralgia**: Severe and disabling arthralgia has been reported in patients taking DPP-4 inhibitors. Consider alogliptin therapy as a possible cause for severe joint pain and consider discontinuation.
Storage	Store between 15° to 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Linagliptin

Generic Name	Linagliptin
Dosage Form/Strengths	Tablets: 5mg. And in combinations.
Route of Administration	*Oral*
Pharmacologic Category	Antidiabetic Agent, Dipeptidyl Peptidase 4 (DPP-4) Inhibitor. ATC: A10BH05.
Indications	Improve glycemic control in adults with type 2 diabetes mellitus in adjunct to diet and exercise.
Dosage Regimen	**Adult dosing** **Oral:** 5mg once daily. **Pediatrics:** The safety and efficacy in children and adolescents < 18 years old have not been established.
Dosage Adjustment	**Renal impairment** No dose adjustment is required. **Hepatic impairment** No dose adjustment is required.
Contra-Indications	Hypersensitivity to linagliptin or any of the excipients.
Adverse Drug Reactions	**1% to 10%** • **Endocrine & metabolic**: Increased uric acid (3%). • **Gastrointestinal**: Increased serum lipase (>3 × ULN: 8%). • **Respiratory**: Cough (2%), nasopharyngitis (7%).
Monitoring Parameters	Bloos glucose and glycosylated hemoglobin.
Drug Interactions	***Risk D: Consider therapy modification*** CYP3A4 Inducers (Strong e.g. Barbiturates (phenobarbital), Carbamazepine, Phenytoin, Rifampicin), Insulins P-glycoprotein/ABCB1 Inducers, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy**: Limited data. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. **Lactation**: No data. Asses benefit to potential risk.
Administration	Oral administration: Can be taken with or without food. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	• **Pancreatitis**: There have been postmarketing reports of acute pancreatitis. Patients should be informed about symptom of acute pancreatitis which is persistent, severe abdominal pain, which may radiate to the back. If pancreatitis is suspected, linagliptin should be discontinued and do not restart if pancreatitis is confirmed. Caution should be exercised in patients with a history of pancreatitis. • **Hypoglycemia:** A lower dose of insulin or other antidiabetic products

	(such as thiazolidinedione) may be considered to reduce the risk of hypoglycemia when used in combination with linagliptin. While the dose of metformin should be maintained if combined with linagliptin. • **Heart failure**: Consider the risks and benefits of linagliptin prior to initiating treatment in patients at risk for heart failure such as those with a prior history of heart failure and a history of renal impairment. • **Hypersensitivity reaction:** Serious reactions have been spontaneously reported including anaphylactic reactions, angioedema and exfoliative skin conditions including Stevens-Johnson syndrome and erythema multiforme. • **Bullous pemphigoid**: There have been post-marketing reports of bullous pemphigoid in patients taking DPP-4 inhibitors. Tell patients to report development of blisters or erosions. If bullous pemphigoid is suspected, linagliptin should be discontinued. • **Arthralgia**: Severe and disabling arthralgia has been reported in patients taking DPP-4 inhibitors. Consider linagliptin therapy as a possible cause for severe joint pain and consider discontinuation.
Storage	Store between 15° to 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Saxagliptin

Generic Name	Saxagliptin
Dosage Form/Strengths	Tablets: 2.5 mg, 5mg.
Route of Administration	*Oral.*
Pharmacologic Category	Antidiabetic Agent, Dipeptidyl Peptidase 4 (DPP-4) Inhibitor ATC: A10BH03
Indications	Improve glycemic control in adults with type 2 diabetes mellitus in adjunct to diet and exercise.
Dosage Regimen	**Adult dosing** Oral: 2.5 mg or 5 mg once daily. **Pediatrics**: The safety and efficacy in children and adolescents < 18 years old have not been established.
Dosage Adjustment	**Renal impairment** • Mild renal impairment: No dose adjustment is required. • Moderate to severe renal impairment: 2.5 mg once daily. • End-stage renal disease requiring hemodialysis: Use is not recommended. **Hepatic impairment** • mild hepatic impairment: No dose adjustment is required. • Moderate hepatic impairment: Caution. No dose adjustment is required. • Severe hepatic impairment: Use is not recommended.
Contra-Indications	Hypersensitivity to the active substance or to any of the excipients.
Adverse Drug Reactions	**1% to 10%** • **Cardiovascular**: Peripheral edema (4%). • **Endocrine & metabolic**: Hypoglycemia (6%). • **Genitourinary**: Urinary tract infection (7%). • **Hematologic & oncologic**: Lymphocytopenia (≤2%). • **Hypersensitivity**: Hypersensitivity reaction (2%; including facial edema and urticaria). • **Nervous system**: Headache (7%).
Monitoring Parameters	• Bloos glucose and glycosylated hemoglobin. • Renal function prior to initiation and periodically thereafter.
Drug Interactions	***Risk X: Avoid combination*** Fexinidazole. ***Risk D: Consider therapy modification*** CYP3A4 Inhibitors (Strong e.g. Barbiturates (phenobarbital), Carbamazepine, Phenytoin, Rifampicin), Fusidic Acid (Systemic), Insulins, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy**: Limited data. Studies in animals have shown reproductive toxicity at high doses. Should not be used during pregnancy unless clearly necessary. **Lactation**: No data. Asses benefit to potential risk.

Administration	**Oral administration**: Tablets can be taken with or without a meal. Tablets must not be split or cut. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	• **Pancreatitis**: There have been postmarketing reports of acute pancreatitis. Patients should be informed about symptom of acute pancreatitis which is persistent, severe abdominal pain, which may radiate to the back. If pancreatitis is suspected, saxagliptin should be discontinued and do not restart if pancreatitis is confirmed. Caution should be exercised in patients with a history of pancreatitis. • **Hypoglycemia:** A lower dose of insulin or other antidiabetic products (such as sulphonylurea) may be considered to reduce the risk of hypoglycemia when used in combination with saxagliptin. • **Heart failure**: Consider the risks and benefits of saxagliptin prior to initiating treatment in patients at risk for heart failure such as those with a prior history of heart failure and a history of renal impairment. • **Hypersensitivity reaction:** Serious reactions have been spontaneously reported including anaphylactic reactions, angioedema and exfoliative skin conditions including Stevens-Johnson syndrome and erythema multiforme. • **Bullous pemphigoid**: There have been post-marketing reports of bullous pemphigoid in patients taking DPP-4 inhibitors including saxagliptin. Tell patients to report development of blisters or erosions. If bullous pemphigoid is suspected, saxagliptin should be discontinued. • **Arthralgia**: Severe and disabling arthralgia has been reported in patients taking DPP-4 inhibitors. Consider saxagliptin therapy as a possible cause for severe joint pain and consider discontinuation.
Storage	Store between 15°-30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Sitagliptin

Generic Name	Sitagliptin
Dosage Form/Strengths	Tablets: 50mg, 100mg. And in combinations.
Route of Administration	*Oral*
Pharmacologic Category	Antidiabetic Agent, Dipeptidyl Peptidase 4 (DPP-4) Inhibitor. ATC: A10BH01
Indications	Improve glycemic control in adults with type 2 diabetes mellitus in adjunct to diet and exercise.
Dosage Regimen	**Adult dosing** **Oral**: 100mg once daily. **Pediatrics**: The safety and efficacy in children and adolescents < 18 years old have not been established.
Dosage Adjustment	**Renal impairment** • Mild to moderate impairment (GFR >45 mL/min): No dose adjustment is required. • Moderate renal impairment (GFR 30 to < 45 mL/min): 50 mg once daily. • Severe renal impairment (eGFR less than 30 mL/min), or with end-stage renal disease including those requiring hemodialysis or peritoneal dialysis: dose of sitagliptin is 25 mg once daily. **Hepatic impairment** • Mild to moderate hepatic impairment: No dose adjustment is required. • Severe hepatic impairment: Not studied.
Contra-Indications	Hypersensitivity to the active substance or to any of the excipients
Adverse Drug Reactions	**1% to 10%** • **Endocrine & metabolic**: Hypoglycemia (1%). • **Respiratory**: Nasopharyngitis (5%). **Frequency not defined** • **Gastrointestinal**: Diarrhea, nausea.
Monitoring Parameters	• Bloos glucose and glycosylated hemoglobin. • Renal function prior to therapy and in and periodically thereafter.
Drug Interactions	***Risk D: Consider therapy modification*** Insulins, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy**: Limited data. Studies in animals have shown reproductive toxicity at high doses. Should not be used during pregnancy unless clearly necessary. **Lactation**: No data. Asses benefit to potential risk.
Administration	**Oral administration** Tablets can be taken with or without food. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	• **Pancreatitis**: There have been postmarketing reports of acute pancreatitis. Patients should be informed about symptom of acute pancreatitis which is persistent, severe abdominal pain, which may

	radiate to the back. If pancreatitis is suspected, sitagliptin should be discontinued and do not restart if pancreatitis is confirmed. Caution should be exercised in patients with a history of pancreatitis. • **Hypoglycemia**: When Sitagliptin is used in combination with a sulphonylurea or with insulin, a lower dose of the sulphonylurea or insulin may be considered to reduce the risk of hypoglycemia. while the dose of metformin should be maintained if combined with sitagliptin. • **Heart failure**: Consider the risks and benefits of sitagliptin prior to initiating treatment in patients at risk for heart failure such as those with a prior history of heart failure and a history of renal impairment. • **Hypersensitivity reaction:** Serious reactions have been spontaneously reported including anaphylactic reactions, angioedema and exfoliative skin conditions including Stevens-Johnson syndrome and erythema multiforme. • **Bullous pemphigoid**: There have been post-marketing reports of bullous pemphigoid in patients taking DPP-4 inhibitors. Tell patients to report development of blisters or erosions. If bullous pemphigoid is suspected, sitagliptin should be discontinued. • **Arthralgia**: Severe and disabling arthralgia has been reported in patients taking DPP-4 inhibitors. Consider sitagliptin therapy as a possible cause for severe joint pain and consider discontinuation.
Storage	Store between 15°-30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Vildagliptin

Generic Name	Vildagliptin
Dosage Form/Strengths	Tablets: 50 mg. And in combinations.
Route of Administration	*Oral*
Pharmacologic Category	Antidiabetic Agent, Dipeptidyl Peptidase 4 (DPP-4) Inhibitor. ATC: A10BH02
Indications	Improve glycemic control in adults with type 2 diabetes mellitus in adjunct to diet and exercise.
Dosage Regimen	**Adults dosing** **Oral**: 50mg twice daily. When used dual combination with a sulphonylurea: 50 mg once daily (with a lower dose of the sulphonylurea). **Pediatrics**: The safety and efficacy in children and adolescents < 18 years old have not been established.
Dosage Adjustment	**Renal impairment** • Mild renal impairment (Crcl ≥ 50 ml/min): No dose adjustment is required. • Moderate or severe renal impairment or with end-stage renal disease (ESRD): 50 mg once daily. **Hepatic impairment** Use is not recommended.
Contra-Indications	Hypersensitivity to the active substance or to any of the excipients.
Adverse Drug Reactions	**1% to 10%** • **Cardiovascular**: Peripheral edema. • **Endocrine & metabolic**: Hypoglycemia. • **Hypersensitivity**: Hypersensitivity reaction (2%; including facial edema and urticaria). • **Nervous system**: headache, dizziness. • **Respiratory:** Nasopharyngitis. • **Gastrointestinal**: Constipation, nausea, gastro-oesophageal reflux disease, diarrhea, abdominal pain, vomiting. • **Skin and subcutaneous tissue disorders**: Hyperhidrosis, rash, pruritis, dermatitis. • **Musculoskeletal**: Arthralgia, myalgia.
Monitoring Parameters	• Bloos glucose and glycosylated hemoglobin. • Renal function test prior to therapy and in and periodically thereafter. • Liver function test prior to therapy and at three-month intervals during the first year and periodically thereafter.
Drug Interactions	***Risk D: Consider therapy modification*** Sulfonylureas.

Pregnancy and Lactation	**Pregnancy**: Limited data. Studies in animals have shown reproductive toxicity at high doses. Should not be used during pregnancy unless clearly necessary. **Lactation**: No data. Asses benefit to potential risk.
Administration	**Oral administration**: Tablets can be administered with or without a meal. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	• **Pancreatitis**: There have been postmarketing reports of acute pancreatitis. Patients should be informed about symptom of acute pancreatitis which is persistent, severe abdominal pain, which may radiate to the back. If pancreatitis is suspected, sitagliptin should be discontinued and do not restart if pancreatitis is confirmed. Caution should be exercised in patients with a history of pancreatitis. • **Hypoglycemia**: When vildagliptin is used in combination with a sulphonylurea, a lower dose of the sulphonylurea may be considered to reduce the risk of hypoglycemia. • **Heart failure**: Consider the risks and benefits of vildagliptin prior to initiating treatment in patients at risk for heart failure such as those with a prior history of heart failure and a history of renal impairment. • **Hypersensitivity reaction:** Serious reactions have been spontaneously reported including anaphylactic reactions, angioedema and exfoliative skin conditions including Stevens-Johnson syndrome and erythema multiforme. • **Bullous pemphigoid**: There have been post-marketing reports of bullous pemphigoid in patients taking DPP-4 inhibitors. Tell patients to report development of blisters or erosions. If bullous pemphigoid is suspected, sitagliptin should be discontinued. • **Arthralgia**: Severe and disabling arthralgia has been reported in patients taking DPP-4 inhibitors. Consider vildagliptin therapy as a possible cause for severe joint pain and consider discontinuation. • **Liver functions monitoring**: Rare cases of hepatic dysfunction have been reported and patients were generally asymptomatic. Liver function test results returned to normal after discontinuation of treatment. Treatment should be discontinued and not reinitiated if increase in AST or ALT were three times the normal level or greater or in Patients who develop jaundice or other liver dysfunction signs.
Storage	Store between 15°-30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Antidiabetic Agent, Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Dulaglutide

Generic Name	Dulaglutide
Dosage form/strengths	Solution for SC injection: 0.75mg/0.5ml, 1.5mg/0.5ml
Route of Administration	SC.
Pharmacologic Category	Antidiabetic Agent, Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist. ATC: A10BJ05
Indications	Biological medicine should be prescribed and dispensed by brand name. **Treatment of Diabetes mellitus, type 2:** as an adjunctive agent or alternative monotherapy [if metformin inappropriate
Dosage Regimen	**Dosing adult** **SC:** Initial: 0.75 mg once weekly; may increase to 1.5 mg once weekly if needed. May be increased in 4-week intervals to 3mg or further increased to 4.5mg maximum dose to achieve targeted glycemic goals. Not recommended for use in pediatric patients younger than 18 years
Dosage Adjustment	**Dosing: Altered kidney function: Adult** No dosage adjustment is necessary. Caution. **Dosing: Hepatic impairment: Adult** No dosage adjustment is necessary. Caution.
Contra-indications	• Hypersensitivity to Dulaglutide or any component of the formulation. • Medullary thyroid carcinoma or family history, or thyroid C-cell tumors. • Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)
Adverse Drug Reactions	**>10%** • Endocrine & metabolic: Hypoglycemia (≤77%; highest incidence seen with adjunctive use of insulin or sulfonylureas; severe hypoglycemia: ≤3%; highest incidence seen with adjunctive use of prandial insulin). • Gastrointestinal: Diarrhea, vomiting (9%-13%), nausea (12%-21%). **1% to 10%** • Cardiovascular: First-degree atrioventricular block (2%), prolongation P-R interval on ECG (3%), sinus tachycardia (6%), sustained tachycardia (2%). • Endocrine & metabolic: Diabetic retinopathy (2%; more common in patients with a history of diabetic retinopathy at baseline. • Gastrointestinal: Abdominal distension (2%-3%), abdominal pain (7%-9%), constipation (4%), decreased appetite (5%-9%), dyspepsia (4%-6%), eructation (2%), flatulence (3%), gastroesophageal reflux disease (2%). • Immunologic: Antibody development (children, adolescents, and adults: 2% to 6%; neutralizing: ≤1%). • Local: Injection-site reaction (adults: <1%; children and adolescents: 4%) • Nervous system: Fatigue (4% to 6%).

Monitoring Parameters	• Blood glucose, Glycosylated hemoglobin A1c (HbA1c). • Renal function (in patients reporting severe GI reactions). • Signs/symptoms of pancreatitis. • Monitor patients with a history of diabetic retinopathy for complications.
Drug Interactions	***Risk X: Avoid combination*** Liraglutide, Semaglutide. ***Risk D: Consider therapy modification*** Insulins, Meglitinides, Sincalide, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy**: Avoid. Toxicity in animal studies. Should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Lactation**: Avoid. No human data.
Administration	**SC**: Administer once weekly at any time of day with or without food Inject subcutaneously in the abdomen, thigh, or upper arm. When using dulaglutide concomitantly with insulin, administer it as separate injections. Never mix them. **N.B.** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• Acute kidney injury: may cause loss of fluids (dehydration) which may cause kidney problems to get worse. Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions. • Hypersensitivity reactions: Rapid or delayed, including anaphylaxis and angioedema. Discontinue and seek medical advice. • Medullary thyroid carcinoma: Dulaglutide may cause thyroid C-cell tumors at clinically relevant doses. Counsel patients regarding the potential risk of MTC with the use of Dulaglutide and inform them of symptoms of thyroid tumors (e.g., mass in the neck, dysphagia, dyspnea, persistent hoarseness) • Pancreatitis: Discontinue if symptoms of acute pancreatitis occur, such as persistent, severe abdominal pain. Do not restart if pancreatitis is confirmed. • Cardiovascular effects: Increased resting heart rate has been observed in placebo-controlled trials; monitoring is recommended. • Severe gastrointestinal disease: Gastrointestinal symptoms are the most common adverse reactions. Increased risk with higher doses and Rapid titration. Has not been studied in these patients including pre-existing gastroparesis therefore not recommended in these patients. • Severe renal impairment: Not recommended for use in patients with end-stage renal disease due to limited experience. • Diabetic Ketoacidosis: Serious and life-threatening cases have been reported in patients on a combination of Dulaglutide and insulin, particularly after discontinuation or rapid dose reduction of concomitant insulin. Stepwise dose reduction of insulin should be done with careful blood glucose self-monitoring.

	• Diabetic Retinopathy Complications: Have been reported. Monitor patients with a history of diabetic retinopathy.
Storage	• Store at (2°C to 8°C). Do not freeze. Do not use it if it has been frozen. Protect from light. • After initial use, it can be stored between 15-30 °C for 14 days. **N.B**. Refer to manufacturer PIL if there are specific considerations.

Exenatide

Generic Name	Exenatide
Dosage form/strengths	Powder for Suspension for Injection in prefilled pen (extended-release): 2mg
Route of Administration	SC
Pharmacologic Category	Antidiabetic Agent, Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist ATC: A10BJ01
Indications	**Diabetes mellitus, type 2, Management** (extended-release): As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients ≥10 years of age and combination with glucose-lowering medicinal products including basal insulin.
Dosage Regimen	**Dosage: Adult, Children ≥10 years and Adolescents** **Extended-release** Subcutaneous: 2 mg once weekly without regard to meals. If changing the day of administration is necessary, allow at least 3 days between 2 doses.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult or pediatric** CrCl 30 to 50 mL/minute: No dosage adjustment necessary; use caution, and monitor for hypovolemia. CrCl <30 mL/minute: Use is not recommended. **Dosage: Hepatic Impairment: Adult** No dose adjustment is necessary.
Contra-indications	• Hypersensitivity to Exenatide or any component of the formulation. • History of or family history of medullary thyroid carcinoma. • Multiple endocrine neoplasia syndrome type 2. • Severe renal impairment (GFR < 30mL/min).
Adverse Drug Reactions	**>10%** • Gastrointestinal: Diarrhea, nausea. • Immunologic: Antibody development (antibody titers commonly decrease with continued use, though a small percentage of patients had increased titers; an attenuated glycemic response may be seen with antibody formation). • Local: Injection-site nodule, injection-site reaction. **1% to 10%** • Endocrine & metabolic: Hypoglycemia. • Gastrointestinal: Constipation, dyspepsia, gallbladder disease, vomiting. • Local: Erythema at the injection site, injection-site pruritus. • Nervous system: Dizziness, headache.
Monitoring Parameters	• Serum glucose. • Kidney function, volume status, weight. • Triglycerides.

	• Signs/symptoms of pancreatitis, signs/symptoms of gallbladder disease.
Drug Interactions	***Risk X: Avoid combination*** Liraglutide, Semaglutide, Tirzepatide. ***Risk D: Consider therapy modification*** Hormonal Contraceptives, Insulins, Meglitinides, Sincalide, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy**: Not recommended. No human data. Agents other than exenatide are currently recommended to treat diabetes mellitus in pregnancy. **Lactation**: Not recommended. No human data. Consider benefits and risks.
Administration	**SC** injection in the upper arm, thigh, or abdomen; rotate injection sites. **Extended-release:** May be administered without regard to meals or time of day. Administer immediately after mixing. If a dose is missed, it should be administered only if the next regularly scheduled dose is due in 3 days or more. **N.B**. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hypersensitivity**: Serious hypersensitivity reactions have been reported; discontinue therapy. Serious injection-site reactions have been reported with use. • **Renal impairment**: Use is not recommended in patients with a CrCl <30 mL/minute or end-stage renal disease (ESRD). If used in renal transplant recipients, monitor for hypovolemia. **Renal effects:** Cases of acute renal failure and chronic renal failure exacerbation, including severe cases requiring hemodialysis, have been reported. Cases may be reversible by discontinuation. Risk factors include experiencing events that may affect hydration, including nausea, vomiting, and/or diarrhea and/or receiving medicinal products known to affect renal function/hydration status. **Gastrointestinal symptoms**: Symptoms may be dose-related and may decrease in frequency/severity with gradual titration and continued use. Use is not recommended in patients with severe gastrointestinal disease or gastroparesis. • **Pancreatitis**: Cases of acute pancreatitis have been reported; Monitor for signs and symptoms of pancreatitis (e.g. persistent severe abdominal pain that may radiate to the back). If pancreatitis is suspected, discontinue use. Resolution of pancreatitis has been observed with supportive treatment, but very rare cases of necrotizing or hemorrhagic pancreatitis and/or death have been reported. **Hypoglycemia**: When used in combination with sulfonylurea or insulin, consider lowering the dose of the sulfonylurea or insulin to reduce risk of hypoglycemia. • **Immunogenicity**: Patients may develop antibodies to Exenatide. If there is worsening glycemic control or failure to achieve target glycemic control, consider alternative antidiabetic therapy. Pediatric patients are at more risk. • **Rapid weight loss:** Rapid weight loss at a rate of > 1.5 kg per week has been reported in patients treated with Exenatide. Weight loss of this rate may have harmful consequences. Patients with rapid weight loss should be monitored for signs and symptoms of cholelithiasis.

	• **Drug-induced thrombocytopenia**: DITP is an immune-mediated reaction that is caused by drug-dependent platelet-reactive antibodies. These antibodies cause destruction of platelets in the presence of the sensitizing drug. • **Thyroid tumors:** Thyroid C-cell tumors have developed in animal studies with Exenatide extended release; it is not known if it causes thyroid C-cell tumors, including medullary thyroid carcinoma in humans. • **Appropriate use**: Not for use in patients with type 1 diabetes mellitus or diabetic ketoacidosis. • A reduction in systolic blood pressure and an increase in heart rate has been observed.
Storage	Store at 2°C to 8°C. **Before mixing powder with solvent:** May store for up to 4 weeks below 30 °C. **After mixing powder with solvent:** use immediately as a single dose. Do not freeze (discard if freezing occurs). Protect from light. **N.B**. Refer to manufacturer PIL if there are specific considerations.

Liraglutide

Generic Name	Liraglutide
Dosage form/strengths	Solution for S.C injection: 6 mg/mL
Route of Administration	SC
Pharmacologic Category	Antidiabetic Agent, Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist ATC: A10BJ02
Indications	**N.B**. Biological medicine should be prescribed and dispensed by brand name. ● Victoza**: Treatment of diabetes mellitus, type 2**: as an adjunct to diet and exercise for adults, adolescents, and children aged 10 years and above. ● Saxenda**: Chronic weight management**: Adjunct to other non-pharmacologic parameters in: ○ Adult patients with either: - An initial body mass index of ≥30 kg/m^2 - An initial body mass index of ≥27 kg/m^2 in the presence of at least 1 comorbidity (e.g. hypertension, type 2 diabetes mellitus, dyslipidemia) ○ Or in adolescents ≥12 years of age with body weight >60 kg and an initial body mass index corresponding to ≥30 kg/m^2
Dosage Regimen	**Diabetes mellitus, type 2** (Victoza) Initial S.C: 0.6 mg once daily for 1 week, then increase to 1.2 mg once daily; if optimal glycemic response is not achieved after an additional week of treatment, may increase further to 1.8 mg once daily. **Chronic weight management** (Saxenda): Initial S.C: 0.6 mg once daily; increased by 0.6 mg daily at weekly intervals to a target dose of 3 mg once daily or maximum tolerated dose.
Dosage Adjustment	**Dosing: Altered kidney function** Mild to moderate: No adjustments are necessary. CrCl ≤ 30 mL/minute: Use is not recommended. **Dosing: Hepatic impairment** No dosage adjustment is necessary; use with caution due to limited experience. Severe impairment: Use is not recommended.
Contra-indications	• Hypersensitivity to Liraglutide or any component of the formulation. • Medullary thyroid carcinoma or family history, or thyroid C-cell tumors. • Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
Adverse Drug Reactions	**>10%** • Cardiovascular: Increased heart rate (>10 bpm from baseline: 34%; >20 bpm from baseline: 5%). • Endocrine & metabolic: Hypoglycemia (monotherapy without type 2 diabetes: adolescents: 15%, adults: 2%; monotherapy with type 2 diabetes: adults: 13%; combination therapy with sulfonylurea: adults: 28%; severe hypoglycemia [requiring the assistance of another person] in combination therapy: adults: ≤2%).

	• Gastrointestinal: Constipation (adolescents: 5%; adults: 19%), diarrhea (adolescents and adults: 21% to 22%), gastroenteritis (adolescents and adults: 5% to 13%), nausea (adolescents and adults: 39% to 42%), vomiting (adolescents: 34%; adults: 16%). • Immunologic: Antibody development (adolescents: 12%; adults: 3%). • Local: Injection-site reaction (including erythema at injection site, injection site pruritus, rash at injection site) (1% to 14%). • Nervous system: Headache (14%). **1% to 10%** • Cardiovascular: Circulatory shock (≤1%), hypotension (≤1%), orthostatic hypotension (≤1%). • Dermatologic: Skin rash (adolescents: 3%). • Endocrine & metabolic: Altered hormone level (1%; increased serum calcitonin), dyslipidemia (adolescents: 5%). • Gastrointestinal: Abdominal distension (5%), abdominal distress (adolescents: 5%), abdominal pain (adults: 5%), cholelithiasis (2%), dyspepsia (adolescents and adults: 4% to 10%), eructation (5%), flatulence (adolescents and adults: 3% to 4%), gastroesophageal reflux disease (5%), increased serum lipase (adolescents and adults: 2% to 5%), upper abdominal pain (5%), viral gastroenteritis (3%), xerostomia (2%) • Genitourinary: Urinary tract infection (4%). • Nervous system: Asthenia (2%), depression (adolescents: 4%), dizziness (adolescents and adults: 7% to 10%), fatigue (adolescents and adults: 5% to 8%). • Neuromuscular & skeletal: Increased creatine phosphokinase in blood specimens (adolescents: 3%), limb pain (adolescents: 4%). • Respiratory: Cough (adolescents: 4%) • Miscellaneous: Fever (adolescents: 8%).
Monitoring Parameters	• Blood glucose, Glycosylated hemoglobin A1c (HbA1c). • Signs/symptoms of pancreatitis and gallbladder disease. • Weight. • Renal function (in patients reporting severe GI reactions).
Drug Interactions	***Risk X: Avoid combination*** Glucagon-Like Peptide-1 Agonists, Semaglutide. ***Risk D: Consider therapy modification*** Insulins, Meglitinides, Sincalide, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy**: Avoid use. No human data. Toxicity occurred in animal models. **Lactation**: Avoid. No human data.
Administration	• **Subcutaneous**: Inject in the abdomen, thigh, or upper arm. • Administer once daily at any time of day, independently of meals. **N.B**. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hazardous agent** (NIOSH 2016 [group 2]): Black Box warning for thyroid C-cell tumors, with supporting evidence in laboratory studies; also, in laboratory studies, teratogenic at or below the Maximum Recommended Human Dose (MRHD). • **Acute kidney injury:** May cause loss of fluids (dehydration) which may cause kidney problems to get worse. Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions.

	• **Gallbladder disease:** with high doses or long use**,** symptoms include pain in the right or middle upper stomach area, nausea and vomiting, fever, and yellowing of the white part of the eyes. Caution in patients with known gallbladder disease or a history of cholelithiasis. • **Hypersensitivity reactions:** Rapid or delayed**,** including anaphylaxis and angioedema. • **Medullary thyroid carcinoma:** Liraglutide may cause thyroid C-cell tumors at clinically relevant doses. Counsel patients regarding the potential risk of MTC with the use of Liraglutide and inform them of symptoms of thyroid tumors (e.g., mass in the neck, dysphagia, dyspnea, persistent hoarseness). • **Pancreatitis:** Discontinue if symptoms of acute pancreatitis occur, such as persistent, severe abdominal pain. • **Dizziness and fatigue:** may occur particularly in the first 3 months of treatment. Caution in driving and machinery use. • **Cardiovascular effects:** Increased resting heart rate has been observed in placebo-controlled trials; monitoring is recommended. No clinical experience in patients with congestive heart failure therefore not recommended for use in these patients. • **Severe gastrointestinal disease**: Gastrointestinal symptoms are the most common adverse reactions. Increased risk with higher doses and Rapid titration. Has not been studied in these patients including pre-existing gastroparesis therefore not recommended in these patients. • **Hepatic impairment and renal impairment:** Use with caution due to limited experience. A higher rate of cholelithiasis and cholecystitis was observed. • **Infection**: Should not be used for more than one person. Always remove the injection needle after each injection and store the pen without a needle attached to prevent the risk of infection. • **Diabetic Ketoacidosis:** Serious and life-threatening cases have been reported in patients on a combination of Liraglutide and insulin, particularly after discontinuation or rapid dose reduction of concomitant insulin. Stepwise dose reduction of insulin should be done with careful blood glucose self-monitoring.
Storage	• Store between 2°C to 8°C. • Do not freeze (discard if freezing occurs). Protect from heat and light. • After initial use of the pen, the pen can be stored for 30 days between (15°C to 30°C) or in a refrigerator (2°C to 8°C). **N.B**. Refer to manufacturer PIL if there are specific considerations.

Semaglutide

Generic Name	Semaglutide
Dosage form/strengths	• Solution for SC injection: 0.25 mg, 0.5 mg • Solution in prefilled pen: 1 mg. • Tablets: 3 mg, 7 mg, 14 mg.
Route of Administration	Oral, SC
Pharmacologic Category	Antidiabetic Agent, Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist. **ATC:** A10BJ06
Indications	N.B. Biological medicine should be prescribed and dispensed by brand name. Treatment diabetes mellitus, type 2. As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Dosage Regimen	**Adult dosing** **SC:** Initially 0.25 mg once weekly for 4 weeks, then increased by doubling in 4-week intervals up to 1 mg once weekly if necessary. **Oral**: Initially 3 mg once daily for 1 month, then increased to 7 mg once daily for at least 1 month, and then increased if necessary to 14 mg once daily, dose to be taken on an empty stomach.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** No dosage adjustment is necessary. Use caution when initiating or escalating doses. **Dosing: Hepatic Impairment: Adult** No dosage adjustment is necessary. Use with caution.
Contra-indications	• Hypersensitivity to Semaglutide or any component of the formulation. • Medullary thyroid carcinoma or family history, or thyroid C-cell tumors. • Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
Adverse Drug Reactions	**>10%** • Gastrointestinal: Abdominal pain (adolescents and adults: 6% to 20%), constipation (oral: 5% to 6%; SC: adolescents: 6%; adults: 3% to 24%), diarrhea (oral: 9% to 10%; SC: adolescents and adults: 9% to 30%), nausea (oral: 11% to 20%; SC: adolescents and adults: 16% to 44%), vomiting (oral: 6% to 8%; SC: adolescents: 36%, adults: 5% to 24%). • Nervous system: Fatigue (SC: 11%), headache (SC: adolescents and adults: 14% to 17%) • Respiratory: Nasopharyngitis (SC: adolescents: 12%). **1% to 10%** • Cardiovascular: Hypotension (SC: adolescents and adults: 1% to 2%; including orthostatic hypotension). • Dermatologic: Alopecia (SC: adolescents and adults: 3% to 4%), skin rash (SC: adolescents: 3%), urticaria (SC: adolescents: 3%). • Endocrine & metabolic: Diabetic retinopathy (complications: 3% to 7%; vitreous hemorrhage: 1%; hypoglycemia (SC: 2% to 6%), severe hypoglycemia (≤1%).

	• Gastrointestinal: Abdominal distension (2% to 7%), cholelithiasis (adolescents and adults: 0% to 4%) (See Table 6), decreased appetite (oral: 6% to 9%), dysgeusia (SC: ≤2%), dyspepsia (oral: 0.6% to 3%; SC: 3% to 9%), eructation (adolescents and adults: ≤7%), flatulence (1% to 6%), gastritis (2% to 4%), gastroenteritis (SC: adolescents and adults: 6% to 7%), gastroesophageal reflux disease (adolescents and adults: 2% to 5%), viral gastroenteritis (SC: 4%). • Genitourinary: Urinary tract infection (SC: adolescents: 4%). • Hepatic: Increased serum alanine aminotransferase (SC: adolescents: 3%). • Immunologic: Antibody development (≤3%). • Infection: Influenza (SC: adolescents: 3%). • Nervous system: Anxiety (SC: adolescents: 4%), dizziness (SC: adolescents and adults: 8%). • Neuromuscular & skeletal: Sprain (ligament: SC: adolescents: 4%). • Respiratory: Sinusitis (SC: adolescents: 4%).
Monitoring Parameters	• Blood glucose, Glycosylated hemoglobin A1c (HbA1c). • Renal function (in patients reporting severe GI reactions). • Signs/symptoms of pancreatitis. • Worsening diabetic retinopathy (in patients with a prior history).
Drug Interactions	***Risk X: Avoid combination*** Glucagon-Like Peptide-1 Agonists (e.g. Liraglutide, Dulaglutide), Tirzepatide. ***Risk D: Consider therapy modification*** Insulins, Meglitinides, Sincalide, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy**: Avoid. Toxicity in animal studies. Contraception should be used during use. **Lactation**: Avoid. No human data.
Administration	**Oral**: Tablets should be taken whole on an empty stomach, with a sip of water (up to half a glass, equivalent to 120 mL). Patients should wait at least 30 minutes after a dose before eating, drinking, or taking other oral medicines. Intake with food or large volumes of water decreases the absorption of Semaglutide. **SC**: Administer injection into the abdomen, thigh, or upper arm at any time of day on the same day each week, with or without food. Do not mix with other products. Rotate injection sites weekly. **N.B**. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Acute kidney injury:** may cause loss of fluids (dehydration) which may cause kidney problems to get worse. Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions • **Hypersensitivity reactions:** rapid or delayed**,** including anaphylaxis and angioedema. Discontinue and seek medical advice. • **Medullary thyroid carcinoma:** Semaglutide may cause thyroid C-cell tumors at clinically relevant doses. Counsel patients regarding the

	potential risk of MTC with the use of Semaglutide and inform them of symptoms of thyroid tumors (e.g., mass in the neck, dysphagia, dyspnea, persistent hoarseness). • **Pancreatitis:** Discontinue if symptoms of acute pancreatitis occur, such as persistent, severe abdominal pain. Do not restart if pancreatitis is confirmed • **Diabetic retinopathy:** Monitor patients with a history of diabetic retinopathy. Complications may occur. • **Cardiovascular effects:** Increased resting heart rate has been observed in placebo-controlled trials; monitoring is recommended. No clinical experience in patients with congestive heart failure therefore not recommended for use in these patients. • **Severe gastrointestinal disease**: Gastrointestinal symptoms are the most common adverse reactions. Risk with higher doses and Rapid titration. Has not been studied in these patients including pre-existing gastroparesis therefore not recommended in these patients. • **Severe hepatic impairment and renal impairment:** Use with caution due to limited experience. Semaglutide is not recommended for use in patients with end-stage renal disease. • **Infection**: Should not be used for more than one person. Always remove the injection needle after each injection and store the pen without a needle attached to prevent the risk of infection. • **Diabetic Ketoacidosis:** Serious and life-threatening cases have been reported in patients on a combination of the GLP-1 receptor Agonists and insulin, particularly after discontinuation or rapid dose reduction of concomitant insulin. Stepwise dose reduction of insulin should be done with careful blood glucose self-monitoring.
Storage	• **Injections**: Before initial use, store at 2°C to 8°C. • After initial use, store at 2°C to 8°C or 15°C to 30°C for up to 56 days; discard after 56 days. Do not freeze (discard if freezing occurs) or store directly adjacent to the refrigerator cooling element. Protect from excessive heat and sunlight. Keep the pen capped when not in use. • **Tablets**: store at 15°C to 30°C. Protect from moisture. **N.B**. Refer to manufacturer PIL if there are specific considerations.

Antidiabetic Agent, Meglitinides

Repaglinide

Generic Name	Repaglinide
Dosage Form/Strengths	Tablets: 0.5mg, 1mg, 2mg.
Route of Administration	*Oral*
Pharmacologic Category	Antidiabetic Agent, Meglitinide Analog ATC: A10BX02
Indications	**Diabetes mellitus, type 2, management in adults:** Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus that can no longer be controlled satisfactorily by diet, weight reduction and exercise. And Repaglinide is also used in combination with metformin in adults with type 2 diabetes mellitus who are not satisfactorily controlled on metformin alone.
Dosage Regimen	**Adult dosing** **Initial** *HbA_{1c} <8%:* **Oral:** 0.5 mg before main meals. *HbA_{1c} ≥8%:* **Oral:** 1 to 2 mg before main meals. Adjust dose with 1-2-week intervals. **Maintenance** Maximum recommended single dose: 4 mg taken before main meals. Maximum total daily dose: 16 mg. **Pediatrics**: Safety and effectiveness have not been established in pediatric patients.
Dosage Adjustment	**Renal impairment** Mild to moderate impairment: No dose adjutments needed. Caution. Severe renal impairment: start with 0.5 mg and carefully titrate dose. **Hepatic impairment** Caution, longer intervals between dose adjustments may be needed. Severe hepatic function: contraindicated.
Contra-Indications	• Hypersensitivity to repaglinide or to any of the excipients. • Concomitant use of gemfibrozil. • Severe hepatic function disorder. **N.B**. Not for treatment of diabetes mellitus type 1 or diabetic ketoacidosis, with or without coma.
Adverse Drug Reactions	**>10%** • **Central nervous system**: Headache (9% to 11%). • **Endocrine & metabolic**: Hypoglycemia (16% to 31%). • **Respiratory**: Upper respiratory tract infection (10% to 16%). **1% to 10%**

	• **Cardiovascular**: Ischemia (4%), chest pain (2% to 3%). • **Gastrointestinal**: Diarrhea (4% to 5%), constipation (2% to 3%). • **Genitourinary**: Urinary tract infection (2% to 3%). • **Hypersensitivity**: Hypersensitivity reaction (1% to 2%). • **Neuromuscular & skeletal**: Back pain (5% to 6%), arthralgia (3% to 6%). • **Respiratory**: Sinusitis (3% to 6%), bronchitis (2% to 6%).
Monitoring Parameters	Blood glucose. Glycosylated hemoglobin.
Drug Interactions	***Risk X: Avoid combination*** Ceftobiprole Medocaril, CYP2C8 Inhibitors (Strong) (e.g. gemfibrozil), Fexinidazole, Leniolisib, Taurursodiol. ***Risk D: Consider therapy modification*** Belumosudil, Bulevirtide, Clopidogrel, Cyclosporine (Systemic), Fusidic Acid (Systemic), Glucagon-Like Peptide-1 Agonists, Trofinetide.
Pregnancy and Lactation	**Pregnancy** Limited data. Not recommended. **Lactation** Limited data. Not recommended.
Administration	**Oral Admnisteration** Repaglinide should be taken before main meals (usually within 15 minutes of the meal, up to 4 meals of the day). Patients who skip a meal (or add an extra meal) should be instructed to skip (or add) a dose for that meal. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	• **Concomitant stress**: Loss of glycemic control may occur with stress such as fever, trauma, infection or surgery. Then, it may be necessary to temporarily discontinue repaglinide and treat with insulin. • **Acute coronary syndrome:** The use of repaglinide might be associated with an increased incidence of acute coronary syndrome (e.g. myocardial infarction). • **Serious cardiovascular adverse reactions with concomitant NPH-insulin**: Repaglinide is not indicated for use in combination with NPH-insulin. • **Concomitant medicines use**: Repaglinide should be used with caution or be avoided in patients receiving medicinal products that affect repaglinide metabolism or induce hypoglycemia or mask signs and symptoms of hypoglycemia. If concomitant use is necessary, close monitoring of blood glucose should be performed.
Storage	Store between 15 to 30 °C. Protect from light and moisture. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Antidiabetic Agent, Sodium-glucose Cotransporter 2 (SGLT2) Inhibitors

Canagliflozin

Generic Name	Canagliflozin
Dosage Form/Strengths	Tablets: 100 mg, 300 mg
Route of Administration	*Oral*
Pharmacologic Category	Antidiabetic Agent, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitor. ATC: A10BK02
Indications	• As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. • To reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease. • To reduce the risk of end-stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria.
Dosage Regimen	**Adult dosing** **Initial**: Oral: 100 mg once daily taken before the first meal of the day. Dose can be increased to 300 mg once daily in patients with CrCl ≥ 60 mL/min and need more glycemic control. **Pediatrics:** The safety and efficacy of canagliflozin in children under 18 years of age have not yet been established.
Dosage Adjustment	**Renal Impairment** **CrCl ≥ 60 (mL/min):** Initiate with 100 mg. Dose can be increased to 300 mg if patients tolerate the initial dose and require additional glycemic control. **CrCl 30 to < 60 (mL/min):** Use 100 mg. **CrCl < 30 (mL/min):** Continue 100 mg for patients already taking canagliflozin. but should not be initiated. **Hepatic Impairment** **Mild or moderate hepatic impairment**: No dose adjustment is required. **Severe hepatic impairment**: Not studied. Not recommended for use in these patients.
Contra-Indications	• Hypersensitivity to the active substance or to any of the excipient.
Adverse Drug Reactions	**>10%** **Infection**: Genitourinary fungal infection (females: 11% to 12%; males: 4%; patients who developed infections were more likely to experience recurrence). **1% to 10%** **Cardiovascular**: Hypotension (3%) **Endocrine & metabolic**: Hypoglycemia (4%), hypovolemia (2% to 3%), increased serum potassium (eGFR 45 to <60 mL/minute/1.73 m^2: >5.4 mEq/L: 5% to 9%; ≥6.5 mEq/L: 1%), increased thirst (2% to 3%) **Gastrointestinal**: Abdominal pain (2%), constipation (2%). **Genitourinary**: Increased urine output (5%), urinary tract infection (6%), vulvovaginal pruritus (2% to 3%).

	Hematologic & oncologic: Increased hemoglobin (3% to 4%). **Hypersensitivity**: Hypersensitivity reaction (4%; severe hypersensitivity reaction: <1%). **Nervous system:** Asthenia (1%), falling (2%). **Neuromuscular & skeletal**: Limb injury (toe, foot, lower limb amputations: 2% to 4%).
Monitoring Parameters	• Renal function (baseline and periodically during treatment) • Volume status (blood pressure, hematocrit, risk of volume depletion): correct prior to initiation. • Monitor for genital mycotic infections and urinary tract infection; assess patients presenting with fever or malaise along with genital or perianal pain, tenderness, erythema, or swelling for necrotizing fasciitis; • Signs/symptoms of ketoacidosis (eg, nausea/vomiting, abdominal pain, malaise, shortness of breath), confirm diagnosis by direct measurement of blood ketones. • Blood glucose. • Glycosylated hemoglobin A1c (HbA1c). • Serum cholesterol profile.
Drug Interactions	***Risk D: Consider therapy modification*** Fosphenytoin, Insulins, Phenobarbital, Phenytoin, Primidone, Rifampin, Ritonavir, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy**: No human data. Reproductive toxicity in animals. Canagliflozin should not be used during pregnancy. Discontinue if pregnancy detected. **Lactation:** No human data. Canagliflozin should not be used during lactation.
Administration	**Oral Administeration** Taken orally once a day preferably before the first meal of the day. Tablets should be swallowed whole. If a dose is missed, it should be taken as soon as the patient remembers; however, a double dose should not be taken on the same day. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	• **Volume depletion:** Canagliflozin increases glucose urinary excretion and induces an osmotic diuresis. That may cause volume depletion and adverse reactions including postural dizziness, orthostatic hypotension, or hypotension**.** Caution**.** *Risk factors* are: Kidney impairment, elderly, concomitant use of diuretics or antihypertensive, initial low systolic blood pressure, low oral fluid intake or increased loss. • **Diabetic ketoacidosis:** Rare cases of diabetic ketoacidosis (DKA), including life-threatening and fatal cases, have been reported in patients treated with SGLT2 inhibitors To minimize risk, follow these advices: ○ Inform patients of the signs and symptoms of DKA, (including rapid weight loss, nausea or vomiting, abdominal pain, fast and deep breathing, sleepiness, a different breath smell, metallic taste), and advise them to seek immediate medical advice if they develop any of these signs.

	○ Test for raised ketones in patients with signs and symptoms of DKA, even if plasma glucose levels are near-normal ○ Use canagliflozin with caution in patients with moderate to severe low renal functions who require insulin. ○ Patients who may be at higher risk of DKA include patients with a low beta-cell function reserve, restricted food intake or severe dehydration, patients for whom insulin doses are reduced and patients with increased insulin requirements due to acute medical illness, surgery or alcohol abuse. SGLT2 inhibitors should be used with caution in these patients. ○ Discontinue treatment if DKA is suspected or diagnosed. ○ Do not restart treatment with any SGLT2 inhibitor in patients who experienced DKA during use, unless another cause for DKA was identified and resolved. • **Renal impairment**: Glycemic efficacy may be decreased in patients with renal impairment. • **Older adults**: Older adults may be predisposed to renal impairment or failure. • **Appropriate use**: Not for use in patients with diabetic ketoacidosis or patients with type 1 diabetes mellitus. • **Surgical procedures**: In patients with diabetes mellitus, consider temporary discontinuation at least 3 days prior to surgery; ensure risk factors for ketoacidosis are resolved prior to reinitiating therapy. • **Infection:** Associated with an increased risk of urinary tract infections (sometimes severe) or genital fungal Infections have occurred. Monitor symptoms and treat promptly. Discontinue therapy if any of the following occur: signs and symptoms of new infection (including osteomyelitis), new pain or tenderness, or sores/ulcers involving the lower limbs. • **Fournier's Gangrene:** Necrotizing fasciitis of the perineum is rare but serious and potentially life-threatening event. Either uro-genital infection or perineal abscess may precede necrotizing fasciitis. If Fournier's gangrene is suspected, canagliflozin should be discontinued and prompt treatment (including antibiotics and surgical intervention) should be taken. Patient should be informed to seek medical advice in case symptoms of severe pain, tenderness, erythema, or swelling in the genital or perineal area, accompanied by fever or malaise. • Increases in Low-Density Lipoprotein Cholesterol (LDL-C) and non-High-Density Lipoprotein Cholesterol (non-HDL-C) were observed with canagliflozin in a dose-related manner. • Decreases in Bone Mineral Density: Consider factors that contribute to bone fracture risk before initiating canagliflozin.
Storage	Store between 15°C to 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Dapagliflozin: Refer to CVS Formulary.

Empagliflozin: Refer to CVS Formulary.

Antidiabetic Agent, Sulfonylureas

Glibenclamide

Generic Name	Glibenclamide
Dosage form/strengths	Tablets: 5 mg. Scored Tablet: 5 mg. And in combination (as 2.5 or 5mg).
Route of Administration	*Oral*
Pharmacologic Category	Antidiabetic Agent, Sulfonylurea ATC: A10BB01
Indications	**Diabetes mellitus, type 2:** Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Dosage Regimen	**Diabetes mellitus, type 2, treatment (alternative agent)** **Note:** May be used as an adjunctive agent or alternative monotherapy for patients in whom initial therapy with lifestyle intervention and metformin failed **or** who cannot take metformin. **Diabetes mellitus, type 2:** Oral - *Initial*: 2.5 to 5 mg/day given normally as a single dose, administered with breakfast or the first main meal of the day. - *Dosage adjustment:* Increase in increments of 2.5 mg-5mg at weekly intervals based on the patient's blood glucose response. - The total daily dosage rarely exceeds 15mg.
Dosage Adjustment	**Elderly, debilitated, or malnourished patients:** initiate with one 2.5mg tablet daily to avoid hypoglycemia. **Dosing: Altered Kidney Function: Adult** Initial and maintenance dosing should be conservative to avoid hypoglycemic reactions. Severe impairment: Avoid use. **Dosing: Hepatic Impairment: Adult** initial and maintenance dosing should be conservative to avoid hypoglycemic reactions. Severe impairment: Avoid use.
Contra-indications	• Hypersensitivity to Glibenclamide or any component of the formulation. • Diabetic ketoacidosis. • Type 1 diabetes mellitus. • Severe impairment of renal, hepatic.
Adverse Drug Reactions	**1% to 10%** • Gastrointestinal: Epigastric fullness (≤2%), heartburn (≤2%), nausea (≤2%). • Hypersensitivity: Hypersensitivity reaction (2%; including erythema, maculopapular rash, morbilliform rash, pruritus, urticaria). **Frequency not defined** • Central nervous system: Disulfiram-like reaction. • Endocrine & metabolic: Hypoglycemia, hyponatremia, weight gain. • Genitourinary: Diuresis (minor).

	• Hematologic & oncologic: Hemolytic anemia. • Hepatic: Cholestatic jaundice, hepatic failure, hepatitis.
Monitoring Parameters	• Blood glucose, signs and symptoms of hypoglycemia. • Glycosylated hemoglobin A1c (HbA1c). • Renal and hepatic functions (baseline for all patients, then periodically in patients with mild-moderate dysfunction).
Drug Interactions	***Risk X: Avoid combination*** Aminolevulinic Acid (Systemic), Bosentan, Leniolisib, Mecamylamine, Mitiglinide**.** ***Risk D: Consider therapy modification*** Alpha-glucosidase inhibitors, Colesevelam, Dipeptidyl Peptidase -IV Inhibitors, Glucagon-Like Peptide-1 Agonists, Metreleptin, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors, Thiazolidinediones.
Pregnancy and Lactation	**Pregnancy**: No human data. Sulfonylureas are not recommended for patients with type 2 diabetes mellitus planning to become pregnant. **Lactation:** Not recommended due to the potential hypoglycemia in infants.
Administration	**Administration: Oral** Administer with meals at the same time each day. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hypoglycemia**: All sulfonylurea drugs are capable of producing severe hypoglycemia. It is also more likely in elderly patients, malnourished or debilitated patients, and in patients with severe renal and hepatic impairment, adrenal and/or pituitary insufficiency; use with caution. • **Hemolytic Anemia**: Treatment of patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency with sulfonylurea agents can lead to hemolytic anemia. Caution and consider a non-sulfonylurea alternative. • **Awareness: Patients** should be informed about the importance of adherence to dietary instructions, of a regular exercise program, and of regular testing of glucose levels. • **Hypersensitivity reactions**: Rashes, pruritus and photosensitivity. Severe manifestations of hypersensitivity include cholestatic jaundice, leucopenia, thrombocytopenia, aplastic anemia, agranulocytosis, hemolytic anemia, erythema multiforme, Stevens-Johnson syndrome and exfoliative dermatitis. • **Weight gain**: Increased appetite and weight gain may occur. • **Renal impairment**: The metabolism and excretion may be slowed and may accumulate in advanced renal insufficiency. Use is not recommended in chronic kidney disease. • **Porphyria and photosensitivity reactions:** have been reported with sulfonylureas. • **Blood and lymphatic system disorders**: Rare reports of anemia, thrombocytopenia, leucopenia and granulocytopenia. Reversible on discontinuation.
Storage	Store between 15°C and 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Gliclazide

Generic Name	Gliclazide
Dosage form/strengths	Tablets: 40mg, 80mg Modified Release Capsules: 30mg Modified release tablets: 30mg, 60mg, 80
Route of Administration	Oral
Pharmacologic Category	Antidiabetic Agent, Sulfonylurea. ATC: A10BB09
Indications	**Diabetes mellitus, type 2, treatment:** Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Dosage Regimen	**Dosing: Adult** *Immediate-release tablet* **Oral:** Initial: 40 to 80 mg once daily with the first main meal *Dosage adjustment:* May increase the dose in 40 to 80 mg increments every 1 to 4 weeks if needed to achieve glycemic goals; usual maintenance dose: 40 to 160 mg/day (maximum: 320 mg/day). **Note:** Administer doses ≥160 mg/day in 2 divided doses. *Modified-release tablet* **Oral:** Initial: 30 mg once daily with the first main meal. *Dosage adjustment:* May increase the dose in 30 mg increments every 1 to 4 weeks if needed to achieve glycemic goals; usual maintenance dose: 30 to 60 mg/day (maximum: 120 mg/day). *Switching between different forms of* tablets • 1 tablet of 80 mg *immediate release* is comparable to 1 tablet of 30 mg modified release Tablets. Switch with careful blood monitoring. • When switching from a hypoglycemic sulfonylurea with a prolonged half-life, a treatment-free period of a few days may be necessary to avoid an additive effect of the two products, which might cause hypoglycemia. **Pediatrics**: The safety and efficacy of Gliclazide in children and adolescents have not been established.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** Mild to moderate impairment: No dosage adjustment necessary. Use with caution with close monitoring. Severe impairment: Use is contraindicated. **Dosing: Hepatic Impairment: Adult** Mild to moderate impairment: No dosage adjustment necessary. Use with caution with close monitoring. Severe impairment: Use is contraindicated.
Contra-indications	• Hypersensitivity to Gliclazide, other sulfonylureas or sulfonamides, or any component of the formulation. • Type 1 diabetes mellitus. • Diabetic ketoacidosis. • Severe renal or hepatic impairment.

Adverse Drug Reactions	**>10%:** Endocrine & metabolic: Hypoglycemia (11% to 12%). **1% to 10%** • Cardiovascular: Hypertension (3% to 4%), angina pectoris (2%), peripheral edema (1%). • Central nervous system: Headache (4% to 5%), dizziness (2%), depression (1% to 2%), insomnia (1% to 2%), neuralgia (≤1%). • Dermatologic: Dermatological disorders (2%), dermatitis (1% to 2%), skin rash (1%; includes maculopapular rash, morbilliform rash), pruritus (≤1%). • Endocrine & metabolic: Hyperglycemia (2%), hyperlipidemia (≤1%), lipid metabolism disorder (≤1%). • Gastrointestinal: Diarrhea (2% to 3%), constipation (1% to 2%), gastroenteritis (1% to 2%), abdominal pain (1%), gastritis (1%), nausea (≤1%). • Genitourinary: Urinary tract infection (3%). • Infection: Viral infection (6% to 8%). • Neuromuscular & skeletal: Back pain (4% to 5%), arthralgia (3% to 4%), asthenia (2% to 3%), arthropathy (2%), myalgia (2%), arthritis (1% to 2%), tendinopathy (1%) • Ophthalmic: Conjunctivitis (1%). • Otic: Otitis media (≤1%). • Respiratory: Bronchitis (4% to 5%), rhinitis (4% to 5%), pharyngitis (4%), upper respiratory tract infection (3% to 4%), cough (2%), pneumonia (1% to 2%), sinusitis (1% to 2%).
Monitoring Parameters	• Blood glucose, Signs and symptoms of hypoglycemia. • Glycosylated hemoglobin A1c (HbA1c). • Renal and hepatic functions (baseline for all patients, then periodically in patients with mild-moderate dysfunction).
Drug Interactions	***Risk X: Avoid combination*** Aminolevulinic Acid (Systemic), Mecamylamine, Mitiglinide. ***Risk D: Consider therapy modification*** Alpha-glucosidase inhibitors, Dipeptidyl Peptidase-IV Inhibitors, Glucagon-Like Peptide-1 Agonists, Metreleptin, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors (e.g. Canagliflozin, Dapagliflozin, Empagliflozin), Thiazolidinediones. **Notes** **Fluoroquinolones:** in case of concomitant use with fluoroquinolone, patients should be warned of the risk of dysglycemia (hypoglycemia and hyperglycemia), and the importance of monitoring blood glucose should be emphasized. **Anticoagulant therapy (e.g. Warfarin):** Sulfonylureas may lead to potentiation of anticoagulation. **Miconazole** (systemic or oromucosal gel) is not recommended due to the risk of hypoglycemia.
Pregnancy and Lactation	**Pregnancy**: No human data. Sulfonylureas are not recommended for patients with type 2 diabetes mellitus planning to become pregnant. **Lactation:** Not recommended due to the potential for hypoglycemia in infant.
Administration	Administer with meals (modified-release tablet should be administered with

	breakfast). **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hypoglycemia**: All sulfonylurea drugs are capable of producing severe hypoglycemia. It is also more likely in elderly patients, malnourished or debilitated patients, and in patients with severe renal and hepatic impairment, adrenal and/or pituitary insufficiency; use with caution. • **Hemolytic Anemia**: Treatment of patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency with sulfonylurea agents can lead to hemolytic anemia. Caution and consider a non-sulfonylurea alternative. • **Awareness: Patients** should be informed about the importance of adherence to dietary instructions, of a regular exercise program, and of regular testing of glucose levels. • **Hypersensitivity reactions**: Rashes, pruritus, and photosensitivity. Severe manifestations of hypersensitivity include cholestatic jaundice, leucopenia, thrombocytopenia, aplastic anemia, agranulocytosis, hemolytic anemia, erythema multiforme, Stevens-Johnson syndrome, and exfoliative dermatitis. • **Renal impairment**: The metabolism and excretion may be slowed and may accumulate in advanced renal insufficiency. Use is not recommended in severe kidney disease. • **Hepato-biliary disorders**: Cholestasis, jaundice, and hepatitis have been reported rarely; • Discontinue treatment if cholestatic jaundice appears. These symptoms usually disappear after discontinuation of treatment. • **Blood and lymphatic system disorders**: Rare reports of anemia, thrombocytopenia, leukopenia, and granulocytopenia. Reversible on discontinuation. • **Lactose intolerance**: Some formulations may contain lactose; avoid use in patients with galactose intolerance, glucose-galactose malabsorption, or congenital lactose deficiency.
Storage	Store between 15°C to 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations.

Glimepiride

Generic Name	Glimepiride
Dosage form/strengths	Tablet: 1 mg ,2 mg, 3 mg, 4 mg, 6mg And in combination
Route of Administration	Oral
Pharmacologic Category	Antidiabetic Agent, Sulfonylurea ATC: A10BB12
Indications	**Diabetes mellitus, type 2, treatment:** As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Dosage Regimen	**Dosing: Adult** **Diabetes mellitus, type 2, treatment** **Oral** Initial: 1 to 2 mg once daily, administered with breakfast or the first main meal. Titration: If adequate glycemic control is not obtained, may increase the dose in 1 to 2 mg increments no more frequently than every 1 to 2 weeks. Maximum: 8 mg/day. **Dosing: Pediatrics**: The available data on safety and efficacy are insufficient in the pediatric population and therefore such use is not recommended.
Dosage Adjustment	**Dosing: Renal Impairment: Adult** Initial: 1 mg once daily; dose titration and maintenance dosing should be conservative to avoid hypoglycemia. Consider alternative therapy if eGFR <15 mL/minute/1.73 m^2. **Dosing: Hepatic Impairment: Adult** Dosage adjustments have not been studied. Initial: 1 mg once daily. Titrate carefully due to the potential for increased hypoglycemia in patients with hepatic impairment.
Contra-indications	• Hypersensitivity to Glimepride, other sulfonylureas or sulfonamides, or any component of the formulation. • Diabetic ketoacidosis. • Diabetes mellitus type 1. • Severe renal or hepatic impairment.
Adverse Drug Reactions	**>10%:** Endocrine & metabolic: Hypoglycemia (4% to 20%). **1% to 10%** • Central nervous system: Dizziness (2%), headache. • Gastrointestinal: Nausea (5%). • Hepatic: Increased serum ALT (2%). • Respiratory: Flu-like symptoms (5%). • Miscellaneous: Accidental injury (6%).
Monitoring Parameters	• Blood glucose, Signs and symptoms of hypoglycemia. • Glycosylated hemoglobin A1c (HbA1c). • Renal and hepatic functions (baseline for all patients, then periodically in patients with mild-moderate dysfunction).

Drug Interactions	***Risk X: Avoid combination*** Aminolevulinic Acid (Systemic), Mitiglinide, Mecamylamine. ***Risk D: Consider therapy modification*** Alpha-Glucosidase Inhibitors, Colesevelam, Dipeptidyl Peptidase-IV Inhibitors, Glucagon-Like Peptide-1 Agonists, Metreleptin, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors, Thiazolidinediones.
Pregnancy and Lactation	**Pregnancy**: No human data. Sulfonylureas are not recommended for patients with type 2 diabetes mellitus planning to become pregnant. **Lactation:** Not recommended due to the potential for hypoglycemia in infants.
Administration	**Administration: Oral** Administer once daily shortly before or during breakfast or the first main meal of the day. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hypoglycemia**: All sulfonylurea drugs are capable of producing severe hypoglycemia. It is also more likely in elderly patients, malnourished or debilitated patients, and in patients with severe renal and hepatic impairment, adrenal and/or pituitary insufficiency; use with caution. • **Hemolytic Anemia**: Treatment of patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency with sulfonylurea agents can lead to hemolytic anemia. Caution and consider a non-sulfonylurea alternative. • **Awareness: Patients** should be informed about the importance of adherence to dietary instructions, of a regular exercise program, and of regular testing of glucose levels. • **Hypersensitivity reactions**: Rashes, pruritus and photosensitivity. Severe manifestations of hypersensitivity include cholestatic jaundice, leucopenia, thrombocytopenia, aplastic anemia, agranulocytosis, hemolytic anemia, erythema multiforme, Stevens-Johnson syndrome and exfoliative dermatitis. • **Weight gain**: Increased appetite and weight gain may occur. • **Renal impairment**: The metabolism and excretion may be slowed and may accumulate in advanced renal insufficiency. Use is not recommended in severe kidney disease. • **Hepato-biliary disorders**: Cholestasis, jaundice, and hepatitis have been reported rarely; • Discontinue treatment if cholestatic jaundice appears. These symptoms usually disappear after discontinuation of treatment. • **Blood and lymphatic system disorders**: Rare reports of anemia, thrombocytopenia, leukopenia, and granulocytopenia. Reversible on discontinuation. • **Cytochrome P450 2C9 (CYP2C9**). Glimepiride metabolism is known to be influenced by the concomitant administration of CYP2C9 inducers (e.g. Rifampicin) or inhibitors (e.g. Fluconazole).
Storage	Store between 15°C and 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Glipizide

Generic Name	Glipizide
Dosage Form/Strengths	Tablets: 5mg. And in combination with metformin.
Route of Administration	*Oral*
Pharmacologic Category	**Antidiabetic Agent, Sulfonylurea** **ATC:** A10BB07
Indications	**Diabetes mellitus, type 2, management in adults:** Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Dosage Regimen	**Adult dosing** **Initial: Oral**: 5 mg daily, given before breakfast or lunch. Mild diabetics, elderly, renal or liver disease patients may start at 2.5 mg. Then adjust based on response of blood glucose levels with several days-intervals. **Maximum recommended single dose** is 15 mg (split dosing if higher doses needed). If insufficient response, splitting the daily doses may be effective. **Pediatric dosing** No data. The safety and efficacy in children and adolescents has not been established.
Dosage Adjustment	**Renal Impairment** May start at conservative doses due to risk of hypoglycemia**.** Severe impairment: Contraindicated. **Hepatic Impairment** May start at conservative doses due to risk of hypoglycemia. Severe impairment: Contraindicated.
Contra-Indications	• Hypersensitivity to the active substance, other sulfonylureas or sulfonamides or to any of the excipients. • Type 1 diabetes mellitus. • Diabetic ketoacidosis. • Severe renal, hepatic or thyroid impairment. • Pregnancy and lactation.
Adverse Drug Reactions	**1% to 10%** **Endocrine & metabolic**: Hypoglycemia (3%). **Gastrointestinal**: Abdominal pain (1%), constipation (<3%), diarrhea (1% to 5%), dyspepsia (<3%), flatulence (3%), nausea (<3%), vomiting (<3%). **Hypersensitivity**: Hypersensitivity reaction (<2%; including eczema, erythema of skin, maculopapular rash, morbilliform rash, pruritus, urticaria). **Nervous system**: Dizziness (2% to 7%), drowsiness (2%), headache (2%), nervousness (4%), tremor (4%). **Frequency not defined**

	Endocrine & metabolic: Increased lactate dehydrogenase. **Hepatic**: Increased serum alkaline phosphatase, increased serum aspartate aminotransferase. **Renal**: Increased blood urea nitrogen, increased serum creatinine.
Monitoring Parameters	• Blood glucose, signs and symptoms of hypoglycemia. • Glycosylated hemoglobin A1c (HbA1c). • Renal and hepatic functions (baseline for all patients, then periodically in patients with mild-moderate dysfunction).
Drug Interactions	***Risk X: Avoid combination*** Aminolevulinic Acid (Systemic), Mecamylamine, Miconazole, Mitiglinide. ***Risk D: Consider therapy modification*** Alpha-Glucosidase Inhibitors (Acarbose), Colesevelam, Dipeptidyl Peptidase-IV Inhibitors (gliptins), Glucagon-Like Peptide-1 Agonists, Metreleptin, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors (e.g., canagliflozin, dapagliflozin, and empagliflozin), Thiazolidinediones (rosiglitazone, pioglitazone). **Note**: Caution during coadministeration of drugs that may increase level of sulphonylurea or increase in hypoglycaemic effect such as NSAIDs, salicylates, angiotensin-converting enzyme inhibitors, cimetidine, fluconazole, monoamine oxidase inhibitors, voriconazole. **Antiadrenergic Drugs** (e.g., beta-blockers) may mask the symptoms of hypoglycemia.
Pregnancy and Lactation	**Pregnancy:** Contraindicated**.** Mildly fetotoxic in rat reproductive studies**.** Insulin is the drug of choice during pregnancy for treatment of diabetes**.** **Lactation**: No data. Contraindicated during breastfeeding due to risk of neonatal hypoglycemia.
Administration	**Oral**: Tablets to be taken 30 minutes before a meal. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	**Hypoglycemia**: All sulfonylurea drugs are capable of producing severe hypoglycemia. It is also more likely in elderly patients, malnourished or debilitated patients, and in patients with severe renal and hepatic impairment, adrenal and/or pituitary insufficiency; use with caution. **Hemolytic Anemia**: Treatment of patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency with sulfonylurea agents can lead to hemolytic anemia. Caution and consider a non-sulfonylurea alternative. **Stress-related states**: It may be necessary to discontinue therapy due to lower effectiveness and administer insulin if the patient is exposed to stress (fever, trauma, infection, surgery). **Awareness:** Patients should be informed about the importance of adherence to dietary instructions, of a regular exercise program, and of regular testing of glucose levels.
Storage	Store between 15- 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Antidiabetic Agent, Thiazolidinedione

Pioglitazone

Generic Name	Pioglitazone
Dosage Form/Strengths	Tablets: 15 mg, 30 mg, 45 mg.
Route of Administration	*Oral*
Pharmacologic Category	Antidiabetic Agent, Thiazolidinedione. ATC: A10BG03
Indications	Improvent of glycemic control in adults with type 2 diabetes mellitus as an adjunct to diet and exercise (as second or third line). May be combined with insulin in type 2 diabetes mellitus adult patients with insufficient glycemic control on insulin for whom metformin is inappropriate
Dosage Regimen	**Adult dosing** **Initial: Oral:** 15 or 30mg once daily. May be increased up to 45mg once daily if needed. Patients should be reviewed after 3 to 6 months to assess adequacy of response to treatment (e.g. reduction in HbA1c). Pioglitazone should be discontinued, if no adequate response. **Pediatrics:** Safety and efficacy of pioglitazone in pediatric patients have not been established.
Dosage Adjustment	**Renal Impairment** No dose adjustments needed. Dialyzed patients: No data. Use is not recommended. **Hepatic Impairment** Use is not recommended.
Contra-Indications	• Hypersensitivity to the active substance or to any of the excipients. • Cardiac failure or history of cardiac failure (NYHA stages I to IV). • Hepatic impairment. • Diabetic ketoacidosis. • Current bladder cancer or a history of bladder cancer. • Uninvestigated macroscopic haematuria.
Adverse Drug Reactions	**>10%** • **Cardiovascular**: Edema (3% to 27%; including exacerbation of edema). • **Endocrine and metabolic**: Hypoglycemia (27%). • **Respiratory**: Upper respiratory tract infection (13%). **1% to 10%** • **Cardiovascular**: Heart failure (8%; including worsening of heart failure). • **Nervous system**: Headache (9%). • **Neuromuscular & skeletal**: Back pain (6%), bone fracture (females: 5%; males: 2%), myalgia (5%). • **Respiratory**: Pharyngitis (5%), sinusitis (6%).
Monitoring Parameters	• Bloos glucose and glycosylated hemoglobin. • Baseline liver disease. Pioglitazone should not be initiated if ALT > 2.5 X

	upper limit of normal) or with any other evidence of liver disease. • Periodic liver enzymes monitoring based on clinical judgement. therapy should be discontinued if ALT levels remained at > 3 X the upper limit. • Monitor patients for signs of heart failure (e.g., excessive, rapid weight gain, dyspnea, and/or edema).
Drug Interactions	***Risk D: Consider therapy modification.*** CYP2C8 Inhibitors (e.g. gemfibrozil), Insulins, Sulfonylureas.
Pregnancy and Lactation	**Pregnancy** Limited data. Foetal growth restriction was apparent in animal studies. Use is not recommended. **Lactation** No data. Use is not recommended.
Administration	**Oral Administeration**: Pioglitazone tablets are taken orally once daily with or without food, and swallowed with a glass of water. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	**Fluid retention and cardiac failure**: Pioglitazone can cause fluid retention, which may exacerbate or precipitate heart failure. For patients with at least one risk factor (e.g. prior myocardial infarction or symptomatic coronary artery disease or the elderly), physicians should start with the lowest dose and increased gradually. Concomitant administration with insulin may increase the risk of oedema. **Bladder cancer**: May increase the risk of bladder cancer. Advise patients to promptly seek the medical advice if macroscopic hematuria or other symptoms such as dysuria or urinary urgency develop during treatment. **Hepatic effects**: Postmarketing reports of hepatic failure, sometimes fatal. If liver injury is detected, promptly interrupt and do not restart if no other probable cause. **Fractures**: Increased incidence in female patients. Apply standards of care with the long-term use for assessing and maintaining bone health. **Weight gain:** A dose related weight gain is observed, which may be due to fat accumulation and in some cases associated with fluid retention. Careful monitoring is needed as it may be a sign of heart failure. **Macular edema**: Postmarketing reports. Recommend regular eye exams in all patients with diabetes according to current standards of care with evaluation for acute visual changes.
Storage	Store between 15 and 30°C. Protect from moisture. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Antithyroid Agent, Sulfur-containing Imidazoles

Carbimazole

Generic Name	Carbimazole
Dosage form/strengths	Tablet 5mg
Route of Administration	Oral
Pharmacologic Category	Antithyroid Agent. ATC: H03BB01
Indications	**Anti-thyroid agents** in adults and children in all conditions where reduction of thyroid function is required, such as: hyperthyroidism, preparation for thyroidectomy in hyperthyroidism, and therapy before and concomitant with radio-iodine treatment.
Dosage Regimen	**Dosing: Adult** **Hyperthyroidism** Oral: Initial: 20 to 60 mg/day given in 2 to 3 divided doses. Continue until the patient becomes euthyroid usually after 4 to 8 weeks. Maintenance: Usual maintenance dose: 5 to 15 mg once daily; adjust dose as needed. continue until the patient becomes euthyroid, reduce the dose gradually, therapy is usually given for 12 to 18 months. **Dosing: Pediatric** **Hyperthyroidism:** Children ≥3 years and Adolescents: Oral: Initial: 15 mg/day; adjust dose according to the response.
Dosage Adjustment	**Dosing: Renal Impairment** There are no dosage adjustments needed. Use caution (half-life may be prolonged). Hemodialysis: Administer post-dialysis due to low protein binding. **Dosing: Hepatic Impairment** **Pre-existing impairment** Mild to moderate hepatic impairment: There are no dosage adjustments needed, use caution (half-life may be prolonged). Severe hepatic impairment: Use is contraindicated. **Hepatotoxicity during treatment:** Discontinue therapy with any signs/symptoms of hepatotoxicity (e.g. upper abdomen pain, anorexia, generalized pruritus) or abnormal hepatic function tests.
Contra-indications	• Hypersensitivity to Carbimazole or any component of the formulation. • Severe blood disorders. • Severe hepatic impairment.
Adverse Drug Reactions	Adverse reactions usually occur in the first eight weeks of treatment. **The most frequently occurring reactions:** Nausea, headache, arthralgia, mild gastric distress, skin rashes and pruritus. These reactions are usually self-limiting and may not require withdrawal of the drug.

	• **Blood and lymphatic system disorders**: Bone marrow depression including neutropenia, eosinophilia, leukopenia and agranulocytosis. Rare cases of pancytopenia/aplastic anemia and thrombocytopenia. Very rare cases of hemolytic anemia have been reported. • **Immune system disorders**: Angioedema and multi-system hypersensitivity reactions such as cutaneous vasculitis, liver, lung and renal effects occur. • Endocrine disorders: Insulin autoimmune syndrome (with pronounced decline in blood glucose level). • **Nervous system disorders**: Headache, neuritis, polyneuropathy. • **Vascular disorders**: Bleeding. • **Gastrointestinal disorders**: Nausea, mild gastrointestinal disturbance. Loss of sense of taste has been observed. Acute salivary gland swelling Acute pancreatitis. • **Hepatobiliary disorders**: Hepatic disorders, including abnormal liver function tests, hepatitis, cholestatic, hepatitis, cholestatic jaundice and most commonly jaundice, have been reported; in these cases, Carbimazole tablets should be withdrawn. • **Skin and subcutaneous tissue disorders**: Skin rashes, pruritus, urticaria. Hair loss has been occasionally reported. Severe cutaneous hypersensitivity reactions have been reported in both adult and pediatric patients, including Stevens-Johnson syndrome. • **Musculoskeletal and connective tissue disorders**: Isolated cases of myopathy have been reported. Patients experiencing myalgia after the intake of Carbimazole should have their creatine phosphokinase levels monitored. • General disorders and administration site conditions: Fever, malaise, Bruising.
Monitoring Parameters	• CBC with differential (baseline and when clinical evidence of infection). • Liver function test at baseline and if symptoms of liver injury occur. • Prothrombin time (periodically and prior to surgery). • Thyroid function tests. • Creatine kinase (as clinically indicated).
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cladribine, Dipyrone, Sodium Iodide I131. ***Risk D: Consider therapy modification*** Deferiprone, Theophylline.
Pregnancy and Lactation	**Pregnancy**: Studies in pregnant women have demonstrated a risk to the fetus. Carbimazole should be used in pregnancy only when propylthiouracil is not suitable. The lowest dose possible should be used, and this can often be discontinued three to four weeks before term, in order to reduce the risk of neonatal complications. **Lactation**: the lowest effective dose is used. neonatal development should be closely monitored.
Administration	Administration: Oral **N.B** Refer to manufacturer PIL if there are specific considerations.

Warnings/ Precautions	• **Bleeding**: This may cause hypoprothrombinemia and bleeding. Monitoring is recommended, especially before surgical procedures. • **Dermatologic reactions**: Antithyroid agents have been associated with rare but severe dermatologic reactions; reactions reported with the use of Carbimazole include cutaneous vasculitis, erythema nodosum, and dermatomyositis, which require prompt discontinuation of therapy. Rash and urticaria are more common dermatologic reactions that may not require discontinuation in all cases. • **Bone marrow depression**: Hematologic abnormalities have been rarely reported, including neutropenia, eosinophilia, leukopenia, pancytopenia, aplastic anemia, thrombocytopenia, hemolytic anemia, and agranulocytosis. Fatal cases of agranulocytosis have been reported, most commonly within 3 months of starting therapy. If signs or symptoms of infection (eg, fever, malaise, pharyngitis) occur, discontinue therapy and obtain a white blood cell count immediately; elderly patients may be at higher risk for agranulocytosis and fatal outcomes. • **Hepatic effects**: Rare hepatic reactions, including cholestatic hepatitis and jaundice, have been reported. Discontinue therapy immediately if signs or symptoms of hepatotoxicity (e.g. upper abdomen pain, anorexia, generalized pruritus) occur or if hepatic function is abnormal. • **Radioiodine therapy**: Temporarily discontinue Carbimazole prior to scheduled administration of radioiodine (to avoid thyroid crisis). • **Hepatic or renal impairment patients**: Use caution in patients with mild to moderate hepatic or renal impairment (half-life may be prolonged); use is contraindicated in severe hepatic impairment. • **Intrathoracic goiter**: Use caution in patients with intrathoracic goiter; Carbimazole may initially enlarge the goiter and cause tracheal obstruction. • **Lactose**: Tablets may contain lactose. • **Thioamide allergy:** Potential for cross-allergy exists with other thioamides (e.g. thiamazole/methimazole, propylthiouracil); avoid the use of other thioamides if a serious hypersensitivity reaction occurs.
Storage	Store between 15-30°C. Protect from light. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Antithyroid Agent, Thiouracil

Propylthiouracil

Generic Name	Propylthiouracil
Dosage form/strengths	Tablets: 50mg
Route of Administration	Oral
Pharmacologic Category	Antithyroid Agent; Thioamide. ATC: H03BA02
Indications	**Management of hyperthyroidism,** including the treatment of Graves' disease and thyrotoxicosis.
Dosage Regimen	**Adult dosing** • **Initial**: 300–400 mg daily in single or divided doses (3 times daily) until the patient becomes euthyroid (may require up to 600-900 mg/day). • **Maintenance**: 50–150 mg daily in divided doses, reduction from the initial dose should be gradual. • Consider Propylthiouracil for patients who experience side effects to Carbimazole, are pregnant or going to be, or have a history of pancreatitis. • When substituting, Carbimazole 1mg is considered equivalent to propylthiouracil 10 mg but the dose may need adjusting according to response. **Dosing: Pediatric** Children: ≥6 years and Adolescents: **Initial** • **6 to 10 years**: Oral: 50 to 150 mg/day divided every 8 hours. • **≥10 years**: Oral: 150 to 300 mg/day divided every 8 hours. **Maintenance** (once euthyroid): The dose should be individualized based on patient response: The usual maintenance dose: is 50 mg twice daily.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** eGFR between 10-50 mL/min: decrease dose by 25%. eGFR < 10 mL/min: decrease dose by 50%. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments needed. Reconsider the use in a patient with liver transaminase (AST and/or ALT) levels more than 5-fold above the upper limit of normal (ULN). Discontinue treatment if evidence of hepatic dysfunction occurs during treatment.
Contra-indications	Hypersensitivity to Propylthiouracil or any component of the formulation.
Adverse Drug Reactions	**Common adverse effect** (mild and reversible): Leukopenia. **The most serious adverse effect (very low incidence) is agranulocytosis**. **Other severe (infrequent**) include systemic vasculitis, aplastic anemia; drug fever; lupus-like syndrome; severe hepatic reactions (including encephalopathy, fulminant hepatic necrosis, and death); periarteritis;

	hypoprothrombinemia; thrombocytopenia and bleeding. **Minor adverse effects include** rash, urticaria, pruritus, abnormal hair loss, skin pigmentation, edema, nausea, vomiting, epigastric distress, loss of taste, arthralgia, myalgia, paresthesia and headache. **Frequency unknown:** Hepatitis, Hepatic Failure, Hypersensitivity reactions.
Monitoring Parameters	• CBC with differential (baseline and when clinical evidence of infection). • Liver function test at baseline and if symptoms of liver injury occur. • Prothrombin time (periodically and before surgery). • Thyroid function tests.
Drug Interactions	***Risk X: Avoid combination*** BCG (Intravesical), Cladribine, Dipyrone, Fexinidazole, Sodium Iodide I131. ***Risk D: Consider therapy modification*** Deferiprone.
Pregnancy and Lactation	**Pregnancy**: Propylthiouracil may be used during the first trimester of pregnancy. Due to the potential for hepatic toxicity, other antithyroid medications could be considered later during pregnancy. Close monitoring is needed. To prevent adverse outcomes, the lowest effective dose is used. Propylthiouracil may be used for the treatment of thyroid storms in pregnant patients. **Lactation**: Maternal use of propylthiouracil is considered acceptable while breastfeeding although it may not be preferred due to the potential risk of maternal hepatic toxicity. The lowest effective dose should be used; maternal doses of propylthiouracil ≤450 mg/day are advised in breastfeeding patients.
Administration	**Administration: Oral** Administer in 3 equally divided doses at approximately 8-hour intervals. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **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. • **Bleeding**: This may cause hypoprothrombinemia and bleeding. Monitoring is recommended, especially before surgical procedures. • **Dermatologic reactions**: Antithyroid agents have been associated with rare but severe dermatologic reactions; reactions reported with use include cutaneous vasculitis which requires prompt discontinuation of therapy. Rash and urticaria are more common dermatologic reactions that may not require discontinuation in all cases. • **Bone marrow suppression:** This may cause significant bone marrow depression; the most severe manifestation is agranulocytosis (usually occurs within the first 3 months of therapy). Aplastic anemia, thrombocytopenia, and leukopenia may also occur. Use with caution in patients receiving other drugs known to cause myelosuppression; discontinue if significant bone marrow suppression occurs, particularly agranulocytosis or aplastic anemia. Discontinue in the presence of unexplained fever. • **Hepatotoxicity**: Severe liver injury and acute liver failure (some fatal) have been reported and have included cases requiring liver transplantation in adult and pediatric patients, including pregnant women. Routine liver function

	monitoring may not reduce risk due to unpredictable and rapid onset. Patients should be counseled to recognize and report symptoms suggestive of hepatic dysfunction (eg. anorexia, pruritus, right upper quadrant pain), especially in the first 6 months of treatment, which should prompt immediate discontinuation. **Radioiodine therapy**: Temporarily withdraw prior to scheduled administration of radioiodine (to avoid thyroid crisis). • **Lupus-like syndrome**: A lupus-like syndrome (including splenomegaly and vasculitis) may occur. • **Vasculitis**: Cases of vasculitis resulting in severe complications and death have been reported. Discontinue use for confirmed or suspected vasculitis. Some cases resolve/improve with drug discontinuation; severe cases may require further treatment (e.g. corticosteroids, immunosuppressant therapy, plasmapheresis). • **Nephritis and Pneumonitis** has been reported; discontinue if these reactions occur. • **Lactose**: Tablets may contain lactose.
Storage	Store between 15°C to 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations.

Contraceptives, combined hormonal products

Ethinyl Estradiol and Etonogestrel

Generic Name	Ethinyl Estradiol and Etonogestrel
Dosage form/strengths	Vaginal Ring: Ethinyl estradiol 2.7 mg; Etonogestrel 11.7 mg
Route of Administration	*Vaginal*
Pharmacologic Category	Contraceptive; Estrogen and Progestin Combination
Indications	**Contraception*:*** For the prevention of pregnancy.
Dosage Regimen	**Adult** **Contraception:** Vaginal It must be removed after 3 weeks of use on the same day of the week as the ring was inserted. After a ring-free interval of one week, a new ring is inserted. The withdrawal bleeding usually starts 2-3 days after removal and may not have finished completely before the next ring insertion is due. **Starting medication:** The woman herself can insert this ring in the vagina according to the instructions of the physician. *Patients with no hormonal contraceptive* use in the past month Woman should insert ring on the first day of menstrual cycle. May also insert on days 2 to 5 of the menstrual cycle but in this case, a barrier method of contraception should be used for the following 7 days. *Changing from a combined hormonal contraceptive* Woman should insert the ring at the latest on the day following the usual free interval of the previous combined hormonal contraceptive (or on any day of the cycle). *Changing from a progestogen-only method* The woman may switch on any day but should use an additional barrier method for the first 7 days of use. *Following first-trimester abortion* The woman may start immediately. *Following delivery or second-trimester abortion* Women should be advised to start during the fourth week after delivery or second-trimester abortion. When starting later, the woman should use a barrier method for the first 7 days of use.
Dosage Adjustment	**Renal Impairment adjustment** No dosage adjustments are available. **Hepatic Impairment adjustment** Known to be poorly metabolized in women with impaired liver function.
Contra-indications	• Hypersensitivity to the active substances or any of the excipients. • Presence or risk of VTE. • Risk factors for VTE include Obesity (body mass index over 30 kg/m^2), Prolonged immobilization, major surgery, Positive family history, cancer,

	systemic lupus erythematosus, haemolytic uraemic syndrome, chronic inflammatory bowel disease (Crohn's disease or ulcerative colitis), sickle cell disease and Increasing age above 35 years. • Presence or risk of arterial thromboembolism (ATE) • Risk factors for ATE include: Increasing age, smoking, hypertension, obesity, positive family history, migraine, diabetes mellitus, hyperhomocysteinaemia, valvular heart disease and atrial fibrillation, dyslipoproteinaemia and systemic lupus erythematosus. • Pancreatitis or a history if associated with severe hypertriglyceridemia. • Presence or history of severe hepatic disease as long as liver function values have not returned to normal. • Presence or history of liver tumors (benign or malignant). • Known or suspected malignant conditions of the genital organs or the breasts, if sex steroid-influenced. • Undiagnosed vaginal bleeding. • Pregnancy. • Concomitant use with medicinal products containing Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir or medicinal products containing Glecaprevir/Pibrentasvir
Adverse Drug Reactions	**>10%** • Endocrine & metabolic: Intermenstrual bleeding (7% to 12%). • Genitourinary: Vaginitis (14%). • Nervous system: Headache (11%; including migraine). **1% to 10%** • Dermatologic: Acne vulgaris (2%). • Endocrine & metabolic: Amenorrhea (≤4%), decreased libido (2%), weight gain (5%). • Gastrointestinal: Abdominal pain (3%), nausea (≤6%), vomiting (≤6%). • Genitourinary: Breast tenderness (≤4%), dysmenorrhea (4%), female birth control device expulsion from genital tract (≤6%), mastalgia (≤4%), vaginal discharge (6%), vaginal discomfort (4%). Nervous system: Foreign body sensation (≤6%; including device discomfort), mood changes (6%; including depression, depressed mood, and emotional lability).
Monitoring Parameters	• Assessment of pregnancy status (before therapy and during therapy if missed doses) • Personal or family history of thrombotic or thromboembolic disorders (prior to therapy) • Blood pressure (prior to therapy and yearly) • Weight (BMI at baseline may be helpful to monitor changes during therapy) • Monitor patient for vision changes; blood pressure; signs and symptoms of thromboembolic disorders; signs or symptoms of depression; glycemic control in patients with diabetes; lipid profiles in patients being treated for hyperlipidemias. • Adequate diagnostic measures, including endometrial sampling, if

	indicated, should be performed to rule out malignancy in all cases of undiagnosed abnormal vaginal bleeding. • Check if the vaginal ring is out of its place.
Drug Interactions	***Risk X: Avoid combination*** Antihepaciviral Combination Products, Dasabuvir, Encorafenib, Exemestane, Fexinidazole, Fezolinetant, Hemin, Indium 111 Capromab Pendetide, Mitotane, Mobocertinib, Omaveloxolone, Ospemifene, Pexidartinib, Raloxifene, Repotrectinib, Taurursodiol, Tranexamic Acid, Ulipristal. ***Risk D: Consider therapy modification*** Aprepitant, Asparaginase Products, Asunaprevir, Atazanavir, Bile Acid Sequestrants, Brigatinib, Carfilzomib, Cobicistat, Cosyntropin, CYP3A4 Inducers, Efavirenz, Elagolix, Exenatide, Felbamate, Ferric Maltol, Fosaprepitant, Fostemsavir, Fusidic Acid (Systemic), Glecaprevir and Pibrentasvir, Griseofulvin, Growth Hormone Analogs, Ivosidenib, Ixazomib, Lamotrigine, Lixisenatide, Lomitapide, Mavacamten, Metyrapone, Mifepristone, Mycophenolate, Nirmatrelvir and Ritonavir, Octreotide, Olutasidenib, Oxcarbazepine, Perampanel, Pitolisant, Protease Inhibitors, Sugammadex, Tazemetostat, Tetrahydrocannabinol and Cannabidiol, Tirzepatide, Tizanidine, Tobacco (Smoked), Topiramate, Tovorafenib, Vaborbactam.
Pregnancy and Lactation	**Pregnancy** Contraindicated. Combination hormonal contraceptives are used to prevent pregnancy; discontinue treatment if pregnancy occurs. **Lactation** Not recommended as it may reduce the amount of breast milk and change its composition.
Administration	**Intravaginal** • The woman herself can insert this ring in the vagina according to instructions of the physician. • Wash hands and remove ring from protective pouch (keep pouch for later ring disposal). • Press the sides of the ring together between thumb and index finger and insert a folded ring into vagina. Alternately, insert using the ring applicator (available separately). Specific placement is not required for the ring to be effective, but the ring should be inserted far enough into the vagina as to be comfortable. • Ring can be removed by pulling it out with the index and middle finger. Vaginal ring cannot be disposed of in the toilet; place used vaginal ring back into foil pouch and dispose of in trash. • If the ring accidentally falls out, it may be rinsed with cool or warm (not hot) water and reinserted within 3 hours. • Regularly check for the presence of the ring in the vagina (eg, before and after intercourse). • Certain barrier methods (eg, diaphragm, cervical cap, female condom) may interfere with proper ring placement, and therefore, are not recommended for use as a back-up method of contraception. • Ensure proper vaginal placement of the ring to avoid inadvertent urinary

	bladder insertion. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Bleeding irregularities**: Amenorrhea, spotting, and unscheduled bleeding may occur, primarily during the first 3 months of therapy. Amenorrhea or oligomenorrhea may occur after discontinuing combination hormonal contraceptives, especially when such a condition is preexistent. • **Chloasma**: A combination hormonal contraceptives, as well as sun exposure and pregnancy, are triggers for chloasma (a condition in which areas of the skin become darker than the surrounding skin). Avoid exposure to sun or UV radiation during therapy in patients with a susceptibility to chloasma or additional risk factors. • **Risk of cholestasis** may be increased with previous cholestatic jaundice of pregnancy or jaundice with prior hormonal contraceptive use. • **Lipid profile**: Combination hormonal contraceptives may adversely affect lipid levels, including serum triglycerides. • **Retinal thrombosis**: Discontinue if unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions occur and immediately evaluate for retinal thrombosis. • **Thromboembolic disorders**: The use of any combined hormonal contraceptive increases the risk of VTE compared with no use. Discontinue use of combination hormonal contraceptives if an arterial or VTE occurs. The risk is greatest during the first year of use and less than the risk associated with pregnancy. Patients with inherited thrombophilias may have increased risk of VTE. Age >35 years, hypertension, obesity, and tobacco use also increase the risk of thromboembolic events in patients taking combination hormonal contraceptives. Combination hormonal contraceptives may also increase the risk of arterial thrombosis (e.g., myocardial infarction, stroke); do not use in patients with a history of stroke or ischemic heart disease. • **Breast cancer:** Available studies have not shown a consistent association with combination hormonal contraceptives and breast cancer risk. However, breast cancer is a hormonal sensitive tumor and the prognosis for patients with a current or recent history of breast cancer may be worse with combination hormonal contraceptive use. • **Use with caution** in patients with risk factors for cardiovascular disease (eg, hypertension, low HDL, high LDL, high triglycerides, older age, diabetes, patients who smoke); use of combination hormonal contraceptives may increase the risk of cardiovascular disease. Use with caution in patients with a high risk of depression; discontinue if serious depression recurs. May impair glucose tolerance; use caution in patients with diabetes. • **Gallbladder disease**: Combination hormonal contraceptives may cause a small increased risk of gallbladder disease or may worsen existing gallbladder disease. • **Hepatic impairment:** Contraceptive steroids may be poorly metabolized in patients with hepatic impairment. Discontinue if jaundice develops during therapy or if liver function becomes abnormal. Use of combination

	hormonal contraceptives may be considered in patients with mild (compensated) cirrhosis. • **Hepatitis**: Initiation of combination hormonal contraceptives is not recommended in patients with acute viral hepatitis or during a flare. Continued use in patients with chronic hepatitis has not been shown to increase the rate or severity of cirrhotic fibrosis or hepatocellular carcinoma. Continued use in patients who are carriers has not been shown to trigger liver failure or severe hepatic dysfunction. • **Angioedema**: Estrogens may induce or exacerbate symptoms in patients with hereditary angioedema. • **Hypertension**: The risk of hypertension may be increased with age, dose, and duration of use. Do not use combination hormonal contraceptives in patients with hypertension and vascular disease, or persistent BP values ≥160 mm Hg systolic or ≥100 mm Hg diastolic. The risks of use may not outweigh the benefits of treatment in patients with less severe hypertension (140 to 159 mm Hg systolic or 90 to 99 mm Hg diastolic) or those with hypertension that is adequately controlled. Consider other risk factors for cardiovascular disease (eg, older age, smoking, diabetes) when prescribing contraceptives. Monitor BP in patients with well-controlled hypertension; discontinue therapy if BP rises significantly. • **Migraine**: Evaluate new, recurrent, severe, or persistent headaches and discontinue use if indicated. The use of combination hormonal contraceptives may be considered in patients who have migraines without aura (including menstrual migraines). **Ovarian and endometrial cancer**: The risk of ovarian cancer is decreased in patients using combination hormonal contraceptives.
Storage	• Store refrigerated between (2°C to 8°C). • After dispensing, it can be stored for up to 4 months or 6 months at 25°C; excursions are permitted between 15°C and 30°C. • Avoid direct sunlight or temperatures above 30°C **N.B** Refer to manufacturer PIL if there are specific considerations.

Ethinylestradiol with Levonorgestrel

Generic Name	Ethinyl estradiol and Levonorgestrel
Dosage form/strengths	**Tablets:** Levonorgestrel 150 mcg; Ethinyl Estradiol 30 mcg **Pack of 3 different sets of tablets:** Levonorgestrel/ Ethinyl Estradiol: 50mcg/30mcg + 125mcg/30mcg + 75mch/40mcg.
Route of Administration	*Oral*
Pharmacologic Category	Contraceptive; Estrogen and Progestin Combination. ATC for preparations, which contain fixed combinations of progestogen and estrogens: **G03AA07** ATC for Preparation with varying contents of progestogens and estrogens adjusted to the normal hormonal cycle: **G03AB03**
Indications	For the prevention of pregnancy.
Dosage Regimen	**Contraception** **Oral**: 1 tablet once daily to be taken daily for 21 consecutive days. Each subsequent pack is started after a 7-day tablet-free interval, during which bleeding usually occurs. **Starting medication:** • *No preceding hormonal contraceptive use [in the past month]:* Administration should be started on day 1 of the natural cycle (the first day of menstrual bleeding). Starting on day 2- 5 is allowed, but in that case a barrier contraceptive (nonhormonal) should be used during the first 7 days of treatment. • *Changing from another combined hormonal contraceptive (combined oral contraceptive (COC), vaginal ring, transdermal patch):* Administration should be started on the day after the last active tablet of the previous COC (or after removal of the ring or patch). • *Changing from a progestogen-only method (oral contraceptive with only progesterone, injection, implant) or progestogen-releasing intrauterine system (IUS):* Administration should be started on any day; the change from an implant or IUS must take place on the day of removal, and from an injectable contraceptive at the time when the next injection would be due. In each case, the use of an additional barrier contraceptive (nonhormonal) is necessary during the first 7 days. • *Following first-trimester abortion* Administration should be started immediately. In this case, no additional contraceptive method is required. • *Following childbirth or second-trimester abortion* Administration should be started 21 to 28 days after delivery or second-trimester abortion. When starting later, an additional barrier contraceptive (nonhormonal) should be used during the first 7 days of tablet-taking.
Dosage Adjustment	**Renal Impairment** No dosage adjustments are available; use with caution and monitor blood pressure closely.

	Hepatic Impairment Contraindicated in patients with hepatic impairment.
Contra-indications	• Hypersensitivity to the active substances or to any of the excipients. • Presence or risk of VTE. • Risk factors for VTE include Obesity (body mass index over 30 kg/m²), Prolonged immobilization, major surgery, Positive family history, cancer, systemic lupus erythematosus, hemolytic uraemic syndrome, chronic inflammatory bowel disease (Crohn's disease or ulcerative colitis), sickle cell disease and Increasing age above 35 years. • Presence or risk of ATE. • Risk factors for ATE include Increasing age, smoking, hypertension, obesity, positive family history, migraine, diabetes mellitus, hyperhomocysteinemia, valvular heart disease and atrial fibrillation, dyslipoproteinaemia and systemic lupus erythematosus. • Pancreatitis or a history associated with severe hypertriglyceridemia. • Presence or history of severe hepatic disease as long as liver function values have not returned to normal. • Presence or history of liver tumors (benign or malignant). • Known or suspected malignant conditions of the genital organs or the breasts, if sex steroid-influenced. • Undiagnosed vaginal bleeding. • Pregnancy. • Concomitant use with medicinal products containing Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir or medicinal products containing Glecaprevir/Pibrentasvir
Adverse Drug Reactions	**1% to 10%** • Endocrine & metabolic: Weight gain. • Gastrointestinal: Nausea (oral: 4%). • Genitourinary: Dysmenorrhea (oral: 2%). • Local: Application site reaction. Nervous system: Headache (oral: 4%).
Monitoring Parameters	• Assessment of pregnancy status (before therapy and during therapy if missed doses) • Personal or family history of thrombotic or thromboembolic disorders (before therapy) • Blood pressure (before therapy and yearly) • Weight (BMI at baseline may be helpful to monitor changes during therapy) • Monitor patient for vision changes; blood pressure; signs and symptoms of thromboembolic disorders; signs or symptoms of depression; glycemic control in patients with diabetes; and lipid profiles in patients being treated for hyperlipidemias. • Adequate diagnostic measures, including endometrial sampling, if indicated, should be performed to rule out malignancy in all cases of undiagnosed abnormal vaginal bleeding.

Drug Interactions	***Risk X: Avoid combination*** Anastrozole, Dasabuvir, Dehydroepiandrosterone, Encorafenib, Erdafitinib, Exemestane, Fexinidazole, Fezolinetant, Fusidic Acid (Systemic), Hemin, Indium 111 Capromab Pendetide, Lactic Acid, Citric Acid, Potassium Bitartrate, Mobocertinib, Omaveloxolone, Ombitasvir, Paritaprevir, Ritonavir, Ombitasvir, Paritaprevir, Ritonavir, Dasabuvir, Ospemifene, Pexidartinib, Raloxifene, Repotrectinib, Taurursodiol, Tranexamic Acid, Uliprista ***Risk D: Consider therapy modification*** Acitretin, Alitretinoin (Systemic), Apalutamide, Aprepitant, Armodafinil, Artemether, Lumefantrine, Asparaginase (E. coli), Asparaginase [Recombinant], Asparaginase, Asunaprevir, Atazanavir, Belzutifan, Bexarotene (Systemic), Bosentan, Brigatinib, Calaspargase Pegol, Carbamazepine, Carfilzomib, Cenobamate, Cholestyramine Resin, Cladribine, Clobazam, Cobicistat, Colesevelam, Colestipol , Cosyntropin, Dabrafenib, Danshen, Darolutamide, Darunavir, Dexamethasone (Systemic), Dicloxacillin, Dipyrone, Echinacea, Efavirenz, Elagolix, Elagolix, Estradiol, and Norethindrone, Enzalutamide, Erlotinib, Eslicarbazepine, Exenatide, Felbamate, Ferric Maltol, Flucloxacillin, Fosamprenavir, Fosaprepitant, Fosphenytoin, Fostemsavir, Ginkgo Biloba, Glecaprevir and Pibrentasvir, Glycerol Phenylbutyrate, Griseofulvin, Isotretinoin (Systemic), Ivosidenib, Ixazomib, LamoTRIgine, Lesinurad, Licorice, Lixisenatide , Lomitapide, Lonapegsomatropin , Lopinavir, Lorlatinib, Lumacaftor, Ivacaftor, Mavacamten, Metyrapone, Mifepristone, Mitapivat, Mitotane, Modafinil, Mycophenolate, Nafcillin, Nelfinavir, Nirmatrelvir, Ritonavir, Octreotide, Olutasidenib, Oxcarbazepine, Palovarotene, Pegaspargase, Perampanel, Phenobarbital, Phenytoin, Pitolisant, Primidone, Rifabutin, Rifampin, Rifapentine, Ritonavir, Rufinamide, Saquinavir, Somapacitan , Somatrogon, Somatropin , Sotagliflozin, Sotorasib, St John's Wort, Sugammadex, Tazemetostat, Tecovirimat, Telotristat Ethyl, Tetrahydrocannabinol, Cannabidiol, Thioridazine, Tipranavir, Tirzepatide, Tizanidine, Tobacco (Smoked), Topiramate, Tretinoin (Systemic), Vaborbactam, Vemurafenib, Zanubrutinib
Pregnancy and Lactation	**Pregnancy** Contraindicated. Combination hormonal contraceptives are used to prevent pregnancy; discontinue treatment if pregnancy occurs. **Lactation** Not recommended as it may reduce the amount of breast milk and change its composition.
Administration	**Oral:** Administer at the same time each day. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	• **Bleeding irregularities**: Amenorrhea, spotting, and unscheduled bleeding may occur, primarily during the first 3 months of therapy. Amenorrhea or oligomenorrhea may occur after discontinuing combination hormonal contraceptives, especially when such a condition was preexistent. • **Chloasma**: Combination hormonal contraceptives, as well as sun exposure and pregnancy, are triggers for chloasma (a condition in which areas of the skin become darker than the surrounding skin). Avoid exposure to sun

or UV radiation during therapy in patients with a susceptibility to chloasma or additional risk factors.

- **Risk of cholestasis** may be increased with previous cholestatic jaundice of pregnancy or jaundice with prior hormonal contraceptive use.
- **Lipid profile**: Combination hormonal contraceptives may adversely affect lipid levels, including serum triglycerides. Patients with hypertriglyceridemia or a family history of hypertriglyceridemia may be at increased risk of pancreatitis when using combination hormonal contraceptives. Consider alternative contraception for patients with uncontrolled dyslipidemia.
- **Retinal thrombosis**: Discontinue if unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions occur and immediately evaluate for retinal thrombosis.
- **Thromboembolic disorders**: The use of any combined hormonal contraceptive increases the risk of VTE compared with no use. Products that contain Levonorgestrel, Norgestimate or Norethisterone are associated with the lowest risk of VTE. Discontinue use of combination hormonal contraceptives if an arterial or VTE occurs. The risk is greatest during the first year of use and less than the risk associated with pregnancy. Patients with inherited thrombophilias may have increased risk of VTE. Age >35 years, hypertension, obesity, and tobacco use also increase the risk of thromboembolic events in patients taking combination hormonal contraceptives. Combination hormonal contraceptives may also increase the risk of arterial thrombosis (eg, myocardial infarction, stroke); do not use in patients with a history of stroke or ischemic heart disease.
- **Breast cancer:** Available studies have not shown a consistent association with combination hormonal contraceptives and breast cancer risk. However, breast cancer is a hormonal sensitive tumor and the prognosis for patients with a current or recent history of breast cancer may be worse with combination hormonal contraceptive use.
- **Use with caution** in patients with risk factors for cardiovascular disease (eg, hypertension, low HDL, high LDL, high triglycerides, older age, diabetes, patients who smoke); use of combination hormonal contraceptives may increase the risk of cardiovascular disease. Use with caution in patients with a high risk of depression; discontinue if serious depression recurs. May impair glucose tolerance; use caution in patients with diabetes.
- **Gallbladder disease**: Combination hormonal contraceptives may cause a small increased risk of gallbladder disease or may worsen existing gallbladder disease.
- **Hepatic impairment:** Contraceptive steroids may be poorly metabolized in patients with hepatic impairment. Discontinue if jaundice develops during therapy or if liver function becomes abnormal. Use of combination hormonal contraceptives may be considered in patients with mild (compensated) cirrhosis.
- **Hepatitis**: Initiation of combination hormonal contraceptives is not

	recommended in patients with acute viral hepatitis or during a flare. Continued use in patients with chronic hepatitis has not been shown to increase the rate or severity of cirrhotic fibrosis or hepatocellular carcinoma. Continued use in patients who are carriers has not been shown to trigger liver failure or severe hepatic dysfunction. • **Angioedema**: Estrogens may induce or exacerbate symptoms in patients with hereditary angioedema. • **Hypertension**: The risk of hypertension may be increased with age, dose, and duration of use. Do not use combination hormonal contraceptives in patients with hypertension and vascular disease, or persistent BP values ≥160 mm Hg systolic or ≥100 mm Hg diastolic. The risks of use may not outweigh the benefits of treatment in patients with less severe hypertension (140 to 159 mm Hg systolic or 90 to 99 mm Hg diastolic) or those with hypertension that is adequately controlled. Consider other risk factors for cardiovascular disease (eg, older age, smoking, diabetes) when prescribing contraceptives. Monitor BP in patients with well-controlled hypertension; discontinue therapy if BP rises significantly. • **Migraine**: Evaluate new, recurrent, severe, or persistent headaches and discontinue use if indicated. The use of combination hormonal contraceptives may be considered in patients who have migraines without aura (including menstrual migraines). • **Ovarian or Endometrial cancer**: The risk of ovarian or endometrial cancer is decreased in patients using combination hormonal contraceptives.
Storage	Store between 15°C to 30°C. • **N.B.** Refer to manufacturer PIL if there are specific considerations.

Contraceptives, devices

Copper releasing Intra-uterine contraceptive devices

Generic Name	Copper containing device
Dosage form/strengths	Intrauterine device (IUD): Copper 208 mm^2; 380 mm^2
Route of Administration	*Intra-uterine*
Pharmacologic Category	Contraceptive ATC: G02BA02
Indications	**Contraception:** For the prevention of pregnancy for up to 10 years
Dosage Regimen	**Contraception** • One device should be inserted at the fundus of the uterine cavity. Exclude pregnancy before insertion. • Device should be removed on or before 10 years from the date of insertion. • Do not leave any one device in place for >10 years. **Starting therapy** • *Start in females not currently using contraception.* ○ At any time during the menstrual cycle. • *Switch to Copper device from an oral, transdermal, or vaginal form of hormonal contraception or an injectable progestin contraceptive.* ○ At any time during the menstrual cycle; discontinue the previous method. • *Switch to Copper device from a contraceptive implant or other intrauterine system* ○ Same day the implant or IUS is removed (insert at any time during the menstrual cycle). • *Insert after abortion or miscarriage.* ○ Immediately after abortion, although immediate placement has a slightly higher risk of expulsion than placement at other times. Insertion after second trimester abortion is associated with a higher risk of expulsion than insertion after a first trimester abortion. • *Insert after Childbirth.* May be inserted immediately postpartum. Insertion before uterine involution is complete, which may not occur until the second postpartum month, has been associated with an increased risk of expulsion. There appears to be an increased risk of perforation in lactating women.
Dosage Adjustment	No dose adjustments are needed.
Contra-indications	• Pregnancy or suspected of pregnancy. • Abnormalities of the uterus resulting in distortion of the uterine cavity. • Acute pelvic inflammatory disease (PID). • Postpartum endometritis or postabortal endometritis in the past 3 months. • Known or suspected uterine or cervical malignancy. • Uterine bleeding of unknown etiology.

	• Untreated acute cervicitis or vaginitis or another lower genital tract infection. • Conditions associated with increased susceptibility to pelvic infections. • Wilson's disease. • A previously placed IUD or IUS that has not been removed. • • Hypersensitivity to any component including copper.
Adverse Drug Reactions	• **Gastrointestinal Disorders**: abdominal distension, nausea • **General Disorders and Administration Site Conditions**: device breakage, pyrexia • **Immune System Disorders**: allergy to metals, hypersensitivity • **Infections and Infestations**: endometritis/uterine infection • **Musculoskeletal and Connective Tissue Disorders**: muscle spasms • **Nervous System Disorders:** dizziness • **Reproductive System and Breast Disorders**: amenorrhea • **Skin and Subcutaneous Tissue Disorders**: Stevens-Johnson syndrome
Monitoring Parameters	**Before insertion** • Assess pregnancy status before insertion. • Monitor for vasovagal reactions following insertion. • Transvaginal ultrasound may be used to check placement. • Evaluate for abdominal or pelvic pain, cramping, tenderness, malodorous discharge, infection, bleeding, fever, or missed period. Assess potential health status changes at routine visits.
Drug Interactions	No known significant interactions.
Pregnancy and Lactation	**Pregnancy** Use during pregnancy is contraindicated. **Lactation** • Copper IUD insertion did not increase copper breast milk content. • An increased risk of perforation in lactating women. There is no information on the effect of copper in a breastfed child or the effect on milk production.
Administration	**Intrauterine device** • Insertion should be done by a trained healthcare provider. • To be inserted into the uterine cavity. • Full administration and removal instructions are provided with the device. • Analgesics may be used to reduce pain during insertion. • Use strict aseptic techniques throughout preparation. • Establish the size and position of the uterus by performing a bi-manual examination. • Insertion of IUS may be associated with pain and/or bleeding or vasovagal reactions (e.g. syncope, bradycardia, or seizure) especially in patients with a predisposition to these symptoms **N.B** Refer to manufacturer PIL if there are specific considerations.

Warnings/ Precautions	• **Ectopic Pregnancy:** Promptly evaluate women who become pregnant for ectopic pregnancy while using copper devices. • **Risks with Intrauterine Pregnancy**: Increased risk of spontaneous abortion, septic abortion, premature delivery, sepsis, septic shock and death if pregnancy occurs. Device should be removed by a healthcare provider if pregnancy occurs while in place. • **Sepsis:** Group A streptococcal infection has been reported; strict aseptic technique is essential during insertion. • **PID and Endometritis**: Before using, consider the risks of PID and endometritis. Symptoms of PID include lower abdominal or pelvic pain, odorous discharge, unexplained bleeding, fever, or genital lesions or sores. In such circumstances, perform a pelvic examination promptly to evaluate for possible pelvic infection. Remove IUD in cases of recurrent PID or endometritis, or if an acute pelvic infection is severe or does not respond to treatment. PID can have serious consequences, such as tubal damage (leading to ectopic pregnancy or infertility), hysterectomy, sepsis, and death. PID or endometritis may be asymptomatic but still result in tubal damage and its sequelae. • **Embedment**: Surgical removal may be necessary. • **Perforation**: Partial or total perforation of the uterine wall or cervix may occur during placement of the device and may not be detected until later. Perforation can cause pregnancy (due to decreased contraceptive efficacy) and migration, which can lead to abscesses, adhesions, intestinal obstruction/penetration, and/or peritonitis. Risk is increased if inserted in lactating women. • **Expulsion**: Partial or complete expulsion may occur. Healthcare provider should consider further diagnostic imaging, such as x-ray. A partially expelled IUD should be removed. • **Bleeding patterns**: May be altered and result in heavier and longer bleeding with spotting. Suitable diagnostic procedures should be conducted to rule out endometrial pathology or device displacement. • **MRI Safety Information**: Patients using copper IUD can be safely scanned with MRI only under the following conditions: a static magnetic field of 3.0 Tesla or 1.5 Tesla, Maximum spatial field gradient of 4,000 gauss/cm^2 (40 Tesla/m^2), Maximum MR system reported, whole body averaged specific absorption rate of 2 W/kg (Normal Operating Mode). • **Actinomycosis:** Actinomycosis has been associated with IUD use. Symptomatic women with known actinomycosis infection should have Paragard removed and receive antibiotics.
Storage	Store between 15°C to 30°C. **N.B.** Refer to manufacturer PIL if there are specific considerations.

Levonorgestrel-releasing intrauterine device

Generic Name	Levonorgestrel-releasing intrauterine device
Dosage form/strengths	Intra-uterine device (IUD): Levonorgestrel 52 mg
Route of Administration	*Intra-uterine*
Pharmacologic Category	Contraceptive; Progestin
Indications	• **Contraception:** Prevention of pregnancy for up to 8 years. • **Treatment of heavy menstrual bleeding:** for women who choose to use intrauterine contraception as their method of contraception for up to 5 years. • **Protection from endometrial hyperplasia during estrogen replacement therapy.**
Dosage Regimen	**Contraception** Levonorgestrel-releasing IUD can be used for contraception and remains effective for 8 years. Should be inserted into the uterine cavity at any time during the menstrual cycle. Following insertion, a barrier method of contraception should be used for the next 7 days to prevent pregnancy. *Postpartum insertion* Not earlier than 6 weeks after delivery. If involution is substantially delayed, consider waiting until 12 weeks postpartum *Insertion after first-trimester abortion* Can be inserted immediately. **Heavy menstrual bleeding** Levonorgestrel-releasing IUD can be used for heavy menstrual bleeding and remains effective for 5 years for the indication of heavy menstrual bleeding. The system should be removed or replaced in case symptoms return. If symptoms have not returned after 5 years of use, continued use of the system may be considered. Remove or replace no later than 8 years after insertion. **Protection from endometrial hyperplasia during estrogen replacement therapy:** should therefore be removed no later than 4 years after insertion. No data beyond 4 years in this indication.
Dosage Adjustment	**Renal impairment** No dosage adjustments are available. Not studied. Caution. **Hepatic Impairment** No dosage adjustments are available; the use of the intrauterine device is contraindicated with active hepatic disease or hepatic tumor.

Contra-indications	• Hypersensitivity to the active substance or any of the excipients. • Known or suspected pregnancy. • Confirmed or suspected hormone-dependent tumors including breast cancer. • Current or recurrent pelvic inflammatory disease. • Cervicitis. • Current genital infection. • Postpartum endometritis, infected abortion during the past three months. • Conditions associated with increased susceptibility to infections. • Cervical dysplasia. • Uterine or cervical malignancy. • Undiagnosed abnormal genital bleeding. • Congenital or acquired abnormality of the uterus including fibroids if they distort the uterine cavity. • Liver tumor or other acute or severe liver disease. • Acute malignancies affecting the blood or leukemias except when in remission. • Recent trophoblastic disease while hCG levels remain elevated.
Adverse Drug Reactions	**>10%** • Dermatologic: Acne vulgaris (7% to 15%). • Endocrine & metabolic: Amenorrhea (≤40%; increases with duration of treatment). • Gastrointestinal: Abdominal pain (≤23%). • Genitourinary: Bacterial vaginosis (19%), gynecological bleeding (including decreased, increased, heavy, irregular, prolonged, unscheduled, frequent and infrequent uterine bleeding), ovarian cyst (1% to 22%), pelvic pain (≤23%), vaginal discharge (4% to 15%), vaginal mycosis (19%), vulvovaginitis (11% to 24%). • Nervous system: Headache (≤16%), migraine (≤16%). **1% to 10%** • Dermatologic: Alopecia (1%), seborrhea (1% to 2%). • Endocrine & metabolic: Hirsutism (<5%), weight gain (6%). • Gastrointestinal: Abdominal distress, nausea, vomiting. • Genitourinary: Bacterial reproductive infection (1% to 4%), breast tenderness (including discomfort: ≤10%), dysmenorrhea (6% to 9%), dyspareunia (9%), endometritis (≤2%), female birth control expulsion from genital tract (3% to 9%; partial and complete), mastalgia (≤10%), pelvic inflammatory disease (<5%), uterine spasm (2%). • Nervous system: Anxiety (9%), depressed mood (≤6%), depression (≤8%), mood changes (6%). • Neuromuscular & skeletal: Back pain (6% to 8%).
Monitoring Parameters	• A complete personal and family medical history should be taken. • Physical (including pelvic and breast) examination (refer to contraindications).

	• Blood glucose (Glucose tolerance may be decreased). • Monitor for thromboembolic disorders (particularly at immobilization), Vision changes, depression and breast cancer in patients receiving long-term high doses. • Evaluate abnormal bleeding that persists or is severe. • Blood pressure, Liver functions. • Lipid profiles in patients being treated for hyperlipidemias. • Pregnancy status (before therapy, ectopic pregnancy during therapy). • Assess changes in health status at routine follow-up visits. • Re-examine following insertion (4 to 6 weeks) and then when clinically needed. Evaluate patients presenting with lower abdominal pain for ectopic pregnancy (especially in association with missed periods) and ovarian cysts.
Drug Interactions	***Risk X: Avoid combination*** Ulipristal. ***Risk D: Consider therapy modification*** Metyrapone.
Pregnancy and Lactation	**Pregnancy** It is contraindicated to use this product if you are pregnant or suspected to be pregnant. **Lactation** In general, no adverse effects on the growth or development of the infant have been observed. There have been isolated reports of decreased milk output. It is not likely that there will be a risk for the child with the dose released from the IUD.
Administration	-it should only be inserted into the uterine cavity by healthcare professionals who are experienced in IUD insertions. -Consider administering analgesics or cervical anesthetic before insertion. -If necessary, dilate the cervical canal and consider using a paracervical block. To ensure adequate implantation, transvaginal ultrasonography may be utilized. -Remove if not positioned properly and insert a new IUD; do not reinsert the removed IUD. -Exclude uterine perforation if exceptional pain or bleeding occurs after insertion. Ensure the device is intact after removal. -Check expiration of IUD before insertion. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Medical Examination**: Before insertion, a complete personal and family medical history should be taken. Physical examination should be guided by this and by the contraindications and warnings for use. • **Perforation:** If perforation is suspected the system should be removed • as soon as possible; surgery may be required**.** Risk is increased if inserted in lactating women and may be increased if inserted in women with fixed retroverted uteri or postpartum. • **Bradycardia** The procedure of insertion/removal may precipitate fainting

as a vasovagal reaction, or a seizure in an epileptic patient. Persistent bradycardia may be controlled with intravenous Atropine. If oxygen is available it may be administered; use with caution in patients predisposed to these conditions.

- **Smoking**: Women using hormonal contraception should be encouraged to give up smoking.
- **Conditions that the removal of the system should be considered**
  - Migraine with aura.
  - Unusually severe or unusually frequent headache.
  - Jaundice.
  - A marked increase in blood pressure.
  - Malignancies affecting the blood or leukemia in remission.
  - Use of chronic corticosteroid therapy.
  - History of symptomatic functional ovarian cysts.
  - Active or previous severe arterial disease, such as stroke or myocardial infarction.
  - Severe or multiple risk factors for arterial disease.
  - Thrombotic arterial or any current embolic disease.
  - Acute venous thromboembolism.
- **Complications leading to failure**
  - Expulsion: Symptoms of the partial or complete expulsion of IUD may include bleeding or pain. However, a system can be expelled from the uterine cavity without the woman noticing it, leading to a loss of contraceptive protection. As the system decreases menstrual flow, an increase in menstrual flow may be indicative of an expulsion.
  - Lost threads: If the retrieval threads are not visible at the cervix on follow-up examination -first, exclude pregnancy.
- **Pelvic Infection**: An increased incidence of group A streptococcal sepsis, pelvic inflammatory disease (PID) and endometritis (may be asymptomatic) has been reported with use. It is critical to use an aseptic procedure during insertion to reduce the risk of severe infections. PID occurs more frequently within the first year and most often within the first month after insertion. If PID is diagnosed, follow current guidelines and reevaluate in 48 to 72 hours. If there is no clinical improvement, antibiotics should be continued and the device should be removed. Remove the IUD if you have recurrent endometritis, or if an acute pelvic infection is severe or does not respond to therapy.
- **Bleeding irregularities:** It usually achieves a significant reduction in menstrual blood in 3 to 6 months of treatment. If Increased menstrual flow persists then the woman should be re-examined as it may be indicative of expulsion.
- **Psychiatric disorders:** In patients with risk of depression, use with caution; may be more sensitive to suicidal behaviour and suicide; monitor particularly shortly after initiation.
- **Glucose tolerance***:* Low-dose levonorgestrel may affect glucose tolerance and the blood. Glucose concentration should be monitored in diabetic users of IUDs.

	• **Pregnancy**: The healthcare provider should remove the IUD if pregnancy occurs during use. If pregnancy occurs, there is an increased risk of ectopic pregnancy including loss of fertility, pregnancy loss, septic abortion (including septicemia, shock, and death), and premature labor and delivery. • **Partial or complete expulsion** may occur leading to loss of contraceptive efficacy. Expulsion may be associated with symptoms of increased bleeding or pain, or it may be asymptomatic and go unnoticed. • **Ovarian Cysts**: Most cysts are asymptomatic, although some may be accompanied by pelvic pain or dyspareunia. In most cases, the ovarian cysts disappear spontaneously during 2-3 months of observation. Evaluate persistent ovarian cysts. Surgical intervention is not usually required.
Storage	Store between 15–30°C. **N.B** Refer to manufacturer PIL if there are specific considerations.

Contraceptives, emergency

Ulipristal

Generic Name	Ulipristal
Dosage form/strengths	Tablets: 5mg, 30mg.
Route of Administration	*Oral*
Pharmacologic Category	Contraceptive; Progestin Receptor Modulator. ATC: G03AD02
Indications	**Emergency contraception** - Prevention of pregnancy following unprotected intercourse within 120 hours (5 days) or a known or suspected contraceptive failure. - It is not intended for routine use as a contraceptive in patients who may become pregnant. **Uterine fibroids** - Intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women who have not reached menopause when uterine fibroid embolization and/or surgical treatment options are not suitable or have failed.
Dosage regimen	**Dosage in Adults** **Emergency contraception** **Oral**: 30 mg as soon as possible, but within 120 hours (5 days) of unprotected intercourse or contraceptive failure. **Intermittent treatment of moderate to severe symptoms of uterine fibroids** **Oral:** 5 mg once daily for treatment courses of up to 3 months each. Initiate the first treatment course during the first week of menstruation. The re-treatment courses should start at the earliest during the first week of the second menstruation following the previous treatment course completion. **Dosage in Older Adults** For use in patients of reproductive potential, not indicated for use post-menopause.
Dosage Adjustment	**Renal Impairment** - No dosage adjustments are available; however, dosage adjustment may not be necessary since renal elimination of ulipristal is minimal. Severe renal impairment: Close monitoring due to lack of data. **Hepatic Impairment** -No dosage adjustments available. - Do not initiate treatment: if ALT or AST exceeds 2 x ULN (isolated or in combination with bilirubin >2 x ULN).

	-Discontinue treatment if: (ALT or AST) > 3 times the upper limit of normal during treatment and closely monitor hepatic functions.
Contra-indications	**Uterine fibroids indication** • Pregnancy (known or suspected). • Hypersensitivity to Ulipristal or any component of the formulation. • Genital bleeding of unknown etiology or for reasons other than uterine fibroids. • Uterine, cervical, ovarian, or breast cancer. • Underlying hepatic disorder. **Emergency contraception Indication** • Pregnancy (known or suspected.
Adverse Drug Reactions	**>10%** • Endocrine & metabolic: Suppressed menstruation (>7 days later than expected: 19%). • Gastrointestinal: Abdominal pain (8% to 15%, including upper abdominal pain), nausea (12% to 13%). • Genitourinary: Dysmenorrhea (7% to 13%). • Nervous system: Headache (18% to 19%). **1% to 10%** • Endocrine & metabolic: Intermenstrual bleeding (9%). • Genitourinary: Early menses (>7 days earlier than expected: 7%). • Nervous system: Dizziness (5%), fatigue (6%).
Monitoring Parameters	• Evaluate for pregnancy or ectopic pregnancy if expected menses is delayed for ≥1 week following emergency contraception, or if lower abdominal pain (3 to 5 weeks after administration) or persistent irregular bleeding develops. • A pregnancy test is recommended if withdrawal bleeding does not occur within 3 weeks following use as an emergency contraceptive. • Liver function before therapy and monthly for the first two courses. • Ultrasound for endometrium monitoring.
Drug Interactions	***Risk X: Avoid combination*** CYP3A4 Inducers or inhibitors (Moderate, Strong), Felbamate, Fexinidazole, Fusidic Acid (Systemic), Griseofulvin, Oxcarbazepine, Progestins, Topiramate.
Pregnancy and Lactation	**Pregnancy** Use is contraindicated during a known or suspected pregnancy. **Lactation** - No human data. Not recommended. - Ulipristal may be used for emergency contraception in patients who are breastfeeding; however, breast milk should be discarded for 24 hours after the dose.
Administration	**Oral**

	- Administered with or without food at any time during the menstrual cycle. - If vomiting occurs within 3 hours of administration, repeating the dose may be considered. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Bleeding irregularities**: Menstrual bleeding patterns may be altered but return to normal in subsequent cycles. - Intermenstrual bleeding (spotting) has also been observed. The possibility of pregnancy should be considered if menstruation is delayed for >7 days of the expected menstrual period. • **Endometrial changes**: Changes in the histology of the endometrium may be observed in patients treated with ulipristal acetate. These changes are reversible after treatment discontinuation. The treatment courses should each not exceed 3 months as the risk of adverse impact on the endometrium is unknown if treatment is continued without interruption. • **Appropriate use**: Repeated use within the same menstrual cycle is not recommended. • **High Alert Medication**: as it increases the risk of causing significant patient harm when used in error. • **Severe asthma**: Use in women with severe asthma insufficiently controlled by oral glucocorticoids is not recommended. • **Concomitant use** with potent CYP3A4 inducers (e.g. Rifampicin, Rifabutin, Carbamazepine, Oxcarbazepine, Phenytoin, Fosphenytoin, Phenobarbital, Primidone, St John's Wort, Efavirenz, Nevirapine) is not recommended • **Concomitant use** with moderate CYP3A4 inhibitors (e.g. Erythromycin, Grapefruit Juice, Verapamil) or potent CYP3A4 inhibitors (e.g. Ketoconazole, Ritonavir, Nefazodone, Itraconazole, Telithromycin, Clarithromycin) is not recommended.
Storage	• Store between 15°C to 30°C. • Protect from light. **N.B** Refer to manufacturer PIL if there are specific considerations.

Contraceptives, progestogen

Etonogestrel-releasing implant

Generic Name	Etonogestrel-releasing implant
Dosage form/strengths	Subdermal Implant: Etonogestrel 68 mg
Route of Administration	*Subdermal*
Pharmacologic Category	Contraceptive; Progestin ATC: G03AC08
Indications	-**Contraception:** Prevention of pregnancy
Dosage regimen	**Contraception** **Subdermal:** 1 implant, which can be left in place up to three years. Overweight women: Consider earlier replacement of the implant. The implant should be administered by healthcare providers trained in the insertion and removal procedure. Timing of insertion (after ruling out pregnancy) -**Patients not currently using a hormonal contraceptive:** Implant is inserted between days 1 through 5 of menstruation, even if the patient is still bleeding. A barrier method of contraception should be used for the first 7 days after insertion if deviating from the recommended timing of insertion. If intercourse has already occurred, pregnancy should be excluded. **-Switching from combination hormonal contraceptive** Oral tablet: The implant is inserted on the day after the last active tablet (containing an active substance). Transdermal system or vaginal ring: Insert on the day of the removal of the transdermal system or vaginal ring. -**Switching from a progestin-only contraceptive** Oral tablet: Any day during the month; Do not skip days between the last tablet and implant insertion. Implant or intrauterine device (IUD): The implant is inserted on the same day as removal of the implant or IUD. Injection: The implant is inserted on the day the next injection is due. -**First-trimester abortion or miscarriage**: The implant is inserted within the first 5 days following the first-trimester abortion or miscarriage.

	-**Second-trimester abortion or miscarriage**: An implant is inserted between 21 and 28 days following second-trimester abortion or miscarriage. -**Postpartum**: If not breastfeeding, Implant is inserted between 21 to 28 days postpartum. If breastfeeding, insert after the fourth postpartum week and use a second non-hormonal form of contraception for the first 7 days of insertion.
Dosage Adjustment	**Renal impairment** No dosage adjustments are needed. **Hepatic Impairment** Use is contraindicated.
Contra-indications	• Hypersensitivity to Etonogestrel or any component of the formulation. • Breast cancer (known, suspected, or personal history). • Progestin-sensitive cancer (current or a history). • Hepatic tumors (benign or malignant) or active hepatic disease. • Pregnancy (known or suspected); • Active venous thromboembolic disorder. • Undiagnosed abnormal vaginal bleeding.
Adverse Drug Reactions	**>10%** • Dermatologic: Acne vulgaris (14%). • Endocrine & metabolic: Weight gain (14%). • Gastrointestinal: Abdominal pain (11%). • Genitourinary: Gynecological bleeding (including amenorrhea: 22%; frequent bleeding: 7%; heavy menstrual bleeding; infrequent uterine bleeding: 34%; prolonged menstrual bleeding: 18%; spotty menstruation: 12% to 37%), mastalgia (13%), vaginitis (15%). • Nervous system: Headache (25%). • Respiratory: Pharyngitis (11%). **1% to 10%** • Gastrointestinal: Nausea (6%). • Genitourinary: Dysmenorrhea (7%), leukorrhea (10%). • Hypersensitivity: Hypersensitivity reaction (5%). • Local: Application-site reaction (implant site: 9%; including bruise: 2%; localized erythema: 3%; hematoma: 3%; local pain: 1% to 5%; local swelling: <1%). • Nervous system: Depression (6%), dizziness (7%), emotional lability (7%), nervousness (6%), pain (6%). • Neuromuscular & skeletal: Back pain (7%). • Respiratory: Flu-like symptoms (8%).
Monitoring Parameters	• A complete personal and family medical history should be taken. • Physical (including pelvic and breast) examination (refer to contraindications). • Blood glucose (Glucose tolerance may be decreased). • Evaluate Vision changes, depression, and breast cancer in patients receiving long-term high doses.

	• Evaluate abnormal bleeding that persists or is severe. • Blood pressure: Remove implant if uncontrolled significant hypertension. • Liver functions: Remove implant if jaundice occurs. • Signs and symptoms of thromboembolic disorders: remove in event of thrombosis. • Lipid profiles in patients being treated for hyperlipidemias. • Pregnancy status (prior to therapy, ectopic pregnancy during therapy).
Drug Interactions	***Risk X: Avoid combination*** Encorafenib, Erdafitinib, Fexinidazole, Fusidic Acid (Systemic), Mobocertinib, Omaveloxolone, Pexidartinib, Repotrectinib, Taurursodiol, Tranexamic Acid, Ulipristal. ***Risk D: Consider therapy modification*** Aprepitant, Asparaginase Products, Asunaprevir, Atazanavir, Brigatinib, Carfilzomib, Cobicistat, CYP3A4 Inducers, Efavirenz, Elagolix, Exenatide, Felbamate, Fosaprepitant, Griseofulvin, Ivosidenib, Ixazomib, Lixisenatide, Mavacamten, Metyrapone, Mifepristone, Mycophenolate, Nirmatrelvir and Ritonavir, Octreotide, Olutasidenib, Oxcarbazepine, Perampanel, Pitolisant, Protease Inhibitors, Sugammadex, Tazemetostat, Tetrahydrocannabinol and Cannabidiol, Tirzepatide, Topiramate, Vaborbactam.
Pregnancy and Lactation	**-Pregnancy** Use is contraindicated during pregnancy. **-Lactation** - Available data show no adverse effects on infant growth and development. Nevertheless, the development and growth of the child should be carefully followed. It may be used during lactation and should be inserted after the 4th postpartum week.
Administration	**-For subdermal insertion by health care providers trained in the insertion and removal procedure:** -The healthcare provider inserts the implant subdermally just under the skin at the inner side of the non-dominant upper arm overlying the triceps muscle ~8 to 10 cm (3 to 4 inches) from the medial epicondyle of the humerus and 3 to 5 cm (1.25 to 2 inches) posterior to the sulcus between the biceps and triceps muscles. This location is intended to avoid the large blood vessels and nerves lying within and surrounding the sulcus. If it is not possible to insert at this location (e.g., in patients with thin arms), insert as far posteriorly from the sulcus as possible. -To ensure proper placement just under the skin, view the advancement of the needle from the side, not from above the patient. -Implant must be palpable after insertion.

	- X-ray, CT scan, ultrasound scanning, or MRI may also be used to confirm the location of the implant if it is not palpable. Deeply placed implants (deeper than subdermally) should be localized and removed as soon as possible. -Removal of deeply placed implants, implants that are not palpable, or implants that cannot be grasped during removal should be performed by health care providers trained in complex removal procedures. Use of a non-hormonal contraceptive (eg, condom) is required until the presence of the implant can be verified. -Perform removal under aseptic conditions. -Inject local anesthetic under (not over) the implant. -When removing the implant, confirm that the entire implant has been removed by measuring its length (4 cm). Remove all pieces if the implant has broken. - A new implant may be inserted in the same arm through the same incision as long as the site is in the correct location. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Thromboembolic disorders**: There may be a slightly, but not statistically significant increased risk of venous thromboembolism (deep venous thrombosis, pulmonary embolism) associated with the use of progestogen-only contraception. The implant should be removed if an arterial or venous thromboembolic event occurs. • **Bleeding irregularities**: Vaginal bleeding including spotting, menorrhagia and/or metrorrhagia and amenorrhea. They occur in ≥ 10 % of users. • **Ectopic pregnancy**: The possibility of ectopic pregnancy should be considered in patients with lower abdominal pain. • **Persistent ovarian cysts**: May occur during the use. Some follicles are accompanied by pelvic pain or dyspareunia. In most cases, the enlarged follicles disappear spontaneously during two to three months of observation however, surgery may rarely be required. • **Depressed mood and depression** are well-known undesirable effects of hormonal contraception. Monitor in patients with a history of depression. Consider removing the implant if serious depression occurs. • **Liver tumor**: In rare cases benign, and in even rarer cases, malignant liver tumors have been observed after the use of combined hormonal contraceptives. • **Breast tumors**: There is a small increase in the risk of having breast cancer diagnosed in women using, or who have recently used oral contraceptives. This relative risk may be due to an earlier diagnosis. The most important risk factor

	appears to be the age at which the contraceptive is stopped rather than the duration of use; the risk disappears gradually during the 10 years after stopping and there is no excess risk by 10 years. A possible small increase in the risk of breast cancer should be weighed against the benefits. • **Elevated Blood Pressure**: Women with a history of hypertension-related diseases or renal disease should be discouraged from using hormonal contraception. Use can be considered for women with well-controlled hypertension with close monitoring. If sustained hypertension develops during the use, or if a significant increase in blood pressure does not respond adequately to antihypertensive therapy, the implant should be removed. • **Weight gain**: Use commonly results in an average weight gain of ~2.8 pounds after 1 year and ~3.7 pounds after 2 years of treatment. • **Caution**: Use with caution in patients with risk factors for cardiovascular disease (eg, hypertension, hypercholesterolemia, morbid obesity, diabetes, patients who smoke or patients with diseases that may be exacerbated by fluid retention). Diabetes: May impair glucose tolerance; use caution in patients with diabetes or prediabetes. • **Hepatic impairment**: Etonogestrel may be poorly metabolized in patients with hepatic impairment. Discontinue if jaundice develops during therapy or if liver function becomes abnormal. • **Surgical patients**: Consider removal during periods of prolonged immobilization due to surgery or illness. • **Chloasma**: Women with a tendency to chloasma should avoid exposure to the sun or ultraviolet radiation whilst using
Storage	Store between 15°C and 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations.

Levonorgestrel

Generic Name	Levonorgestrel
Dosage form/strengths	Tablets: 0.030 mg, 0.75 mg, 1.5mg
Route of Administration	*Oral*
Pharmacologic Category	Contraceptive; Progestin ATC: G03AC03 ATC for emergency use packages: G03AD01
Indications	**Emergency contraception** (0.75 mg, 1.5mg)**:** Emergency contraception within 72 hours of unprotected sexual intercourse or failure of a contraceptive method. **Prevention of pregnancy** (0.030 mg).
Dosage Regimen	**Emergency contraception** **Oral**: 1.5 mg for 1 dose, taken as soon as possible after coitus, preferably within 12 hours and no later than after 72 hours. **Oral**: 1 tablet (0.75 mg) as a first dose as soon as possible after intercourse (i.e., preferably within 12 to 24 hours after the event). (The efficacy lasts for up to 5 days). Must give a second dose 12 hours after the initial dose. **Contraception** **Oral:** One tablet 0.03mg daily, starting on the first day of the menstrual cycle. All subsequent tablets must then be taken at the same time each day without interruption, and without regard to bleeding. *Changing from a combined contraceptive*, vaginal ring, or transdermal patch: - Oral contraceptive: The first tablet of Levonorgestrel should be taken on the first day after the last active tablet. - Vaginal ring or transdermal patch: Start Levonorgestrel on the day of removal of the last vaginal ring or transdermal patch. *Changing from another progestogen-only parenteral method (implant, injection):* The switch should be made before or when the next injection or implant is due. *Post-partum use***:** start up to 21 days post-partum (no additional contraceptive is required). If started after 21 days additional barrier contraceptive methods should be used for 7 days. *Post-abortion or miscarriage use***:** start at the time of the abortion or miscarriage. If started after this time, barrier contraceptive methods should be used for 7 days.

Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** No dosage adjustments are needed. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments available. It should be avoided in severe impairment. Emergency contraception may be used with caution.
Contra-indications	**Emergency contraception** • Hypersensitivity to the active substance or any of the excipients. **Contraception** • Known or suspected pregnancy. • Presence or history of active severe hepatic disease or liver tumors. • History of or existing thromboembolic processes (e.g. stroke, myocardial infarction). • Known or suspected sex- steroid-influenced malignancies (e.g. current or history of breast cancer). • Undiagnosed abnormal vaginal bleeding. • Severe diabetes with vascular changes. • Hypersensitivity to the active substance or to any of the excipients.
Adverse Drug Reactions	**>10%** • Endocrine & metabolic: Irregular menses (26%; including delayed menstruation, heavy menstrual bleeding [14%], hypomenorrhea [13%], and spotting). • Gastrointestinal: Abdominal pain (18%), nausea (23%), diarrhea. • Genitourinary: Breast tenderness (11%). • Nervous system: Dizziness (11%), fatigue (17%), headache (17%). **1% to 10%** • Gastrointestinal: Diarrhea (5%), vomiting (6%).
Monitoring Parameters	• A complete personal and family medical history should be taken. • Physical (including pelvic and breast) examination (refer to contraindications). • Blood glucose (Glucose tolerance may be decreased). • Monitor for thromboembolic disorders, Vision changes, depression, and breast cancer in patients receiving long-term high doses. • Evaluate abnormal bleeding that persists or is severe. • Blood pressure, Liver functions. • Lipid profiles in patients being treated for hyperlipidemias. • Pregnancy status (before therapy, ectopic pregnancy during therapy).
Drug Interactions	***Risk X: Avoid combination*** Encorafenib, Erdafitinib, Fexinidazole, Fusidic Acid (Systemic), Mobocertinib, Omaveloxolone, Pexidartinib, Repotrectinib, Taurursodiol, Tranexamic Acid, Ulipristal.

	Risk D: Consider therapy modification Aprepitant, Asparaginase Products, Asunaprevir, Atazanavir, Brigatinib, Carfilzomib, Cobicistat, CYP3A4 Inducers, Efavirenz, Elagolix, Exenatide, Felbamate, Fosaprepitant, Griseofulvin, Ivosidenib, Ixazomib, Lixisenatide, Mavacamten, Metyrapone, Mifepristone, Mycophenolate, Nirmatrelvir and Ritonavir, Octreotide, Olutasidenib, OXcarbazepine, Perampanel, Pitolisant, Protease Inhibitors, Retinoic Acid Derivatives, Sugammadex, Tazemetostat, Tetrahydrocannabinol and Cannabidiol, Tirzepatide, Topiramate, Vaborbactam.
Pregnancy and Lactation	**Pregnancy** Not for use in patients confirmed to be pregnant. Adverse effects on the mother or fetus have not been observed following inadvertent exposure during pregnancy. **Lactation**: Available data show no adverse effects on infant growth and development. Progestogen-only methods are considered the next choice category after non-hormonal methods.
Administration	**Administration: Oral** • If the pill was taken 3 hours after the due time (> 27 hours since the last pill was taken) a barrier contraceptive method for the next 7 days and continue normal pill taking. • If vomiting occurs within 2 hours of taking a tablet, another pill should be taken as soon as possible **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	• **Thromboembolic disorders**: There may be a slightly, but not statistically significant increased risk of venous thromboembolism (deep venous thrombosis, pulmonary embolism) associated with the use of progestogen-only contraception. • **Bleeding irregularities**: Vaginal bleeding including spotting, menorrhagia and/or metrorrhagia and amenorrhea. They occur in ≥ 10 % of users. • **Ectopic pregnancy**: Levonorgestrel is not recommended for patients with a history of ectopic pregnancy. The possibility of ectopic pregnancy should be considered in patients with lower abdominal pain. • **Persistent ovarian cysts**: May occur during the use. Some follicles are accompanied by pelvic pain or dyspareunia. In most cases, the enlarged follicles disappear spontaneously during two to three months of observation. • **Depressed mood and depression** are well-known undesirable effects of hormonal contraception. Monitor in patients with a history of depression. • **Liver tumor**: In rare cases benign, and in even rarer cases, malignant liver tumors have been observed after the use of hormonal contraceptives. • **Breast tumors**: There is a small increase in the risk of having breast cancer diagnosed in women using, or who have recently used oral contraceptives. This relative risk may be due to an earlier diagnosis. The most important

	risk factor appears to be the age at which the contraceptive is stopped rather than the duration of use; the risk disappears gradually during the 10 years after stopping and there is no excess risk by 10 years. A possible small increase in the risk of breast cancer should be weighed against the benefits. • **Obese patients** can generally use any type of contraceptive but Levonorgestrel may be less efficacious in obese women. It is unclear if dosage adjustment is required based on weight. • **Diabetes**: May impair glucose tolerance; use caution in patients with diabetes or prediabetes. • Use with caution in patients with diseases that may be exacerbated by fluid retention. • **Hepatic disorders**: Levonogestrel may be poorly metabolized in patients with hepatic impairment. Discontinue if jaundice develops during therapy or if liver function becomes abnormal. • **Visual disorders**: Discontinue if sudden disturbances of vision or hearing or other perceptual disorders occured.
Storage	Store between 15°C and 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations.

Medroxyprogesterone Acetate

Generic Name	Medroxyprogesterone Acetate
Dosage form/strengths	Tablets: 5mg Suspension for injection: 150mg/ml Suspension in prefilled syringe: 104 mg/0.65ml
Route of Administration	*Oral, IM*
Pharmacologic Category	Contraceptive; Progestin ATC: G03DA02, G03AC06
Indications	***Oral*:** • **Dysfunctional uterine bleeding, secondary amenorrhea:** Treatment of non-acute abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathologies, such as fibroids or uterine cancer. • **Mild to moderate endometriosis, and to reduce the incidence of endometrial hyperplasia in non-hysterectomized postmenopausal women receiving daily oral conjugated estrogens** • **Hormone replacement therapy (HRT):** In combination with an estrogen product for estrogen deficiency symptoms in peri- and post-menopausal women. ***Injection*** • **Contraception (104 mg/0.65 mL and 150 mg/mL injection):** For the **prevention** of pregnancy for at least 12 weeks. **N.B.** Consider, the return to fertility (ovulation) may be delayed for up to one year.
Dosage Regimen	• **Dysfunctional uterine bleeding** **Oral:** 5 to 10 mg daily for 5 to 10 days; starting between the calculated 16th to 21st day of the menstrual cycle for two consecutive cycles. Progestin withdrawal bleeding usually occurs within three to seven days after discontinuing therapy. • **Secondary amenorrhea** **Oral:** 5 to 10 mg daily for 5 to 10 days starting at any time. Progestin withdrawal bleeding usually occurs within three to seven days after discontinuing therapy. • **Reduction of Endometrial Hyperplasia in Postmenopausal Women Receiving Daily 0.625 mg Conjugated Estrogens** **Oral**: 5 or 10 mg daily for 12 to 14 consecutive days per month, either beginning on the 1st day of the cycle **or** the 16th day of the cycle. • **Mild to moderate endometriosis** **Oral**: 10 mg three times a day for 90 consecutive days beginning on the first day of the menstrual cycle. • **Hormone replacement therapy** **Oral**: 10 mg a day for the last 14 days of each 28day cycle to reduce the risk to the endometrium in women with an intact uterus.

	• **Contraception** **IM:** 150 mg every 3 months **SC:** 104 mg every 3 months **Note**: If administration is ≤5 days since menstrual bleeding started, no additional contraception is needed. Otherwise, additional contraceptive protection is needed. **Postpartum**: The initial dose is given within 5 days if not breastfeeding. Or just after 6 weeks if the woman is breastfeeding.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** No dosage adjustments are needed. **Dosing: Hepatic Impairment: Adult** Elimination of Medroxyprogesterone is reduced in patients with liver dysfunction. Medroxyprogesterone should be avoided in patients with severe hepatic dysfunction. Discontinue if jaundice or deterioration in liver function develops.
Contra-indications	• Hypersensitivity to Medroxyprogesterone or any of its excipients. • Acute hepatic disease. • Cerebrovascular disease (current or history). • Active thromboembolic disorders (current or history). • Thromboembolism e.g. Stroke or myocardial infarction. • Undiagnosed vaginal bleeding. • Estrogen- or progesterone-dependent tumor (e.g. Breast cancer). • Pregnancy or incomplete abortion. Porphyria.
Adverse Drug Reactions	**>10%:** • Endocrine & metabolic: Amenorrhea (6% to 68%), hot flash (≤36%), weight gain (7% to 38%), weight loss (≤12%). • Gastrointestinal: Abdominal pain (4% to 11%). • Genitourinary: Gynecological bleeding (IM: 32% to 57%; SUBQ: 18%; including irregular, increase or decrease flow, and spotting). • Nervous system: Headache (9% to 17%), nervousness (11%). **1% to 10%:** • Cardiovascular: Edema (2%). • Dermatologic: Acne vulgaris (1% to 4%), alopecia (1%), skin rash (1%). • Endocrine & metabolic: Decreased libido (3% to 6%) • Gastrointestinal: Bloating (2%), nausea (3%). • Genitourinary: Bacterial vaginosis (≤5%), breast tenderness (≤2%), dysmenorrhea (≤2%), leukorrhea (3%), mastalgia (≤3%), urinary tract infection (4%), vaginitis (≤5%), vulvovaginal candidiasis (≤5%). • Local: Atrophy at injection site (≤1%), induration at injection site (≤1%), injection-site reaction (5% to 6%). • Nervous system: Anxiety (1%), asthenia (≤4%), depression (2% to 3%), dizziness (1% to 6%), fatigue (≤4%), insomnia (1%), irritability (1%). Neuromuscular & skeletal: Arthralgia (1%), back pain (2% to 3%), lower limb cramp (4%).

Monitoring Parameters	• A complete personal and family medical history should be taken. • Physical (including pelvic and breast) examination (refer to contraindications). • Blood glucose (Glucose tolerance may be decreased). • Evaluate depression and breast cancer in patients receiving long-term high doses. • Evaluate abnormal bleeding that persists or is severe.
Drug Interactions	***Risk X: Avoid combination*** Encorafenib, Erdafitinib, Fexinidazole, Fusidic Acid (Systemic), Indium 111 Capromab Pendetide, Mobocertinib, Omaveloxolone, Pexidartinib, Repotrectinib, Taurursodiol, Tranexamic Acid, Ulipristal. ***Risk D: Consider therapy modification*** Aprepitant, Asparaginase Products, Asunaprevir, Atazanavir, Brigatinib, Carfilzomib, Cobicistat, CYP3A4 Inducers (Barbiturates (phenobarbital), Carbamazepine, Corticosteroids, Phenytoin, Rifampicin, St John's wort), Efavirenz, Elagolix, Exenatide, Felbamate, Fosaprepitant, Gallium Ga 68 PSMA-11, Griseofulvin, Ivosidenib, Ixazomib, Lixisenatide, Mavacamten, MetyraPone, Mifepristone, Mycophenolate, Nirmatrelvir and Ritonavir, Octreotide, Olutasidenib, Oxcarbazepine, Perampanel, Piflufolastat F18, Pitolisant, Protease Inhibitors, Sugammadex, Tazemetostat, Tetrahydrocannabinol and Cannabidiol, Tirzepatide, Topiramate, Vaborbactam. **Laboratory interactions**: These include gonadotrophin levels (decreased), plasma progesterone levels (decreased), urinary pregnanediol levels (decreased), plasma estrogen levels (decreased), plasma cortisol levels (decreased), glucose tolerance test, metyrapone test, liver function tests (may increase), thyroid function tests (protein bound iodine levels may increase and T3 uptake levels may decrease). Coagulation test values for prothrombin (Factor II), and Factors VII, VIII, IX and X may increase.
Pregnancy and Lactation	**Pregnancy:** Medroxyprogesterone is contraindicated for use during known *pregnancy* or *suspected pregnancy*. No increased risk of birth defects in women who have inadvertently been exposed to Medroxyprogesterone acetate contraceptive injections in early pregnancy. **Lactation**: Medroxyprogesterone contraceptive injections may be used safely during breast-feeding.
Administration	**Administration: IM** Contraception: Administer the first dose during the first 5 days of menstrual period, or within the first 5 days postpartum if not breastfeeding, or at the sixth week postpartum if breastfeeding exclusively. Shake vigorously before administration. Administer by deep IM injection in the gluteal or deltoid muscle. Rotate the administration site with each injection. Injection must be administered by a health care professional only. Patients should return every 3 months for subsequent doses; the interval between injections should not exceed 13 weeks. **Administration: Subcutaneous** Administer the first dose during the first 5 days of the menstrual period, or at the sixth week postpartum if breastfeeding. Shake vigorously for at least 1

	minute prior to administration. Administer by SC injection in the upper anterior thigh or abdomen; avoid boney areas and the umbilicus. Administer slowly over 5 to 7 seconds. Do not rub the injection area. SC injection should be administered by a health care professional; however, patient administration is also an option. **Administration: Oral** Administer with food. **Missed dose:** Take it as soon as they remember. However, if it is time for the next dose, patients should be advised not to take the missed dose but to continue to take the tablets as prescribed. A missed dose may increase the likelihood of breakthrough bleeding and spotting. **Dietary Considerations** Ensure adequate calcium and vitamin D intake. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Thromboembolic disorders**: There may be a slightly, but not statistically significant increased risk of venous thromboembolism (deep venous thrombosis, pulmonary embolism) associated with the use. If developed during use, do not re-administer. • **Bleeding irregularities**: Break-through bleeding and spotting may occur during the first months of treatment. If it appears after some time on therapy, or continues after treatment has been discontinued, the reason should be investigated. An endometrial biopsy to exclude endometrial malignancy may be needed. • **Ectopic pregnancy**: The possibility of ectopic pregnancy should be considered in patients with lower abdominal pain. • **Depressed mood and depression** are well-known undesirable effects of hormonal contraception. Monitor in patients with a history of depression. • **Breast tumors**: There is a small increase in the risk of having breast cancer diagnosed in women using, or who have recently used oral contraceptives. The risk increased with duration of use and appeared to return to baseline in about 5 years after stopping treatment. A possible small increase in the risk of breast cancer should be weighed against the benefits. • **Hypertriglyceridemia:** In patients using estrogen plus progesterone therapy, triglycerides may be increased in patients with preexisting hypertriglyceridemia; discontinue if pancreatitis occurs. • **Exacerbation of other conditions** Estrogen plus progestin therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomas and should be used with caution in women with these conditions. • **Fluid retention**: Use with caution in patients with diseases that may be exacerbated by fluid retention including cardiac or renal dysfunction. • **Hepatic disorders**: Discontinue if jaundice develops during therapy or if liver function becomes abnormal. • **Visual Abnormalities**: Discontinue if sudden disturbances of vision or hearing or other perceptual disorders occurred. If examination reveals

	papilledema or retinal vascular lesions, medication should not be readministered. • **Adrenal suppression**: May cause suppression of HPA axis, resulting in decreased plasma cortisol concentrations, decreased cortisol secretion, and low plasma ACTH concentrations. Cushingoid symptoms may occur. • **Hypersensitivity reactions**: Anaphylaxis or anaphylactoid reactions have been reported with use of the injection; medication for the treatment of hypersensitivity reactions should be available for immediate use. • **Diabetes**: Medroxyprogesterone therapy may have adverse effects on glucose tolerance; monitor patients with diabetes mellitus. • **Porphyria**: Use estrogen plus progestogen therapy with caution in patients with porphyria; may exacerbate disease. • **Body weight**: Dose adjustment is not required based on body weight. • **Surgery**: Whenever possible, discontinue progestogens in combination with estrogens at least 4 to 6 weeks prior to surgery associated with an increased risk of thromboembolism or during periods of prolonged immobilization. • **Endometrial carcinoma**: Use for endometrial carcinoma is contraindicated when used as part of an oestrogen-containing HRT regimen. The effects of long-term use on adrenal, hepatic, ovarian, pituitary, and uterine function is not known. Use for endometrial carcinoma may mask the onset of menopause.
Storage	Store between 15°C to 30°C. Do not refrigerate or freeze. Used immediately after opening. **N.B** Refer to manufacturer PIL if there are specific considerations.

Norethisterone (Norethindrone)

Generic Name	Norethisterone (Norethindrone)
Dosage form/strengths	Norethisterone Acetate: Tablets: 5 mg; 10 mg
Route of Administration	*Oral*
Pharmacologic Category	Contraceptive; Progestin Oral: G03DC02
Indications	**N.B** Norethindrone acetate is a prodrug that is rapidly converted to Norethindrone in the body; on a weight basis, Norethindrone acetate is twice as potent as Norethindrone. • Dysfunctional uterine bleeding • Polymenorrhea • Menorrhagia • Metropathia • Haemorrhagia • Pre-menstrual syndrome • Postponement of menstruation • endometriosis • At high doses: Disseminated carcinoma of the breast.
Dosage Regimen	**Adult** • **Dysfunctional uterine bleeding, polymenorrhoea, menorrhagia, dysmenorrhoea and metropathia haemorrhagia** Oral: 5 mg 3 times a day for 10 days; bleeding usually stops within 48 hours. Oral: 5 mg twice daily, to be taken from day 19 to day 26 of the two subsequent cycles to prevent recurrence of the condition • **Endometriosis** -Oral: 5 mg 3 times a day for at least 6 months; increased to 20–25 mg daily if required, dose only increased if spotting occurs and reduced once bleeding has stopped. • **Postponement of menstruation** Oral: Females of childbearing potential: 5 mg 3 times a day, to be started 3 days before expected onset onset of menstruation (menstruation occurs 2–3 days after stopping).

	• **Pre-menstrual syndrome:** 5mg daily from days 16 to 25 of the menstrual cycle. ***High dose*** • **For disseminated breast carcinoma**: Initial dose: 40mg per day increasing to 60mg if no regression is observed.
Dosage Adjustment	**Renal Impairment** No dosage adjustments available. Use with caution. **Hepatic Impairment** No dosage adjustments available. However, use is contraindicated in patients with hepatic tumors or impairment.
Contra-indications	• Hypersensitivity to Norethindrone or any component of the formulation. • Breast cancer (known, suspected, or history of). • undiagnosed abnormal genital bleeding. • Pregnancy. • Deep vein thrombosis or pulmonary embolism (current or history of) • Active or recent history of arterial thromboembolic disease (eg, stroke, myocardial infarction). • Hepatic impairment or disease. • Severe pruritus or pemphigoid gestationis. • Porphyria.
Adverse Drug Reactions	**≥1%**: Menstrual cycle irregularities **Frequency not known**: Hepatic cancer, Thromboembolism, Appetite change, depression, fatigue, gastrointestinal disorder, headaches, hypertension, Libido disorder, nervousness.
Monitoring Parameters	• A complete personal and family medical history should be taken. • Physical (including pelvic and breast) examination (refer to contraindications). • Blood glucose (Glucose tolerance may be decreased). • Evaluate abnormal bleeding that persists or is severe. • Monitor for thromboembolic disorders, Vision changes, depression and breast cancer in patients receiving long-term high doses. • Blood pressure, Liver functions. • Lipid profiles in patients being treated for hyperlipidemias. • Pregnancy status (prior to therapy, ectopic pregnancy during therapy).
Drug Interactions	***Risk X: Avoid combination***

	Abametapir, Encorafenib, Fexinidazole, Fusidic Acid (Systemic), Mobocertinib, Omaveloxolone, Pexidartinib, Repotrectinib, Taurursodiol, Tranexamic Acid, Ulipristal. ***Risk D: Consider therapy modification*** Aprepitant, Asparaginase Products, Asunaprevir, Atazanavir, Brigatinib, Carfilzomib, Cladribine, Cobicistat, Colesevelam, CYP3A4 Inducers (Barbiturates (phenobarbital) Carbamazepine, Corticosteroids, Phenytoin, Rifampicin St John's wort), Efavirenz, Elagolix, Exenatide, Felbamate, Fosaprepitant, Griseofulvin, Ivosidenib, Ixazomib, Lixisenatide, Mavacamten, Metyrapone, Mifepristone, Mycophenolate, Nirmatrelvir and Ritonavir, Octreotide, Olutasidenib, OXcarbazepine, Perampanel, Pitolisant, Protease Inhibitors, Retinoic Acid Derivatives, Sugammadex, Tazemetostat, Tetrahydrocannabinol and Cannabidiol, Tripeptide, Topiramate.
Pregnancy and Lactation	**Pregnancy** Use is contraindicated during pregnancy. -First trimester exposure of progestins may cause genital abnormalities. Changes in external genitalia have been reported in female infants exposed to Norethindrone acetate. **Lactation** -Norethindrone is present in breast milk. Caution during use.
Administration	**Oral:** Administer at the same time each day. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Thromboembolic disorders**: There may be a slightly increased risk of venous thromboembolism (deep venous thrombosis, pulmonary embolism) associated with the use. If developed during use, discontinue therapy. • **Bleeding irregularities**: Irregular menstrual bleeding patterns are common with progestin-only contraceptives; nonpharmacologic causes of abnormal bleeding should be ruled out. • **Ectopic pregnancy**: The possibility of ectopic pregnancy should be considered in patients with lower abdominal pain. • **Depressed mood and depression** are well-known undesirable effects of hormonal contraception. Monitor in patients with a history of depression. • **Breast tumors**: There is a small increase in the risk of having breast cancer diagnosed in women using, or who have recently used, a progestogen only contraceptive pill; this relative risk may be due to an

	earlier diagnosis. The most important risk factor appears to be the age at which the contraceptive is stopped rather than the duration of use; the risk disappears gradually during the 10 years after stopping and there is no excess risk by 10 years. A possible small increase in the risk of breast cancer should be weighed against the benefits • **Hyperlipidemias:** May have adverse effects on lipid metabolism; use caution in patients with hyperlipidemias. • **Exacerbation of other conditions** Estrogen plus progestin therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomas and should be used with caution in women with these conditions. • **Fluid retention**: Use with caution in patients with diseases that may be exacerbated by fluid retention including cardiac or renal dysfunction. • **Hepatic disorders**: Discontinue if jaundice develops during therapy or if liver function becomes abnormal. • **Visual Abnormalities**: Discontinue if sudden disturbances of vision or hearing or other perceptual disorders occurred. If examination reveals papilledema or retinal vascular lesions, medication should not be readministered. • **Diabetes**: Medroxyprogesterone therapy may have adverse effects on glucose tolerance; monitor patients with diabetes mellitus.
Storage	Store between 15° to 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations.

Progesterone

Generic Name	Progesterone
Dosage form/strengths	• Vaginal Gel: 8 % w/w. • Rectal or vaginal pessaries: 200 mg; 400 mg. • Soft Gelatin Capsule: Progesterone micronized: 100 mg, 200 mg, 400 mg. • Oral or Vaginal soft gelatin capsule: Progesterone micronized 200 mg • Vaginal Tablets: 100 mg. • Oily solution for IM injection: 25mg, 50 mg, 100 mg. • Rectal Suppositories: 200 mg
Route of Administration	*Oral; Vaginal; I.M, Rectal*
Pharmacologic Category	Progestin ATC: G03DA04
Indications	**Oral** • Adjunctive use with an Estrogen in post-menopausal women with an intact uterus, as hormone replacement therapy. **Intramuscular** • Treatment of dysfunctional uterine bleeding. • Maintenance of early pregnancy in cases of documented history of 3 or more prior consecutive unexplained miscarriages • For luteal support as part of an ART treatment program in infertile women who are unable to use or tolerate vaginal preparations **Vaginal Gel** • Treatment of infertility due to inadequate luteal phase. • For use during in-vitro fertilization. **Vaginal tablet:** For luteal support as part of an ART treatment program for infertile women. **Vaginal or rectal pessaries:** • Treatment of premenstrual syndrome, including premenstrual tension and depression (micronized). • Treatment of puerperal depression (micronized). • Luteal phase support as part of an ART treatment for women.
Dosage regimen	**Oral** **Adjunctive use with Estrogen, as hormone replacement therapy.**

- Oral: 200mg at bedtime for 12 days beginning on Day 15 of the cycle and ending on Day 26). Withdrawal bleeding may occur in the following week.
- Alternatively, 100mg can be given at bedtime from Day 1 to Day 25 of each therapeutic cycle, withdrawal bleeding is less with this treatment schedule.

Intramuscular

- **Dysfunctional *uterine bleeding***

IM: 5-10mg daily for 5-10 days until 2 days before anticipated onset of menstruation.

- **Maintenance *of pregnancy***

Twice a week (up to once daily) injections of 25-100mg from approximately day 15, or day of transfer of embryo or gametes usually until 8 - 16 weeks of pregnancy.

Daily dosage can be increased to 200mg at the direction of the physician.

- ***For luteal support as part of an ART treatment program in infertile women***

Once daily injection of 25 mg from day of oocyte retrieval, usually until 12 weeks of confirmed pregnancy.

Vaginal gel

- ***Treatment of infertility due to inadequate luteal phase***

  Apply (1.125 g of 8% gel) every day, starting after ovulation or arbitrarily on the 18^{th} – 21^{st} day of the cycle.

- ***Use during in-vitro fertilization***

  Apply the 8% gel and should be continued for 30 days if there is laboratory evidence of pregnancy

Vaginal tablet

- ***Treatment of infertility due to inadequate luteal phase***

Vaginal: 100 mg three times daily starting at oocyte retrieval. Continue for 30 days, if pregnancy has been confirmed.

Vaginal or rectal insertion

- ***For the treatment of premenstrual syndrome and puerperal depression***

200mg daily to 400mg twice a day.

For premenstrual syndrome: Start treatment on day 12-14 of menstrual cycle and continue treatment until onset of menstruation.

	• ***For luteal phase support as part of an ART treatment*** 400 mg administered vaginally twice a day starting at oocyte retrieval. The administration of Progesterone should be continued for 38 days, if pregnancy has been confirmed.
Dosage Adjustment	**Renal Impairment** Systemic, Vaginal: Has not been studied. Use with caution. Risk of fluid retention. **Hepatic Impairment** **Systemic**: Use is contraindicated in hepatic impairment. **Vaginal, rectal:** Contraindicated in severe impairment. Caution in mild and moderate.
Contra-indications	**Systemic, vaginal, rectal** • Hypersensitivity to Progesterone or any component of the formulation. • Undiagnosed abnormal vaginal bleeding. • Breast cancer (known, suspected, or history) or genital tract cancer. • Active deep vein thrombosis, pulmonary embolism, or history of these conditions. • Active or history of arterial thromboembolic disease (e.g., stroke, MI) or thrombophlebitis. • Hepatic impairment or disease (severe impairment in vaginal and rectal). • Missed abortion or ectopic pregnancy. • Cerebral hemorrhage. • Porphyria.
Adverse Drug Reactions	**Intramuscular injection** **<10%** • Reproductive system and breast disorders: Uterine spasm Vaginal hemorrhage. • General disorders and administration site conditions: Administration site reactions. **1% to 10%** • Nervous system disorders: Headache. • Gastrointestinal disorders: Abdominal distension, Abdominal pain, Nausea, Vomiting and Constipation. • Reproductive system and breast disorders: Breast tenderness, Breast pain, Vaginal discharge, Vulvovaginal pruritus, Vulvovaginal discomfort, Vulvovaginal inflammation, and Ovarian hyperstimulation syndrome (OHSS). • General disorders and administration site conditions: Injection site hematoma. • Injection site induration, Fatigue.

Oral

10%

- Gastrointestinal: Abdominal pain (20%), bloating (12%)
- Genitourinary: Breast tenderness (27%), mastalgia (6% to 16%), urinary tract abnormality (11%).
- Infection: Viral infection (12%).
- Nervous system: Depression (19%), dizziness (15% to 24%), headache (16% to 31%).
- Neuromuscular & skeletal: Musculoskeletal pain (12%).

1% to 10%

- Cardiovascular: Chest pain (7%).
- Gastrointestinal: Cholecystectomy (2%), constipation (3%), diarrhea (7% to 8%), nausea and vomiting (≤8%).
- Genitourinary: Breast carcinoma (2%), vaginal discharge (10%).
- Nervous system: Anxiety (8%), fatigue (8%), irritability (8%).
- Respiratory: Cough (8%).

Vaginal gel

>10%

- Gastrointestinal: Abdominal pain (12%), constipation (27%), nausea (7% to 22%).
- Genitourinary: Breast hypertrophy (40%), mastalgia (13%), nocturia (13%), perineal pain (17%).
- Nervous system: Depression (11%), drowsiness (27%), headache (13% to 17%), nervousness (16%).
- Neuromuscular & skeletal: Muscle cramps (15%).

1% to 10%

- Endocrine & metabolic: Decreased libido (10%).
- Gastrointestinal: Bloating (7%), diarrhea (8%), vomiting (5%).
- Genitourinary: Dyspareunia (6%), genital candidiasis (5%), vaginal discharge (7%), vulvovaginal pruritus (5%), Breast tenderness, itching or burning.
- Nervous system: Dizziness (5%), pain (8%).
- Neuromuscular & skeletal: Arthralgia (8%).
- Local: skin rash, vaginal irritation.

Vaginal pessaries

1% to 10%

- Nervous system disorder: somnolence.
- Vascular disorders: hot flush.
- Gastrointestinal disorders: Abdominal distension, abdominal pain, constipation.

	• Reproductive system and breast disorders: Breast pain. • General disorders and administration site conditions: Fatigue. **Vaginal tablets** **>1%** • Nervous system disorders: Headache, Dizziness, Insomnia. • Gastrointestinal disorders: Abdominal distension, Abdominal pain, Nausea, Diarrhea, constipation. • Skin and subcutaneous tissue disorder: Urticaria, Rash. • Reproductive system and breast disorders: Uterine spasm, Vulvovaginal disorders, Vaginal mycosis, Breast disorders, genital Pruritus. • General disorders and administration site conditions: peripheral Edema.
Monitoring Parameters	• A complete personal and family medical history should be taken. • Physical (including pelvic and breast) examination (refer to contraindications). • Blood glucose (Glucose tolerance may be decreased). • Evaluate abnormal bleeding that persists or is severe. • Monitor for thromboembolic disorders, Vision changes, depression and breast cancer in patients receiving long-term high doses. • Blood pressure, Liver functions. • Lipid profiles in patients being treated for hyperlipidemias. • Pregnancy status (prior to therapy, ectopic pregnancy during therapy). • Duration of treatment should be evaluated at least annually.
Drug Interactions	***Risk X: Avoid combination*** Antifungal Agents (Vaginal), Ulipristal. ***Risk D: Consider therapy modification*** Metyrapone, Sincalide.
Pregnancy and Lactation	**Pregnancy** Limited data, should not be used during pregnancy. May be used in the first trimester of pregnancy as part of an ART regimen. **Lactation** Avoid. Progesterone is present in breast milk. Consider benefits and risks.
Administration	**Intramuscular** -Inject deeply into a large muscle mass. - It should be injected deep into large muscle mass as buttock, rather than the thigh or deltoid, using a 1.5inch (3.8cm) needle. Rotate sites of injection. The product should be injected slowly to minimize local tissue damage. -May cause injection-site irritation.

	Oral Administer at bedtime with a full glass of water, should not be taken with food. **Intravaginal** • ***Vaginal gel***: Gel is administered directly from an applicator. • ***Vaginal tablets:*** place directly into the vagina by the applicator provided. • ***Vaginal or rectal pessaries:*** Use rectally if barrier methods of contraception are used. Use rectally if patients suffer from vaginal infection or recurrent cystitis or have recently given birth. Use vaginally if patients suffer from colitis or fecal incontinence. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hazardous agent (NIOSH 2016 [group 2]):** Use appropriate precautions for receiving, handling, storage, preparation, dispensing, transporting, administration, and disposal. IARC Group 2B: reasonably anticipated to be human carcinogen. • **Thromboembolic disorders**: There may be a slightly increased risk of venous thromboembolism (deep venous thrombosis, pulmonary embolism) associated with the use. If developed during use, discontinue therapy. • **Bleeding irregularities**: Irregular menstrual bleeding patterns are common with progestin-only contraceptives; non-functional causes of abnormal bleeding should be ruled out. • **Ectopic pregnancy**: The possibility of ectopic pregnancy should be considered in patients with lower abdominal pain. • **Depressed mood and depression** are well-known undesirable effects of hormonal contraception. Monitor in patients with a history of depression. Abrupt withdrawal may increase anxiety and moodiness. • **Breast tumors**: There is a small increase in the risk of having breast cancer diagnosed in women using, or who have recently used, a progestogen only contraceptive pill; this relative risk may be due to an earlier diagnosis. The most important risk factor appears to be the age at which the contraceptive is stopped rather than the duration of use; the risk disappears gradually during the 10 years after stopping and there is no excess risk by 10 years. A possible small increase in the risk of breast cancer should be weighed against the benefits • **Hyperlipidemias:** May have adverse effects on lipid metabolism; use caution in patients with hyperlipidemias. • **Exacerbation of other conditions** Estrogen plus progestin therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine,

	porphyria, systemic lupus erythematosus, and hepatic hemangiomas and should be used with caution in women with these conditions. • **Fluid retention**: Use with caution in patients with diseases that may be exacerbated by fluid retention including cardiac or renal dysfunction. • **Hepatic disorders**: Discontinue if jaundice develops during therapy or if liver function becomes abnormal. Cautious use in severe hepatic insufficiency for vaginal or rectal. Avoid systemic use in hepatic disorders. • **Visual Abnormalities**: Discontinue if sudden disturbances of vision or hearing or other perceptual disorders occurred. If examination reveals papilledema or retinal vascular lesions, medication should not be re-administered. • **Diabetes**: Medroxyprogesterone therapy may have adverse effects on glucose tolerance; monitor patients with diabetes mellitus. • **Abortion**: It is not indicated in threatened abortion. Treatment should be discontinued in the event of a missed abortion. • **Continuation of therapy**: In all cases, a careful appraisal of the risks and benefits should be undertaken at least annually. • **Caution** in conditions of uterine fibroids or endometriosis. The drug should be withdrawn immediately in these cases: Jaundice or deterioration in liver function, Significant increase in blood pressure, new onset of migraine-type headache, Pregnancy, Sudden or gradual, partial or complete loss of vision, Proptosis or diplopia, Papilledema, Retinal vascular lesions.
Storage	• Store between 15°C to 30°C. • Protect capsules from excessive moisture. • Store in the original container to protect from light. **N.B** Refer to manufacturer PIL if there are specific considerations.

Corticosteroids

Betamethasone

Generic Name	Betamethasone
Dosage form/strengths	Topical Aerosol Foam: 0.12 gm Topical Ointment or cream: 1 mg/gm (0.1 gm/100g), 0.5 mg/gm Topical Gel: 0.5 mg/gm Topical Solution: 0.1 gm Tablets: 0.5mg Solution for deep I.M, I.V slow Injection/Infusion, Subconjunctival, and local injection in soft tissue: 4 mg/mL Solution for I.M Injection, I.V Injection/Infusion: 8mg/2mL And in combinations
Route of Administration	*Oral, IV, IM, Topical, intra-articular, intralesional*
Pharmacologic Category	Corticosteroid **ATC code:** D07AC01: Topical H02AB01: Systemic A07EA04: For the treatment of intestinal inflammatory diseases.
Indications	**Systemic** Congenital adrenal hyperplasia and Suppression of inflammatory and allergic disorders *Indications may include:* Bronchial asthma, severe hypersensitivity reactions, anaphylaxis • rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease (excluding systemic sclerosis), polyarteritis nodosa • inflammatory skin disorders, including pemphigus vulgaris, bullous pemphigoid and pyoderma gangrenosum • minimal change nephrotic syndrome, acute interstitial nephritis • ulcerative colitis, Crohn's disease, sarcoidosis • rheumatic carditis • hemolytic anemia (autoimmune), acute and lymphatic leukemia, malignant lymphoma, multiple myeloma, idiopathic thrombocytopenic purpura • immunosuppression in transplantation. **Intra-articular or soft tissue administration** Adjunctive therapy for short-term administration in acute gout flares, acute and subacute bursitis, acute nonspecific tenosynovitis, epicondylitis, rheumatoid arthritis, synovitis of osteoarthritis **Topical** For adults and children over 1 year: Eczema and dermatitis of all types. Psoriasis of scalp and chronic plaque psoriasis of hands and feet, excluding widespread plaque psoriasis. **N.B** Betamethasone has very high glucocorticoid activity and insignificant mineralocorticoid activity.

Dosage Regimen	– Dose depends upon the condition being treated, severity and response of the patient. – Gradual discontinuation is recommended. **General Dosing** • **Oral**: Usual dose 0.5–5 mg daily (smaller doses for children). • **Local injections**: 4-8mg (smaller doses for children). • **Topical**: Once to twice daily. (for adults and children). If used in children or on the face courses should be limited to 5 days. • **I.M, I.V slow Injection/Infusion**: ○ **Adult**: 4–20 mg, repeated up to 4 times in 24 hours. ○ **Pediatric**: Child 1–11 months: Initially 1 mg, repeated up to 4 times in 24 hours according to response. Child 1–5 years: Initially 2 mg, repeated up to 4 times in 24 hours according to response. Child 6–11 years: Initially 4 mg, repeated up to 4 times in 24 hours according to response. Child 12–17 years: 4–20 mg, repeated up to 4 times in 24 hours according to response. **Weight based dosing:** Initial: 0.02 to 0.3 mg/kg/day in three or four divided doses (0.6 to 9 mg/m^2 /day).
Dosage Adjustment	**Dosing: Altered Kidney Function** There are no dosage adjustments needed. **Dosing: Hepatic Impairment** There are no dosage adjustments needed. **Elderly** Lower initial doses.
Contra-indications	**Systemic** • Hypersensitivity to any component of this medicine. • Infections (e.g. Herpes simplex of the eye; systemic fungal infections; vaccinia; cerebral malaria; use in areas with local infection). • Idiopathic thrombocytopenia purpura (IM administration only). **Topical** • Hypersensitivity to any component of this medicine. • Infections of skin. • Rosacea, acne, perioral dermatitis, perianal and genital pruritus.
Adverse Drug Reactions	**Systemic** **Allergic Reactions:** Anaphylactoid reaction, anaphylaxis, angioedema **Cardiovascular**: Bradycardia, cardiac arrest, cardiac arrhythmias, cardiac enlargement, circulatory collapse, congestive heart failure, fat embolism, hypertension, hypertrophic cardiomyopathy in premature infants, myocardial rupture following recent myocardial infarction, pulmonary edema, syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis.

Dermatologic: Acne, allergic dermatitis, cutaneous and subcutaneous atrophy, dry scaly skin, ecchymoses and petechiae, edema, erythema, hyperpigmentation, hypopigmentation, impaired wound healing, increased sweating, rash, sterile abscess, striae**,** suppressed reactions to skin tests, thin fragile skin, thinning scalp hair, urticaria.
Endocrine: Decreased carbohydrate and glucose tolerance, development of cushingoid state, glucosuria, hirsutism, hypertrichosis, increased requirements for insulin or oral hypoglycemic adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery, or illness), suppression of growth in pediatric patients.
Fluid and Electrolyte Disturbances: Congestive heart failure in susceptible patients, fluid retention, hypokalemic alkalosis, potassium loss, sodium retention**.**
Gastrointestinal: Abdominal distention, bowel/bladder dysfunction (after intrathecal administration), elevation in serum liver enzyme levels (usually reversible upon discontinuation), hepatomegaly, increased appetite, nausea, pancreatitis, peptic ulcer with possible perforation and hemorrhage, perforation of the small and large intestine (particularly in patients with inflammatory bowel disease), ulcerative esophagitis.
Metabolic: Negative nitrogen balance due to protein catabolism.
Musculoskeletal: Aseptic necrosis of femoral and humeral heads, calcinosis (following intraarticular or intralesional use), Charcot-like arthropathy, loss of muscle mass, muscle weakness, osteoporosis, pathologic fracture of long bones, post-injection flare (following intra-articular use), steroid myopathy, tendon rupture, vertebral compression fractures.
Neurologic/Psychiatric: Convulsions, depression, emotional instability, euphoria, headache, increased intracranial pressure with papilledema (pseudotumor cerebri) usually following discontinuation of treatment, insomnia, mood swings, neuritis, neuropathy, paresthesia, personality changes, psychic disorders, vertigo. Arachnoiditis, meningitis, paraparesis/paraplegia, and sensory disturbances have occurred after intrathecal administration.
Ophthalmic: Intraocular pressure may become elevated in some individuals. If steroid therapy is continued for more than 6 weeks, intraocular pressure should be monitored.
Other: Abnormal fat deposits, decreased resistance to infection, hiccups, increased or decreased motility and number of spermatozoa, malaise, moon face, weight gain
Topical
>10%: Local: Application-site reaction (includes application-site atrophy, application-site burning, application-site irritation, application-site pain, application-site pruritus, stinging of the skin)
1% to 10%
Dermatologic: Acne vulgaris, alopecia, pruritus (≤2%), xeroderma (4%)
Nervous system: Paresthesia
Ophthalmic: Conjunctivitis

Monitoring Parameters	**Systemic** • Blood pressure • Blood glucose. • Electrolytes, Serum Potassium. • Ophthalmic examination. • Injection site reactions. • Growth rate in children. • HPA axis suppression, adrenal insufficiency or hypercortisolism. • Risk of infection. **Frequent patient monitoring is necessary in patients with the following conditions:** • Osteoporosis (post-menopausal females are particularly at risk). • Hypertension, dyslipidemia or congestive heart failure. • Existing or previous history of severe affective disorders (especially previous steroid psychosis). • Diabetes mellitus (or a family history of diabetes). • History of tuberculosis. • Glaucoma (or a family history of glaucoma). • Myasthenia gravis or previous corticosteroid-induced myopathy. • Liver failure - blood levels of corticosteroid may be increased. • Renal insufficiency. • Epilepsy. • Peptic ulceration. • Hypothyroidism
Drug Interactions	***Systemic*** ***Risk X: Avoid combination*** Aldesleukin, BCG Products, Brivudine, Chikungunya Vaccine (Live), Cladribine, Dengue Tetravalent Vaccine (Live), Desmopressin, Macimorelin, Mifamurtide, Mifepristone, Mumps- Rubella- or Varicella-Containing Live Vaccines, Natalizumab, Nadofaragene Firadenovec, Pimecrolimus, Poliovirus Vaccine (Live/Trivalent/Oral), Ritlecitinib, Ruxolitinib (Topical), Tacrolimus (Topical), Talimogene Laherparepvec, Tertomotide, Typhoid Vaccine, Yellow Fever Vaccine. ***Risk D: Consider therapy modification*** Abrocitinib, Baricitinib, CAR-T Cell Immunotherapy, Coccidioides immitis Skin Test, COVID-19 Vaccine (Adenovirus Vector), COVID-19 Vaccine (mRNA), Denosumab, Desirudin, Deucravacitinib, Filgotinib, Hyaluronidase, Immune Checkpoint Inhibitors, Influenza Virus Vaccines, Leflunomide, Metyrapone, Neuromuscular-Blocking Agents (Nondepolarizing), Polymethylmethacrylate, Rabies Vaccine, Sipuleucel-T, Tofacitinib, Upadacitinib, Vaccines (Inactivated/Non-Replicating), Vaccines (Live).
Pregnancy and Lactation	**Pregnancy** **Systemic**: Corticosteroids have been shown to be teratogenic in many

	species when given in doses equivalent to the human dose. An increased incidence of cleft palate in the offspring occured. Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. If used during pregnancy, observe infants carefully for signs of hypoadrenalism. Chronic high doses should be avoided. **Topical**: In general, the use of topical corticosteroids is not associated with a significant risk of adverse pregnancy outcomes. However, there may be an increased risk of low birth weight infants following maternal use of potent or very potent topical products, especially in high doses, although this risk is likely to be low. **Lactation** **Systemic:** Could suppress growth or interfere with endogenous corticosteroid production. Caution. When systemic corticosteroids are needed in a lactating patient for rheumatic disorders, low doses of non-fluorinated corticosteroids (e.g., Prednisone) are preferred. **Topical:** Corticosteroids are generally considered acceptable for use in patients who are breastfeeding.
Administration	**IM:** Shake well prior to use. **IV:** May be administered as an IV injection over 30 seconds to 1 minute **or** as a diluted infusion. **Topical** Apply a thin film to the affected skin areas once or twice daily. Discontinue therapy when control is achieved. Do not use occlusive dressings unless directed by a physician. **N.B** Refer for the product PIL for more specific considerations.
Warnings/ Precautions	• **Immunosuppressant Effects:** Increased Susceptibility to Infections and may mask symptoms of infection. Caution in immunosuppressant agents. • **Endocrine Effects:** Prolonged, high dose therapy may result in hypothalamic-pituitary-adrenal (HPA) suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. HPA axis suppression may lead to adrenal crisis. Discontinuation of a corticosteroid should be done slowly and carefully. • **Diabetes mellitus**: Corticosteroids can increase blood glucose level and worsen pre-existing diabetes. • **Psychiatric Effects:** May appear with corticosteroids use. Symptoms include euphoria, insomnia, mood swings, personality changes, severe depression and frank psychotic manifestations. • **Cardiovascular disease:** Use has been associated with fluid retention, electrolyte disturbances, and hypertension. Use with caution in patients with heart failure, hypertension or renal insufficiency. • **Gastrointestinal disease**: Use with caution in patients with GI diseases (diverticulitis, fresh intestinal anastomosis, active or latent peptic ulcer, ulcerative colitis, abscess or other pyogenic infection) due to perforation risk. • **Musculoskeletal Effects:** Osteoporosis is associated with long term and

large dose uses of glucocorticoids. All corticosteroids increase calcium excretion. Use may cause transient worsening of myasthenia gravis; monitor for worsening of case. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. Acute myopathy is reported with high doses. Clinical improvement after discontinuation may require weeks to years.

• **Ocular disorders**: Prolonged use of corticosteroids may enhance eye disorders including cataract, glaucoma, or eye infections. Monitor for visual disturbances. Do not use in active ocular herpes simplex.

• **Thyroid disease**: Changes in thyroid status may necessitate dosage adjustments; metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid ones.

• **Withdrawal of systemic treatment:** Abrupt withdrawal is not recommended after long term use. Withdraw therapy with gradual tapering of dose. Symptoms of abrupt withdrawal include: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss, and/or hypotension.

• **Kaposi sarcoma**: Prolonged treatment with corticosteroids has been associated with the development of Kaposi's sarcoma (case reports); if noted, discontinuation of therapy should be considered.

• Menstrual irregularities may occur and in postmenopausal women vaginal bleeding has been observed.

• **Anaphylactoid reactions:** Rare cases of anaphylactoid reactions have been observed in patients receiving corticosteroids. Cases of serious anaphylaxis, including death, have been reported with Triamcinolone acetonide.

• **Elderly:** Use cautiously in older adults with the smallest possible effective dose for the shortest duration.

• **Pediatrics**: May slow growth rate; growth should be routinely monitored in pediatric patients.

• **Intra-Articular Injection:** Corticosteroids should not be injected into unstable joints. Severe joint destruction with necrosis of bone may occur if repeated intra-articular injections are given over a long period of time. Caution when given into tendon sheaths to avoid injection into the tendon itself. Repeated injection into inflamed tendons should be avoided as it has been shown to cause tendon rupture.

• **Septic arthritis:** May occur as a complication to intra-articular or soft tissue administration. Local swelling, further restriction of joint motion, fever, and malaise are suggestive of septic arthritis. institute appropriate antimicrobial therapy as required.

• **Local nasal effects:** Nasal septal perforation, nasal ulceration, epistaxis, and localized Candida albicans infections of the nose and/or pharynx may occur. Monitor patients periodically for adverse nasal effects.

• **Sensitization:** Topical use has been associated with local sensitization (redness, irritation); discontinue if sensitization is noted.

• **Systemic effects** may be associated with high doses or prolonged topical use which include: Cushing's syndrome, Cushingoid features, adrenal suppression, hyperglycemia. Absorption is increased by the use of occlusive dressings, or application to large surface areas.

	• **Appropriate use**: For intramuscular, intra-articular or intralesional use only, do not administer intravenously or epidurally (see Epidural injection). • **Topical steroids use in psoriasis may be hazardous** due to: Rebound relapses following development of tolerance, risk of pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin. If used in psoriasis, careful patient supervision is important**.**
Storage	Store between 15°C and 30°C. Protect from light. **N.B** Refer for the product PIL for more specific considerations.

Budesonide

Generic Name	Budesonide
Dosage form/strengths	**Inhalation** Inhalation powder, or Powder for Inhalation in Hard Capsule: 200 mcg, 400 mcg Suspension Aerosol for Inhalation: 200 mcg/dose Suspension for inhalation in nebules: 0.25 mg/ml, 0.25mg/2ml, 0.5mg/ml, 0.5 mg/2ml, 1 mg/2ml. Suspension for inhalation in Respules: 0.5mg, 1mg. **Oral** Oral Hard Gelatin Capsule: 3mg Oral Modified-Release Tablet: 9mg **Rectal** Enema: 2 mg **Nasal** spray: 32 mcg/metered dose, 64mcg/metered dose
Route of Administration	*Oral Inhalation, Oral, Rectal, Nasal Inhalation*
Pharmacologic Category	Corticosteroid ATC, Oral Inhalant : R03BA02 ATC, Rectal: D07AC09 ATC, Nasal: R01AD05 ATC, Systemic: A07EA06
Indications	*Oral Inhalation* **Bronchial Asthma** Maintenance and prophylactic treatment of asthma in patients ≥6 years of age (dry powder inhaler) or 3 months age and above (nebulization suspension). *Rectal enema* **Ulcerative colitis:** Ulcerative colitis involving rectal and recto-sigmoid disease. *Nasal* Treatment and prevention of symptoms of seasonal and perennial allergic rhinitis (**upper respiratory allergies** e.g., nasal congestion, runny nose, itchy nose, sneezing) in adults and children ≥6 years of age. Treatment of signs and symptoms of **nasal polyps.** *Oral* **Ulcerative colitis or Crohn's disease** (mild to moderate) involving the ileum and/or the ascending colon (delayed-release capsule) **Active microscopic colitis** in adults aged ≥ 18 years.
Dosage regimen	***Oral Inhalation*** Note: Titrate to the lowest effective dose once asthma is stable. **Dosing: Adult** **Asthma** *Powder for Inhalation* *Initial*: Individualize daily starting budesonide dose based on severity of symptoms

- Low doses (200-400 mcg/day) for mild persistent asthma;
- Low to medium doses (>400 to 800 mcg/day) for moderate persistent asthma;
- High doses (>800 mcg/day up to 1600 micrograms/day.) for severe persistent asthma.

Maintenance

- Twice daily dosing: usual maintenance dose is 100-400 mcg twice daily up to 800 mcg twice daily in severe periods of asthma.
- Once daily dosing: usual maintenance dose is 200-400 mcg once daily up to 800 mcg once daily.

Oral suspension inhalation (alternative agent)
Initial: 1 to 2 mg twice daily; dose may be increased if needed.
Maintenance: 0.5 - 1mg twice daily.

Dosing: Pediatric
Asthma
Powder for Inhalation
Initial: Children 6 to 11 years of age: 200-400 mcg/day. Increased if needed up to 800 mcg/day.
Maintenance
Twice daily dosing: Children 6 to 11 years: The usual maintenance dose is 100-200 mcg and up to 400 mcg twice daily.
Once daily dosing: The usual maintenance dose is 200-400 micrograms once daily.

Oral suspension inhalation (alternative agent)
Initial: Children 3 months to 12 years: 0.5 – 1 mg twice daily.
Maintenance: Children 3 months to 12 years: 0.25 - 0.5 mg twice daily.

Rectal: Dosing Adult
One Enema once daily at night prior to bedtime for 4 weeks. Full effect is usually achieved within 2–4 weeks. Otherwise, the treatment period may be prolonged to 8 weeks.

Intranasal
Upper respiratory symptoms and Nasal Polyps
Dosing: Adult and pediatric:
The recommended (initial) dose Adults, adolescents and children from 6 years of age: 256 micrograms (128 mcg in each nostril), may be administered once daily in the morning or divided into two administrations, in the morning and in the evening.

Oral
Crohn disease, mild to moderate (active)
Dosing: Adult and pediatrics 8 years and and Adolescents weighing >25 kg**:**
Oral (delayed-release)
Initial: 9 mg once daily in the morning for 2-4 weeks up to 8 weeks if needed.

	Maintenance: 6 mg once daily in the morning, or the lowest effective dose for up to 2- 3 months in adults or for 2 weeks for pediatrics. *Discontinuation*: If maintained for prolonged dosing intervals, dose should be reduced gradually for the last 2 to 4 weeks of therapy. **Active Microscopic colitis in adults** *Initial*: 9 mg once daily in the morning up to 8 weeks. *Maintenance*: 6 mg once daily in the morning, or the lowest effective dose.
Dosage Adjustment	**Dosing Altered Kidney Function** Specific dosage adjustments are not available; it appears that no dosage adjustments are needed. **Dosing Hepatic Impairment** Budesonide undergoes hepatic metabolism. *Nasal, Inhaled or Rectal products:* No dosage adjustment suggested *Oral:* - Mild Impairment: No dosage adjustment is needed. - Moderate Impairment: Monitor the patient for signs/symptoms of hypercorticism. Discontinue then. Consider reducing the dosage to oral 3 mg once daily. - Severe Impairment: Avoid.
Contra-indications	• Hypersensitivity to budesonide or any component of the formulation. • Hepatic cirrhosis in oral use.
Adverse Drug Reactions	**Systemic** **>10%** Cardiovascular: Hypertension (16%), peripheral edema (14%). Dermatologic: Acne vulgaris (5% to 15%). Endocrine & metabolic: Bruise (5% to 15%), moon face (3% to 11%). Gastrointestinal: Nausea (5% to 11%). Nervous system: Headache (15% to 21%). Neuromuscular & skeletal: Muscle spasm (13%). Respiratory: Respiratory tract infection (11%). **Oral Inhalation** **>10%** Otic: Otitis media (suspension: 12%; powder: 1%). Respiratory: Respiratory infection (suspension: 38%; powder: ≥3%), rhinitis (5% to 12%). **Nasal** **1% to 10%:** Respiratory: Bronchospasm (2%), cough (2%), epistaxis (8%), nasal mucosa irritation (2%), pharyngitis (4%). **Rectal** **>10%:** Endocrine & metabolic: Decreased plasma cortisol (17%).
Monitoring Parameters	**Systemic** • Ophthalmic examinations. • Growth rate in pediatrics.

	• HPA axis suppression, adrenal insufficiency or hypercortisolism. • Risk of infection. **Nasal** • Growth rate in pediatrics. • Monitor patients periodically for signs of adverse effects: Epistaxis, nasal septal perforation, nasal ulceration, infection, impaired wound healing and eye disorders. • HPA axis suppression, adrenal insufficiency or hypercortisolism. • Risk of infection. **Inhalation** • Growth rate in pediatrics. • Ophthalmic examination. • HPA axis suppression, adrenal insufficiency or hypercortisolism. • Risk of infection. • Monitor patients periodically for signs of adverse effects: Oral candidiasis, paradoxical bronchospasm. **Topical** At large surface areas or longer periods: HPA axis suppression (urinary free cortisol, ACTH stimulation tests). **Frequent patient monitoring is necessary in patients with the following conditions:** • Osteoporosis (post-menopausal females are particularly at risk). • Hypertension, dyslipidemia or congestive heart failure. • Existing or previous history of severe affective disorders (especially previous steroid psychosis). • Diabetes mellitus (or a family history of diabetes). • History of tuberculosis. • Glaucoma (or a family history of glaucoma). • Myasthenia gravis or previous corticosteroid-induced myopathy. • Liver failure - blood levels of corticosteroid may be increased. • Renal insufficiency. • Epilepsy. • Peptic ulceration. • Hypothyroidism
Drug Interactions	**Note**: Interactions (Moderate, Strong) may depend on the Route of Administration of Budesonide. ***Risk X: Avoid combination*** CYP3A4 Inhibitors (e.g., Ketoconazole, Itraconazole, Ritonavir, Indinavir, Saquinavir, Erythromycin, and Cyclosporine), Aldesleukin, Desmopressin, Loxapine, Fexinidazole, Fusidic Acid (Systemic), Grapefruit Juice. ***Risk D: Consider therapy modification***

	Esketamine. Antacids, CYP3A4 inducers.
Pregnancy and Lactation	**Pregnancy**: No increased risk for overall congenital malformations from the use of inhaled or intranasal budesonide during early pregnancy by prospective epidemiological studies. **Lactation**: Minor effects on the breast-fed child are anticipated in oral systemic. Data support continued use of Budesonide, oral and rectal administrations, during breast-feeding.
Administration	**Oral systemic** Capsule - Tablet, extended release: Administer in the morning. Some products recommended to be taken about half an hour before breakfast. Swallow whole; do not open, crush, break or chew. **Rectal, Nasal or inhalation:** Refer to product instructions. N.B. Refer to product PIL for other specific considerations.
Warnings/ Precautions	• **Immunosuppressant Effects:** Increased Susceptibility to Infections and may mask symptoms of infection. Caution in immunosuppressed patients. • **Endocrine Effects:** Prolonged, high dose therapy may result in hypothalamic-pituitary-adrenal (HPA) suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. HPA axis suppression may lead to adrenal crisis. Pediatrics and patients with hepatic impairment may be at increased risk. • **Diabetes mellitus**: Corticosteroids can increase blood glucose level and worsen pre-existing diabetes. • **Psychiatric Effects:** May appear with corticosteroids use. Symptoms include euphoria, insomnia, mood swings, personality changes, severe depression and frank psychotic manifestations. • **Gastrointestinal disease**: Use with caution in patients with GI diseases (diverticulitis, fresh intestinal anastomosis, active or latent peptic ulcer, ulcerative colitis, abscess or other pyogenic infection) due to perforation risk. • **Systemic effects** may be associated with high doses or prolonged use which include: Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, Osteoporosis, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). • **Withdrawal of systemic treatment:** Dose should normally be reduced for the last 2 to 4 weeks of therapy. Withdrawal phase includes pain in muscles and joints and in rare cases, symptoms such as tiredness, headache, nausea and vomiting. • **Withdrawal Symptoms in Transferred Patients** from Other Systemic Corticosteroids: Taper slowly from corticosteroids with high systemic effects; monitor for withdrawal symptoms e.g adrenocortical suppression and unmasking of allergies (rhinitis, eczema). • **Ocular disorders**: Prolonged use of corticosteroids (nasal, inhalation, topical or systemic) may enhance eye disorders including cataract, glaucoma, increased intraocular pressure, rare diseases such as central serous

	chorioretinopathy (CSCR) or eye infections. Use with caution. Monitor for visual disturbances. Corticosteroids should not be used in active ocular herpes simplex. • **Rare hereditary problems patients**: Fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency patients should not take oral budesoinde.
Storage	Store between 15°C to 30°C. Protect from light. N.B. Refer to product PIL for other specific considerations.

Dexamethasone

Generic Name	Dexamethasone
Dosage form/strengths	Solution for I.M or I.V. Injection: 8mg/2ml, 4 mg/ml, 6.65 mg/ml Tablets: 0.5mg, 0.75 mg, 8mg Oral Syrup: 0.25 mg/5ml, 10 mg/100ml Eye / Ear Drops: 1 mg/ml Eye Ointment: 0.050 % Intravitreal Implant in Applicator: 700 mcg And in combinations.
Route of Administration	Oral, IM, IV, Ophthalmic, Intravitreal.
Pharmacologic Category	**Systemic**: Anti-inflammatory Agent; Antiemetic; Corticosteroid. **Ophthalmic**, Otic: Anti-inflammatory Agent; Corticosteroid. **ATC:** Hormonal: H02AB02 Ophthalmic: S01CB01 Ophthalmological and otological preparations: S03BA01
Indications	**Oral, IV, or IM injection** **Anti-inflammatory or immunosuppressant agent** in the treatment of a variety of diseases, including: Allergic, hematologic (e.g. immune thrombocytopenia), dermatologic, neoplastic (leukemias, lymphomas, and multiple myeloma), rheumatic, autoimmune, nervous system, renal, and respiratory origin. **Management of shock, cerebral edema.** **(COVID19) in adult and adolescent patients** (aged 12 years and older with body weight at least 40 kg) who require supplemental oxygen therapy. **Palliative treatment of malignant tumors.** **Severe infections with toxic conditions** (e.g. tuberculosis, typhoid) only with concomitant anti-infective therapy. **Intra-articular or soft tissue injection** As adjunctive therapy for short-term administration in synovitis of osteoarthritis, rheumatoid arthritis, acute and subacute bursitis, acute gouty arthritis, epicondylitis, acute nonspecific tenosynovitis, and posttraumatic osteoarthritis. **Ophthalmic** For treatment of non-infectious inflammatory conditions affecting the anterior segment of the eye such as allergic conjunctivitis, iritis, or cyclitis; symptomatic treatment of corneal injury from chemical, radiation, or thermal burns, or penetration of foreign bodies. **Otic** 0.1% ophthalmic solution is indicated for otic use to treat steroid-responsive inflammatory conditions of the external auditory meatus. **N.B** Dexamethasone has very high glucocorticoid activity and insignificant mineralocorticoid activity.

Dosage regimen	The dose depends upon the condition being treated, severity, and response of the patient. **General adult dosing** **Oral, IV, IM** • **Usual dosage range:** 4 to 20 mg/day given in a single daily dose or 2 to 4 divided doses. • **High dose***:* 0.4 to 0.8 mg/kg/day (usually not to exceed 40 mg/day, up to 80 mg in initial treatment of cerebral edema). Followed by gradual decreasing doses. • **Covid-19 management**: 6 mg IV or oral, once a day for up to 10 days. (from 12 years of age and above) **Ophthalmic** • **Usual dose range:** 1 drop 4 to 6 times daily in the affected eye. • **Severe cases**: May start with 1 drop every hour; reduce to one drop every 4 hours when favorable response is observed. Duration: few days up to 14 days. Gradual decreasing of doses is recommended to avoid relapse.
Dosage Adjustment	**Dosing: Altered Kidney Function** There is no dosage adjustment needed. Hemodialysis, intermittent (thrice weekly): No supplemental dose or dosage adjustment necessary. **Dosing: Hepatic Impairment** There are no dosage adjustments needed.
Contra-indications	**Systemic** • Hypersensitivity to Dexamethasone or any component of the formulation. • Systemic infections. • Idiopathic thrombocytopenia purpura (IM administration only). **Ophthalmic** • Hypersensitivity. • Infections of the eye (bacterial, fungal, or viral). • Solution should also not be used for otic indications if perforation of a drum membrane is present.
Adverse Drug Reactions	**Adverse reactions (significant) considerations** **Adrenal suppression (tertiary adrenal insufficiency):** glucocorticoid-induced adrenal insufficiency usually resolves with discontinuation of dexamethasone, but symptoms may persist for 6 to 12 months. Adrenal crisis, a life-threatening emergency that may present like a hypotensive shock state. **CNS and psychiatric/behavioral effects:** patients receiving high-dose regimens may develop apathy or depression. More commonly, patients develop excitatory psychiatric disturbances. Discontinuation or dose reductions generally resolve symptoms over days to weeks. *Onset:* varied; most cases occur early in treatment (within the first 5 days), average of 11.5 days. The majority develop within 6 weeks of initiation

Cushingoid features/Cushing syndrome: *onset:* delayed; may develop within the first 2 months of dexamethasone therapy.

GI effects

Hyperglycemia: may provoke new-onset hyperglycemia in patients without a history of diabetes and may cause an exacerbation of diabetes mellitus. *Onset:* rapid; 4 hours.

Infection: have immunosuppressive and anti-inflammatory effects that are reversible with discontinuation.

Neuromuscular and skeletal effects: ranging from osteoporosis and vertebral compression fracture to myopathy to osteonecrosis in adult and pediatric patients. *Onset:* delayed; vertebral fracture risk is increased within 3 months of initiation and peaks at 12 months.

Ocular effects: include increased intraocular pressure (IOP), glaucoma (open-angle), and subcapsular posterior cataract in adult and pediatric patients. Cataracts may persist after discontinuation of glucocorticoid therapy.

Systemic adverse events

Frequency not defined

Cardiovascular: bradycardia, cardiac arrhythmia, cardiomegaly, circulatory shock, edema, embolism (fat), heart failure (in susceptible patients), hypertension, myocardial rupture (after recent myocardial infarction), syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis.

Dermatologic: acne vulgaris, allergic dermatitis, alopecia, atrophic striae, diaphoresis, ecchymoses, erythema of skin, facial erythema, fragile skin, hyperpigmentation, hypertrichosis, hypopigmentation, inadvertent suppression of skin test reaction, perianal skin irritation (itching, burning, tingling; following rapid iv injection; more common in females, with higher doses; sudden onset with resolution in <1 minute), skin atrophy, skin rash, subcutaneous atrophy, urticaria, xeroderma.

Endocrine & metabolic: decreased serum potassium, fluid retention, growth, suppression (children), hirsutism, hypokalemic alkalosis, menstrual disease, negative nitrogen balance (due to protein catabolism), sodium retention, weight gain.

Gastrointestinal: hiccups, increased appetite, nausea, pancreatitis, pruritus ani (following iv injection).

Genitourinary: defective spermatogenesis (increased or decreased), glycosuria.

Hematologic & oncologic: Kaposi sarcoma, petechia.

Hepatic: hepatomegaly, increased serum transaminases.

Hypersensitivity: anaphylaxis, angioedema, non-immune anaphylaxis.

Infection: sterile abscess.

Local: post injection flare (intra-articular use).

Nervous system: amyotrophy, emotional lability, euphoria, headache, increased intracranial pressure, intracranial hypertension (idiopathic; usually following discontinuation), malaise, myasthenia, neuritis, neuropathy, paresthesia, personality changes, seizure, vertigo.

Neuromuscular & skeletal: Charcot arthropathy, rupture of tendon.

Ophthalmic: exophthalmos.

	Respiratory: pulmonary edema. **Miscellaneous**: wound healing impairment. **Intraocular implant/injection** **>10%** **Cardiovascular**: hypertension (implant: 13%). **Ophthalmic**: cataract (implant: 5% to 68%; incidence increases in patients requiring a second injection), conjunctival hemorrhage (implant: 22% to 23%), corneal edema (injection: 5% to 15%; implant: ≤1%), increased intraocular pressure (3% to 28%), iritis (injection: 5% to 15%). **Ophthalmic solution/suspension** **1% to 10%:** ophthalmic: eye discomfort (10%), eye irritation (1%).
Monitoring Parameters	**Systemic** • Blood pressure. • Blood glucose. • Ophthalmic examination. • Injection site reactions. • Electrolytes, Serum potassium in high doses. • HPA axis suppression, adrenal insufficiency or hypercortisolism. • Growth rate in children. • Risk of infection. **Frequent patient monitoring is necessary in patients with the following conditions** • Osteoporosis (post-menopausal females are particularly at risk). • Hypertension, dyslipidemia or congestive heart failure. • Existing or previous history of severe affective disorders (especially previous steroid psychosis). • Diabetes mellitus (or a family history of diabetes). • History of tuberculosis. • Glaucoma (or a family history of glaucoma). • Myasthenia gravis or previous corticosteroid-induced myopathy. • Liver failure - blood levels of corticosteroid may be increased. • Renal insufficiency. • Epilepsy. • Peptic ulceration. • Hypothyroidism **Ophthalmic**: Intraocular pressure (with use >10 days).
Drug Interactions	***Risk X: Avoid combination*** Aldesleukin, BCG Products, Brivudine, Chikungunya Vaccine (Live), Cladribine, Dengue Tetravalent Vaccine (Live), Desmopressin, Disulfiram, Fexinidazole, Fusidic Acid (Systemic), Lapatinib, Macimorelin, Methotrimeprazine, Mifamurtide Mifepristone, Mumps- Rubella- or Varicella-Containing Live Vaccines, Nadofaragene Firadenovec, Natalizumab, Ornidazole, Pimecrolimus,

	Poliovirus Vaccine (Live/Trivalent/Oral), Rilpivirine, Ritlecitinib, Ruxolitinib (Topical), Secnidazole, Simeprevir, Tacrolimus (Topical), Talimogene Laherparepvec, Tertomotide, Typhoid Vaccine, Yellow Fever Vaccine. ***Risk D: Consider therapy modification*** Abrocitinib, Adenovirus Vaccine, Antacids, Aprepitant, Atogepant, Avelumab, Baricitinib, CAR-T Cell Immunotherapy, Caspofungin, Cobicistat, Coccidioides immitis Skin Test, COVID-19 Vaccine (Adenovirus Vector), COVID-19 Vaccine (mRNA), CYP3A4 Inducers (Strong))e.g. Carbamazepine, Rifampicin(, Denosumab, Desirudin, Deucravacitinib, Elvitegravir, Filgotinib, Fosaprepitant, Fosnetupitant, Fosphenytoin, Hormonal Contraceptives, Hyaluronidase, Imatinib, Immune Checkpoint Inhibitors, Leflunomide, Lenalidomide, Lopinavir, Magaldrate, Mestranol, Metyrapone Netupitant, Neuromuscular-Blocking Agents (Nondepolarizing), Phenobarbital, Phenytoin, Poliovirus Vaccine, Polymethylmethacrylate, Rabies Vaccine, Rotavirus Vaccine, Saquinavir, Sipuleucel-T, Thalidomide, Tofacitinib, Ubrogepant, Upadacitinib, Vaccines (Inactivated/Non-Replicating), Vaccines (Live).
Pregnancy and Lactation	**Pregnancy**: Abnormalities in fetal development can't be excluded in long term use. Careful benefit-risks assessment before use. Chronic high doses should be avoided for the treatment of maternal disease. **Lactation**: Single doses of Dexamethasone are considered compatible with breastfeeding; information related to prolonged use is not available. If the disease requires higher doses, breast-feeding should be discontinued.
Administration	**Oral**: May administer with food or milk to decrease GI adverse effects. **Parenteral**: Use preservative-free dosage forms in neonates. **IM**: May be administered undiluted by deep IM injection. **IV**: May be administered as undiluted solution slow IV push, usually over 1 to 4 minutes; rapid administration is associated with perineal discomfort (burning, tingling); may consider further dilution of high doses and administration by IV intermittent infusion over 15 to 30 minutes **Intra-articular or soft tissue injection**: (Dexamethasone sodium phosphate (a short-acting solution)) Intra-articular: Administer into affected joints. Soft tissue: Administer into affected tissue. **Preparation for Administration: Adult** **IV**: May be given undiluted or further diluted in NS or D5W. Dexamethasone dilutions in 50 mL of NS have been used. **Ophthalmic** 0.1% solution or suspension: Remove soft contact lenses prior to using solutions containing benzalkonium chloride. Do not touch the tip of the container to the eye. Shake suspension well prior to use. Apply finger pressure to the lacrimal sac during and for 1 to 2 minutes after installation to decrease risk of absorption and systemic effects. **Otic** Ophthalmic 0.1% solution may also be administered otically. Prior to use, clean the aural canal thoroughly and sponge dry. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Warnings/ Precautions	• **Immunosuppressant Effects:** Increased Susceptibility to Infections and may mask symptoms of infection. Caution in immunosuppressant agents. • **Endocrine Effects:** Prolonged, high dose therapy may result in hypothalamic-pituitary-adrenal (HPA) suppression particularly in younger children and hepatic impaired patients. HPA axis suppression may lead to adrenal crisis. Discontinuation of a corticosteroid should be done slowly and carefully. • **Diabetes mellitus**: Corticosteroids can increase blood glucose level and worsen pre-existing diabetes. • **Psychiatric Effects:** May appear with corticosteroids use. Symptoms include euphoria, insomnia, mood swings, personality changes, severe depression and frank psychotic manifestations. • **Cardiovascular disease:** Use has been associated with fluid retention, electrolyte disturbances, and hypertension. Use with caution in patients with heart failure, hypertension or renal insufficiency. • **Gastrointestinal disease**: Use with caution in patients with GI diseases (diverticulitis, fresh intestinal anastomosis, active or latent peptic ulcer, ulcerative colitis, abscess or other pyogenic infection) due to perforation risk. • **Musculoskeletal Effects:** Osteoporosis is associated with long term and large dose uses of glucocorticoids. Use may cause transient worsening of myasthenia gravis; monitor for worsening of case. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. Acute myopathy is reported with high doses. Clinical improvement after discontinuation may require weeks to years. • **Ocular disorders**: Prolonged use of corticosteroids may enhance eye disorders including cataract, glaucoma, or eye infections. Monitor for visual disturbances. Do not use in active ocular herpes simplex. • **Renal impairment**: Use with caution in patients with renal impairment; fluid retention may occur. • **Thyroid disease**: Changes in thyroid status may necessitate dosage adjustments; metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid ones. • **Withdrawal of systemic treatment:** Abrupt withdrawal is not recommended after long term use. Withdraw therapy with gradual tapering of dose. Symptoms of abrupt withdrawal include: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss, and/or hypotension. • **Kaposi sarcoma**: Prolonged treatment with corticosteroids has been associated with the development of Kaposi's sarcoma (case reports); if noted, discontinuation of therapy should be considered. • **Elderly:** Use cautiously in older adults with the smallest possible effective dose for the shortest duration. • **Pediatrics**: May slow growth rate; growth should be routinely monitored in pediatric patients. • **Pheochromocytoma:** higher risk of pheochromocytoma crisis (may be fatal) in patients with suspected or confirmed pheochromocytoma after administration of systemic corticosteroids. • **Seizure disorders**: Use corticosteroids with caution in patients with a

	history of seizure disorder; seizures have been reported with adrenal crisis. • **Intravitreal implant**: Endophthalmitis, ocular inflammation, intraocular pressure elevations and retinal detachments may occur with intravitreal injection. A risk of implant migration into the anterior chamber may be present if the posterior capsule of the lens is absent or torn. Administer adequate anesthesia and a broad-spectrum microbicide prior to procedure.
Storage	**Injection**: Store intact vials between 15°C to 30°C. Protect from light, heat, and freezing. Diluted solutions should be used within 24 hours. **Oral dosage form**: Store between 15°C to 30°C. Protect from moisture. **Ophthalmic**: Store between 15°C to 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations.

Fludrocortisone

Generic Name	Fludrocortisone
Dosage Form/Strengths	Tablets: 0.1 mg.
Route of Administration	Oral.
Pharmacologic Category	Corticosteroid, Systemic. ATC: H02AA02.
Indications	**Primary adrenal insufficiency (Addison disease):** Partial replacement therapy for primary adrenocortical insufficiency. **Classic congenital adrenal hyperplasia treatment (salt-losing adrenogenital syndrome)**. **N.B**. Fludrocortisone Acetate is a potent mineralocorticoid and is used predominantly for replacement therapy.
Dosage Regimen	Dosage depends on the severity of the disease and the response of the patient. **Dosage adult** **Oral**: 0.05-0.2mg, up to 0.3 mg daily. If hypertension develops, reduce the dose to 0.05mg. May be preferably administered with oral Cortisone or Hydrocortisone. Doses of 0.1 mg three times weekly have been used. **Dosage Pediatrics**: Refer to adult dosing; adjust according to age, weight and severity.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** There are no dosage adjustments needed; use with caution. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments needed; use with caution.
Contra-indications	• Hypersensitivity to Fludrocortisone or any component of the formulation. • Systemic infections.
Adverse Drug Reactions	**Adverse Reactions (Significant) Considerations** Cardiovascular effects. Electrolyte disturbances. **Frequency not defined** • Cardiovascular: Cardiomegaly, edema, heart failure, hypertension • Dermatologic: Allergic skin rash, atrophic striae, diaphoresis, ecchymoses, facial erythema, hyperpigmentation (skin and nails), maculopapular rash, skin atrophy, subcutaneous atrophy, urticaria. • Endocrine & metabolic: Cushing syndrome, growth retardation, hirsutism, HPA-axis suppression, hyperglycemia, hypokalemia, hypokalemic alkalosis, menstrual disease, negative nitrogen balance, prediabetes. • Gastrointestinal: Abdominal distention, esophageal ulcer, pancreatitis, peptic ulcer. • Genitourinary: Glycosuria.

	• Hematologic & oncologic: Bruise, petechia, purpuric disease. • Local: Local acneiform eruptions. • Nervous system: Amyotrophy, headache, intracranial hypertension (idiopathic), mental status changes (severe), myasthenia, seizure, vertigo. • Neuromuscular & skeletal: Aseptic necrosis of femoral head, aseptic necrosis of humeral head, bone fracture (including pathological fracture and vertebral compression fracture), osteoporosis, steroid myopathy. • Ophthalmic: Exophthalmos, glaucoma, subcapsular posterior cataract. • Miscellaneous: Wound healing impairment.
Monitoring Parameters	• Blood pressure. • Blood glucose. • Electrolytes, Serum potassium. • Ophthalmic examination. • Risk of infection. • HPA axis suppression, adrenal insufficiency or hypercortisolism. • Growth rate in children with prolonged therapy. **Frequent patient monitoring is necessary in patients with the following conditions:** • Osteoporosis (post-menopausal females are particularly at risk). • Hypertension, dyslipidemia or congestive heart failure. • Existing or previous history of severe affective disorders (especially previous steroid psychosis). • Diabetes mellitus (or a family history of diabetes). • History of tuberculosis. • Glaucoma (or a family history of glaucoma). • Myasthenia gravis or previous corticosteroid-induced myopathy. myasthenia gravis. • Liver failure - blood levels of corticosteroid may be increased. • Renal insufficiency. • Epilepsy. • Peptic ulceration. • Hypothyroidism
Drug Interactions	***Risk X: Avoid combination*** Aldesleukin, BCG (Intravesical,) Cladribine, Desmopressin, Fexinidazole, Indium 111, Capromab, Pendetide, Macimorelin, Mifamurtide, Mifepristone, Natalizumab, Pimecrolimus, Tacrolimus (Topical), Talimogene, Laherparepvec. ***Risk D: Consider therapy modification*** Antacids, Aprepitant, Baricitinib, Desirudin, Echinacea, Fingolimod, Fosaprepitant, Hyaluronidase, Immune Checkpoint Inhibitors, Leflunomide, Neuromuscular-Blocking Agents (Nondepolarizing), Rabies Vaccine, Roflumilast, Sipuleucel-T, Tisagenlecleucel, Tofacitinib, Vaccines (Inactivated), Vaccines (Live).
Pregnancy and Lactation	**Pregnancy:** Complications, including cleft palate, still birth, and premature abortion, have been reported when corticosteroids were administered during first trimester pregnancy. Fludrocortisone acetate should be given to a pregnant woman only if clearly needed.

	Hypoadrenalism may occur in newborns following maternal use of corticosteroids in pregnancy; monitor. **Lactation:** Corticosteroids distribute into breast milk. Because of the risk of hypoadrenalism in the infant, or other potential adverse effects, Fludrocortisone should be used cautiously during breast-feeding.
Administration	**Oral**: Administer without regard to food; if GI upset, may take with food. Pediatric: Tablets may be crushed and mixed with about 1 teaspoon of water or soft food such as applesauce, chocolate syrup, jelly, or yogurt. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Immunosuppressant Effects:** Increased Susceptibility to Infections and may mask symptoms of infection. Caution in immunosuppressant agents. • **Endocrine Effects:** Prolonged, high dose therapy may result in hypothalamic-pituitary-adrenal (HPA) suppression particularly in pediatrics and hepatic patients. HPA axis suppression may lead to adrenal crisis. Discontinuation of a corticosteroid should be done slowly and carefully. • **Diabetes mellitus**: Corticosteroids can increase blood glucose level and worsen pre-existing diabetes. • **Psychiatric Effects:** May appear with corticosteroids use. Symptoms include euphoria, insomnia, mood swings, personality changes, severe depression and frank psychotic manifestations. • **Cardiovascular disease:** Use has been associated with fluid retention, electrolyte disturbances, and hypertension. Use with caution in patients with heart failure, hypertension or renal insufficiency. • **Gastrointestinal disease**: Use with caution in patients with GI diseases (diverticulitis, fresh intestinal anastomosis, active or latent peptic ulcer, ulcerative colitis, abscess or other pyogenic infection) due to perforation risk. • **Musculoskeletal Effects:** Osteoporosis is associated with long term and large dose uses of glucocorticoids. Use may cause transient worsening of myasthenia gravis; monitor for worsening of case. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. Acute myopathy is reported with high doses. Clinical improvement after discontinuation may require weeks to years. • **Ocular disorders**: Prolonged use of corticosteroids may enhance eye disorders including cataract, glaucoma, or eye infections. Monitor for visual disturbances. Do not use in active ocular herpes simplex. • **Thyroid disease**: Changes in thyroid status may necessitate dosage adjustments; metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid ones. • **Withdrawal of systemic treatment:** Abrupt withdrawal is not recommended after long term use. Withdraw therapy with gradual tapering of dose. Symptoms of abrupt withdrawal include: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss, and/or hypotension. • **Elderly:** Use cautiously in older adults with the smallest possible effective dose for the shortest duration. • **Pediatrics**: May slow growth rate; growth should be routinely monitored in

	pediatric patients. • **Anaphylactoid reactions**: Rare cases of anaphylactoid reactions have been observed in patients receiving corticosteroids. • **Seizure disorders:** Use corticosteroids with caution in patients with a history of seizure disorder; seizures have been reported with adrenal crisis.
Storage	Store between 15°C to 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations.

Hydrocortisone

Generic Name	Hydrocortisone
Dosage Form/Strengths	Lyophilized powder for solution for IM, IV injection: 100mg, 250 mg. Tablets: 10mg. Topical Cream: 0.01g, 0.1 gm/100g (10mg/gm) (1%). Topical Ointment: 0.01 gm (1%). Ophthalmic Ointment: 10 mg. And in combinations.
Route of Administration	IM, IV, Oral, Topical Ophthalmic.
Pharmacologic Category	Corticosteroid, Systemic, Topical, Ophthalmic. ATC: Dermatological: D07AA02 Systemic: H02AB09 Ophthalmic: S01BA02
Indications	**Systemic** 1. **Endocrine Disorders** • Primary or secondary adrenocortical insufficiency. • Congenital adrenal hyperplasia • Non suppurative thyroiditis • Hypercalcemia associated with cancer **2. Rheumatic Disorders** • Psoriatic arthritis • Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy) • Ankylosing spondylitis • Acute and subacute bursitis • Acute nonspecific tenosynovitis • Acute gouty arthritis • Post-traumatic osteoarthritis • Synovitis of osteoarthritis • Epicondylitis **3. Collagen Diseases** During an exacerbation or as maintenance therapy in selected cases of: • Systemic lupus erythematosus • Systemic dermatomyositis (polymyositis) • Acute rheumatic carditis **4. Dermatologic Diseases** • Pemphigus • Bullous dermatitis herpetiformis • Severe erythema multiforme (Stevens-Johnson syndrome) • Exfoliative dermatitis • Mycosis fungoides • Severe psoriasis • Severe seborrheic dermatitis

5. Allergic States

Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment:

- Seasonal or perennial allergic rhinitis
- Serum sickness
- Bronchial asthma
- Contact dermatitis
- Atopic dermatitis
- Drug hypersensitivity reactions

6. Ophthalmic Diseases

Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:

- Allergic conjunctivitis
- Keratitis
- Allergic corneal marginal ulcers
- Herpes zoster ophthalmicus
- Iritis and iridocyclitis
- Chorioretinitis
- Anterior segment inflammation
- Diffuse posterior uveitis and choroiditis
- Optic neuritis
- Sympathetic ophthalmia

7. Respiratory Diseases

- Symptomatic sarcoidosis
- Loeffler's syndrome not manageable by other means
- Berylliosis
- Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy
- Aspiration pneumonitis

8. Hematologic Disorders

- Idiopathic thrombocytopenic purpura in adults
- Secondary thrombocytopenia in adults
- Acquired (autoimmune) hemolytic anemia
- Erythroblastopenia (RBC anemia)
- Congenital (erythroid) hypoplastic anemia

9. Neoplastic Diseases

For palliative management of:

- Leukemias and lymphomas in adults
- Acute leukemia of childhood

10. Edematous States

To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.

11. Gastrointestinal Diseases

To tide the patient over a critical period of the disease in:

- Ulcerative colitis
- Crohn's disease

	• Regional enteritis **12. Miscellaneous** • Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy • Trichinosis with neurologic or myocardial involvement **Topical** • For the topical treatment of eczema and dermatitis.
Dosage Regimen	Dose depends upon the condition being treated, severity and response of the patient. **Dosing: Adults** **Oral** **Initial**: 20 mg to 240 mg daily. Maintenance: When favorable response is observed, reduce in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. Withdraw treatment, when needed, gradually rather than abruptly. **IV** 100 mg to 500 mg, over 1-10 minutes. This dose may be repeated at intervals of 2, 4, or 6 hours as indicated by the patient's response and clinical condition. High-dose corticosteroid therapy should not continue beyond 48 to 72 hours. It may be preferable to replace Hydrocortisone with a corticosteroid such as methylprednisolone sodium succinate as little or no sodium retention occurs. **Dosing Pediatric** **IV:** 25mg daily or more according to severity and response**.** **Oral**: **Congenital adrenal hyperplasia**: 9–15 mg/m^2/day divided in 3 doses, adjusted according to response. **Adrenocortical insufficiency:** 8–10 mg/ m^2/day divided in 3 doses, adjusted according to response. Higher doses may be needed. **Acute emergencies** 60–80 mg every 4–6 hours for 24 hours, then gradually reduce the dose over several days. **Topical** Apply twice daily. For infants, don't exceed 7 days duration of treatment.
Dosage Adjustment	**Renal Impairment: Adults and pediatrics** There are no dosage adjustments needed. **Hepatic Impairment: Adult and pediatrics** Mild and moderate impairment: There are no dosage adjustments needed. Severe hepatic impairment: Monitoring clinical response and adjustment of dose may be necessary.
Contra-	**Systemic**

indications	• Hypersensitivity to Hydrocortisone or any component of the formulation • Systemic infections. • Idiopathic thrombocytopenia purpura (IM administration only). • Sterile Powder is contraindicated for intrathecal administration. • Suspension may be contraindicated for use in premature infants because the formulation may contain benzyl alcohol. **Topical** • Hypersensitivity. • Infection of skin. • Not to be used on open wounds, ulcers or broken skin.
Adverse Drug Reactions	**Systemic** **Frequency not defined** **Cardiovascular**: Bradycardia, cardiac arrhythmia, cardiac failure (especially in susceptible patients), cardiomegaly, circulatory shock, embolism (fat), hypertension, hypertrophic cardiomyopathy (premature infants), myocardial rupture (post-myocardial infarction), syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis. **Dermatologic**: Acne vulgaris, allergic dermatitis, atrophic striae, burning sensation of skin (especially in the perineal area after IV injection), diaphoresis, ecchymoses, erythema of skin, facial erythema, hyperpigmentation, hypertrichosis, hypopigmentation, inadvertent suppression of skin test reaction, skin rash, thinning hair, urticaria, xeroderma. **Endocrine & metabolic**: Adrenocortical insufficiency (secondary unresponsiveness, particularly during trauma, surgery, or illness), Cushing syndrome, decreased serum potassium, drug-induced Cushing's syndrome, fluid retention, glycosuria, growth retardation, hirsutism, HPA-axis suppression, hyperglycemia, hypokalemic alkalosis, impaired glucose tolerance/prediabetes, lipodystrophy, manifestation of prediabetes, menstrual disease, moon face, negative nitrogen balance (due to protein catabolism), pituitary insufficiency (secondary unresponsiveness, particularly during trauma, surgery, or illness), protein catabolism, sodium retention, weight gain. **Gastrointestinal**: Abdominal distention, gastrointestinal perforation (small and large intestine, particularly in patients with inflammatory bowel disease), hiccups, impaired intestinal carbohydrate absorption, increased appetite, nausea, pancreatitis, peptic ulcer (with possible perforation and hemorrhage), ulcerative esophagitis. **Genitourinary**: Asthenospermia, oligospermia. **Hematologic & oncologic**: Leukocytosis, petechia. **Hepatic**: Hepatomegaly, increased liver enzymes (usually reversible on discontinuation). **Hypersensitivity**: Anaphylaxis, angioedema, hypersensitivity reaction, non-immune anaphylaxis. **Infection**: Increased susceptibility to infection, sterile abscess.

	Local: Atrophy at injection site (cutaneous and subcutaneous), post-injection flare (intra-articular use), skin edema. **Nervous system**: Depression, emotional lability, euphoria, headache, increased intracranial pressure (with pseudotumor cerebri; usually following discontinuation), insomnia, malaise, myasthenia, neuritis, neuropathy, paresthesia, personality changes, psychic disorder, seizure, tingling of skin (especially in the perineal area after IV injection), vertigo. **Neuromuscular & skeletal**: Amyotrophy, aseptic necrosis of femoral head, aseptic necrosis of humeral head, Charcot arthropathy, osteoporosis, pathological fracture (long bones), rupture of tendon (particularly rupture of Achilles tendon), steroid myopathy, vertebral compression fracture. **Ophthalmic**: Blindness (rare, periocular injection), exophthalmos, glaucoma, increased intraocular pressure, retinopathy (central serous chorioretinopathy), subcapsular posterior cataract. **Respiratory**: Pulmonary edema. **Miscellaneous**: Wound healing impairment. ***Topical***: **Cream, ointment:** Dermatologic: Acneiform eruption, atrophic striae, burning sensation of skin, folliculitis, hypertrichosis, hypopigmentation, maceration of the skin, miliaria, perioral dermatitis, pruritus, secondary skin infection, skin atrophy, skin irritation, xeroderma.
Monitoring Parameters	**Systemic use** • Blood pressure. • Blood glucose. • Electrolytes, Serum potassium. • Ophthalmic examination. • HPA axis suppression, adrenal insufficiency or hypercortisolism. • Risk of infection. • Growth rate in pediatric patients. **Frequent patient monitoring is necessary in patients with the following conditions:** • Osteoporosis (post-menopausal females are particularly at risk). • Hypertension, dyslipidemia or congestive heart failure. • Existing or previous history of severe affective disorders (especially previous steroid psychosis). • Diabetes mellitus (or a family history of diabetes). • History of tuberculosis. • Glaucoma (or a family history of glaucoma). • Myasthenia gravis or previous corticosteroid-induced myopathy. • Liver failure - blood levels of corticosteroid may be increased. • Renal insufficiency. • Epilepsy. • Peptic ulceration. • Hypothyroidism. **Topical:** • At large surface areas or longer periods: HPA axis suppression (urinary free cortisol, ACTH stimulation tests).

Drug Interactions	**Systemic** **Risk X: Avoid combination** Aldesleukin, BCG Products, Cladribine, Dengue, Tetravalent Vaccine (Live), Desmopressin, Indium 111, Capromab, Pendetide, Macimorelin, Mifamurtide, Mifepristone, Mumps- Rubella- or Varicella-Containing Live Vaccines, Nadofaragene, Firadenovec, Natalizumab, Pimecrolimus, Poliovirus Vaccine (Live/Trivalent/Oral), Ruxolitinib (Topical), Tacrolimus (Topical), Tertomotide, Typhoid Vaccine, Yellow Fever Vaccine. ***Risk D: Consider therapy modification*** Abrocitinib, Antacids, Baricitinib, CAR-T Cell Immunotherapy, Coccidioides immitis Skin Test, Cosyntropin, COVID-19 Vaccine (Adenovirus Vector), COVID-19 Vaccine (mRNA), Denosumab, Desirudin, Deucravacitinib, Filgotinib, Hyaluronidase, Influenza Virus Vaccines, Lutetium Lu 177 Dotatate, Metyrapone, Neuromuscular-Blocking Agents (Nondepolarizing), Polymethylmethacrylate Rabies Vaccine, Sipuleucel-T, Tofacitinib, Upadacitinib, Vaccines (Inactivated /Non-Replicating), Vaccines (Live). **Topical** **Risk X: Avoid combination** Aldesleukin.
Pregnancy and Lactation	**Pregnancy**: No or limited amount of human data. Animal studies have shown reproductive toxicity in nasal form. Use only if benefit outweighs potential risk. Observe infants for hypoadrenalism. Hydrocortisone for replacement therapy can be used during pregnancy. **Lactation**: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Decisions should be made either to discontinue breastfeeding or treatment with this therapy.
Administration	**Administration: IM** Avoid injection into deltoid muscle (high incidence of subcutaneous atrophy). Dermal and/or subdermal skin depression may occur at injection sites. **Administration: IV** • IV bolus: Administer undiluted over at least 30 seconds; for large doses (≥500 mg), administer over 10 minutes. • IV intermittent infusion: Further dilute in a compatible fluid and administer over 20 to 30 minutes. **Preparation for Administration** • IV bolus or IM administration: Reconstitute 100 mg vials with bacteriostatic water or bacteriostatic sodium chloride (not >2 mL). resulting in a concentration ≥ 50 mg/mL. • IV infusion administration: Add reconstituted solutions to an appropriate volume of 5% dextrose, isotonic saline solution, or D5NS. Concentration should generally not exceed 1 mg/mL. **Administration: Oral** Administer with food or milk to decrease GI upset.

	Administration: **Topical** Apply a thin film to the affected area once or twice a day depending on the severity of the condition. Massage gently until the medication disappears. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Immunosuppressant Effects:** Increased Susceptibility to Infections and may mask symptoms of infection. Caution in immunosuppressant agents. • **Endocrine Effects:** Prolonged, high dose therapy may result in hypothalamic-pituitary-adrenal (HPA) suppression particularly in children and hepatic patients. HPA axis suppression may lead to adrenal crisis. Discontinuation of a corticosteroid should be done slowly and carefully. • **Diabetes mellitus**: Corticosteroids can increase blood glucose level and worsen pre-existing diabetes. • **Psychiatric Effects:** May appear with corticosteroids use. Symptoms include euphoria, insomnia, mood swings, personality changes, severe depression and frank psychotic manifestations. • **Cardiovascular disease:** Use has been associated with fluid retention, electrolyte disturbances, and hypertension. Use with caution in patients with heart failure, hypertension or renal insufficiency. • **Gastrointestinal disease**: Use with caution in patients with GI diseases (diverticulitis, fresh intestinal anastomosis, active or latent peptic ulcer, ulcerative colitis, abscess or other pyogenic infection) due to perforation risk. • **Musculoskeletal Effects:** Osteoporosis is associated with long term and large dose uses of glucocorticoids. Use may cause transient worsening of myasthenia gravis; monitor for worsening of case. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. Acute myopathy is reported with high doses. Clinical improvement after discontinuation may require weeks to years. • **Ocular disorders**: Prolonged use of corticosteroids may enhance eye disorders including cataract, glaucoma, or eye infections. Monitor for visual disturbances. Do not use in active ocular herpes simplex. • **Renal impairment**: Use with caution in patients with renal impairment; fluid retention may occur. • **Thyroid disease**: Changes in thyroid status may necessitate dosage adjustments; metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid ones. • **Withdrawal of systemic treatment:** Abrupt withdrawal is not recommended after long term use. Withdraw therapy with gradual tapering of dose. Symptoms of abrupt withdrawal include: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss, and/or hypotension. • **Kaposi sarcoma**: Prolonged treatment with corticosteroids has been associated with the development of Kaposi's sarcoma (case reports); if noted, discontinuation of therapy should be considered. • **Anaphylactoid reactions:** Rare cases of anaphylactoid reactions have been observed in patients receiving corticosteroids. • **Elderly:** Use cautiously in older adults with the smallest possible effective

	dose for the shortest duration. • **Pediatrics**: May slow growth rate; growth should be routinely monitored in pediatric patients. • **Systemic effects** may be associated with high doses or prolonged topical use which include: Cushing's syndrome, Cushingoid features, adrenal suppression, hyperglycemia. Absorption is increased by the use of occlusive dressings, or application to large surface areas. • **Dermal changes:** Avoid injection or leakage into the dermis; dermal and/or subdermal skin depression may occur at the site of injection. Avoid deltoid muscle injection; subcutaneous atrophy may occur. • **Pheochromocytoma**: Pheochromocytoma crisis has been reported with corticosteroids (may be fatal). Consider the risk of pheochromocytoma crisis prior to administering corticosteroids in patients with suspected pheochromocytoma. • **Benzyl alcohol:** Injection products may contain benzyl alcohol. Benzyl Alcohol may cause toxic reactions and anaphylactoid reactions in infants and children up to 3 years old. Refer to product labeling. • **Topical use**: Avoid use of topical preparations with occlusive dressings or on weeping or exudative lesions. Not for treatment of diaper dermatitis.
Storage	**Injection**: • Store intact vials between 15°C to 30°C; protect from light. Heat sensitive. • Reconstituted solutions are stable for 3 days at 15°C to 30°C. • Protect from light. Solutions prepared for IV infusion are stable for at least 4 hours. **Tablet**: Store between 15°C to 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations.

Methyl Prednisolone

Generic Name	Methylprednisolone
Dosage form/strengths	**Suspension for injection** (IM, Intra-articular, soft tissue, Intralesional): 40 mg/ml, 80 mg/2ml **Powder for reconstitution for I.M/IV injection or I.V infusion**: 1.000 gm, 500mg **Tablets**: 4 mg, 8 mg, 16mg
Route of Administration	Oral, IV, IM, Intra-articular, Intralesional
Pharmacologic Category	Corticosteroid. ATC: H02AB04
Indications	**Systemic** **1. Endocrine disorders** • Primary and secondary adrenal insufficiency. • Congenital adrenal hyperplasia. • hypercalcemia associated with cancer. • Nonsuppurative thyroiditis. **2. Rheumatic disorders** • Acute gouty arthritis. • Psoriatic arthritis. • Rheumatoid arthritis. • Juvenile chronic arthritis. • Ankylosing spondylitis. **3. Collagen diseases/arteritis** • Systemic lupus erythematosus. • Systemic dermatomyositis (polymyositis). • Rheumatic fever with severe carditis. • Giant cell arteritis/polymyalgia rheumatica. **4. Dermatological diseases** • Pemphigus vulgaris. • Severe erythema multiforme (Stevens-Johnson syndrome). **5. Allergic states** • Severe seasonal and perennial allergic rhinitis. • Drug hypersensitivity reactions. • Angioneurotic oedema. • Serum sickness. • Allergic contact dermatitis. • Bronchial asthma. • Atopic dermatitis. • Contact dermatitis. **6. Ophthalmic diseases** • Anterior uveitis (iritis, iridocyclitis). • Posterior uveitis. • Optic neuritis. **7. Respiratory diseases**

- Pulmonary sarcoid.
- Fulminating or disseminated tuberculosis (with appropriate anti-tuberculous
- chemotherapy).
- Aspiration of gastric contents.
- Berylliosis, idiopathic eosinophilic pneumonias.

8. Haematological disorders

- Idiopathic thrombocytopenic purpura.
- Haemolytic anaemia (autoimmune).
- Congenital (erythroid) hypoplastic anemia.
- Pure red cell aplasia.

9. Neoplastic diseases

- Leukaemia (acute and lymphatic).
- Malignant lymphoma.

10. Gastro-intestinal diseases

- Ulcerative colitis.
- Crohn's disease.

11. Nervous System:

- Cerebral edema associated with primary or metastatic brain tumor or craniotomy.

12. Renal Diseases:

- To induce diuresis or remission of proteinuria in idiopathic nephrotic syndrome, or that due to lupus erythematosus.

12. Miscellaneous

- Tuberculous meningitis (with appropriate anti-tuberculous chemotherapy).
- Transplantation.
- Trichinosis with neurologic or myocardial involvement.

Intra-articular administration

- Rheumatoid arthritis.
- Osteo-arthritis with an inflammatory component.

Soft tissue administration (intrabursal, periarticular, into tendon sheath)

- Synovitis not associated with infection.
- Epicondylitis.
- Tenosynovitis.
- Plantar fasciitis.
- Bursitis.

Intralesional

- Keloids.
- Localized lichen planus.
- Localized lichen simplex.
- Granuloma annulare.
- Discoid lupus erythematosus.
- Alopecia areata.
- Psoriatic plaques, necrobiosis lipoidica diabeticorum.
- Also, may be useful in cystic tumors of an aponeurosis or tendon (ganglia).

Dosage regimen	**N.B.** Dosage must be individualized and depends on the condition being treated and its severity. **N.B**. Treatment should be limited to the minimum dosage for the shortest period of time. **Oral** **Recommended initial daily dosage** Systemic dermatomyositis: 48 mg Systemic lupus erythematosus: 20 - 100 mg Acute rheumatic fever: 48 mg until ESR normal for one week. Allergic diseases: 12 - 40 mg Bronchial asthma: up to 64 mg single dose/alternate day up to 100mg maximum. Ophthalmic diseases: 12 - 40 mg Haematological disorders and leukaemias: 16 - 100 mg Malignant lymphoma: 16 - 100 mg Ulcerative colitis: 16 - 60 mg Crohn's disease: up to 48 mg per day in acute episodes. Organ transplantation: up to 3.6 mg/kg/day Pulmonary sarcoid: 32 - 48 mg on alternate days. Giant cell arteritis/polymyalgia rheumatica: 64 mg Pemphigus vulgaris: 80 - 360 mg Rheumatoid arthritis: Severe 12 - 16 mg Moderately severe 8 - 12 mg Moderate 4 - 8 mg Children 4 - 8 mg **Intravenous** **Initial dosage**: 10 to 500 mg (according to the severity of the condition). **Treatment of graft rejection reactions following transplantation**: 500mg to 1 g/day may be required (limited to a 48–72-hour period). **Exacerbation episodes or conditions unresponsive to standard therapy, such as: rheumatic disorders, systemic lupus erythematosus, edematous state**s: 250 mg/day (given over a period of at least five minutes) or above for a few days (usually ≤ 5 days). **In multiple sclerosis unresponsive to standard therapy** (or during exacerbation episodes): Pulses of 500 or 1000 mg/day for 3 or 5 days over 30 minutes. **Status asthmaticus:** 40 mg, repeated as dictated by patient response. In some asthmatic patients it may be advantageous to administer by slow intravenous drip over a period of hours. **In cerebral edema** Suggested dosage schedules for oedemas due to brain tumor: Pre-operative: 20 mg IM every 3-6 hours. During Surgery: 20 to 40mg IV hourly. Post-operative: 20 mg IM every 3 hours. Then decrease dose or increase intervals gradually to avoid a rebound increase in intracranial pressure. **Treatment of acute exacerbations of multiple sclerosis in adults:** 500 mg/day or 1 g daily for 3 days (infusion over at least 30 minutes). **Intramuscular –** for sustained systemic effect:

	Allergic conditions (asthma, drug reactions): 80 – 120 mg. Dermatological conditions: 40 – 120 mg. Rheumatic disorders and collagen diseases (rheumatoid arthritis, SLE): 40 – 120 mg per week. **N.B.** On average 80 mg injection may be expected to last approximately two weeks. **Intra-articular** Rheumatoid arthritis, osteo-arthritis: The dose depends upon the size of the joint and the severity of the condition. Repeated injections, if needed, may be given at intervals of 1 to 5 or more weeks depending upon response to initial injection. A suggested dosage is: large joint (knee, ankle, shoulder): 20 – 80 mg Medium joint (elbow, wrist): 10 – 40 mg Small joint: 4 –10 mg. **Intralesional** Dermatological conditions: for administration directly into the lesion for local effect: 20 – 60 mg. For large lesions, the dose may be distributed by repeated local injections of 20 – 40 mg. One to four injections are usually used. The intervals between injections vary with the type of lesion and the duration of improvement produced by the initial injection. **Dosing: Pediatric** **Intramuscular** The range of initial doses is 0.11 to 1.6 mg/kg/day. Dosage must be individualized according to the severity of the disease and response of the patient When a prolonged effect is desired, the weekly dose may be calculated by multiplying the daily oral dose by 7 and given as a single intramuscular injection. **Intravenous** Treatment of graft rejection reactions following transplantation: 10 to 20 mg/kg/day for up to 3 days, to a maximum of 1 g/day. Treatment of status asthmaticus: 1 to 4 mg/kg/day for 1-3 days is recommended. **Note:** **The equivalent milligram dose of the various glucocorticoids (apply to Oral or Intravenous administration):** Cortisone: 25, Triamcinolone: 4, Hydrocortisone: 20, Paramethasone: 2, Prednisolone: 5, Betamethasone: 0.75, Prednisone: 5, Dexamethasone: 0.75, Methylprednisolone: 4
Dosage Adjustment	**Dosing: Renal Impairment** No dosage adjustment is necessary for any degree of kidney impairment. **Dosing: Hepatic Impairment** No dosage adjustment is necessary for liver impairment. Frequent patient monitoring is necessary in patients with liver failure or cirrhosis.
Contra-indications	**Systemic** • Hypersensitivity to Methylprednisolone or any component of the formulation. • Systemic infections (uncontrolled) except when administered as an intra-articular injection for localized joint conditions.

	• Idiopathic thrombocytopenia purpura (IM administration only). • Suspension is contraindicated for intravenous or intrathecal administration. • Suspension may be contraindicated for use in premature infants because the formulation may contain benzyl alcohol.
Adverse Drug Reactions	**Frequency Not Known** **Infections and infestations:** Opportunistic infection **Neoplasms benign, malignant, and unspecified**: Kaposi's sarcoma **Blood and lymphatic system disorders**: Leukocytosis. **Immune system disorders:** Drug hypersensitivity; Anaphylactic reaction; Anaphylactoid reaction **Endocrine disorders:** Cushingoid; Hypothalamic pituitary adrenal axis suppression; Steroid withdrawal syndrome; **Steroid withdrawal syndrome** (if too rapid may lead to acute adrenal insufficiency, hypotension and death). A 'withdrawal syndrome' may also occur including, fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight. **Metabolism and nutrition disorders:** Metabolic acidosis; Sodium retention; Water retention; Alkalosis hypokalaemic; Dyslipidaemia; Glucose tolerance impaired; Increased insulin requirement (or oral hypoglycemic agents in diabetics); Lipomatosis; Increased appetite; Weight increased. **Psychiatric disorders:** Affective disorders (including Depression, Euphoric mood, Affect lability, Drug dependence, Suicidal ideation); Psychotic disorder (including Mania, Delusion, Hallucination, and aggravation of Schizophrenia); Mental disorder; Personality change; Confusional state; Anxiety; Mood swings; Abnormal behaviour; Insomnia; Irritability. **Nervous system disorders:** Epidural lipomatosis; Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri) has been reported, usually after treatment withdrawal of hydrocortisone; Benign intracranial hypertension; Seizure; Amnesia; Cognitive disorder; Dizziness; Headache. **Eye disorders:** Central serous chorioretinopathy; Cataract; Glaucoma; Exophthalmos; Vision blurred; Increased intra-ocular pressure, with possible damage to the optic nerve; Corneal or scleral thinning; Exacerbation of ophthalmic viral or fungal disease. **Ear and labyrinth disorders:** Vertigo **Cardiac disorders:** Cardiac failure congestive (in susceptible patients); Myocardial rupture following a myocardial infarction; Hypertrophic cardiomyopathy in prematurely born infants. **Vascular disorders:** Thrombosis including Thromboembolism; Hypertension; Hypotension **Respiratory, thoracic and mediastinal disorders:** Pulmonary embolism; Hiccups **Gastrointestinal disorders:** Peptic ulcer (with possible Peptic ulcer perforation and Peptic ulcer haemorrhage); Intestinal perforation; Gastric haemorrhage; Pancreatitis; Oesophageal ulceration; Oesophageal candidiasis; Abdominal distension; Abdominal pain; Diarrhoea; Dyspepsia; Nausea **Skin and subcutaneous tissue disorders:** Angioedema; Hirsutism; Petechiae; Ecchymosis; Skin atrophy; Erythema; Hyperhidrosis; Skin striae; Rash; Pruritus; Urticaria; Acne; Skin hypopigmentation; Telangiectasia; Skin hyperpigmentation

	Musculoskeletal and connective tissue disorders: Muscular weakness; Myalgia; Myopathy; Muscle atrophy; Osteoporosis, Osteonecrosis; Pathological fracture; Neuropathic arthropathy; Arthralgia; Growth retardation **Reproductive system and breast disorders:** Menstruation irregular; Amenorrhoea **General disorders and administration site conditions:** Impaired healing; Oedema peripheral; Fatigue, Abscess sterile; Malaise; Injection site reaction **Investigations:** Carbohydrate tolerance decreased; Blood potassium decreased; Urine calcium increased; Alanine aminotransferase increased; Aspartate aminotransferase increased; Blood alkaline phosphatase increased; Blood urea increased; Suppression of reactions to skin tests; Weight increased **Injury, poisoning and procedural complications:** Spinal compression fracture; Tendon rupture (particularly of the Achilles tendon).
Monitoring Parameters	• Blood pressure • Blood glucose • Electrolytes, Serum potassium • Ophthalmic examination. • HPA axis suppression, adrenal insufficiency, or hypercortisolism. • Risk of infection. • Growth rate in pediatric patients. **Frequent patient monitoring is necessary in patients with the following conditions:** • Osteoporosis (post-menopausal females are particularly at risk). • Hypertension, dyslipidemia, or congestive heart failure. • Existing or previous history of severe affective disorders (especially previous steroid psychosis). • Diabetes mellitus (or a family history of diabetes). • History of tuberculosis. • Glaucoma (or a family history of glaucoma). • Myasthenia gravis or previous corticosteroid-induced myopathy. myasthenia gravis. • Liver failure - blood levels of corticosteroid may be increased. • Renal insufficiency. • Epilepsy. • Peptic ulceration. • Hypothyroidism
Drug Interactions	***Risk X: Avoid combination*** Aldesleukin, BCG Products, Brivudine, Chikungunya Vaccine (Live), Cladribine, Dengue Tetravalent Vaccine (Live), Desmopressin, Fexinidazole, Fusidic Acid (Systemic), Indium 111 Capromab Pendetide, Macimorelin, Mifamurtide, Mifepristone, Mumps- Rubella- or Varicella-Containing Live Vaccines, Nadofaragene Firadenovec, Natalizumab, Pimecrolimus, Poliovirus Vaccine (Live/Trivalent/Oral), Ritlecitinib, Ruxolitinib (Topical), Tacrolimus (Topical), Talimogene Laherparepvec, Tertomotide, Typhoid Vaccine, Yellow Fever Vaccine. ***Risk D: Consider therapy modification*** Abrocitinib, Antacids, Aprepitant, Baricitinib, CAR-T Cell Immunotherapy, COVID-19 Vaccine (Adenovirus Vector), COVID-19 Vaccine (mRNA), CYP3A4 Inducers

	(Strong), Denosumab, Desirudin, Deucravacitinib, Filgotinib, Fosaprepitant, Hyaluronidase, Immune Checkpoint Inhibitors (Anti-PD-1, -PD-L1, and -CTLA4 Therapies), Influenza Virus Vaccines, Leflunomide, Lutetium Lu 177 Dotatate, Metyrapone, Neuromuscular-Blocking Agents (Nondepolarizing), Polymethylmethacrylate, Rabies Vaccine, Sipuleucel-T, Tofacitinib, Upadacitinib, Vaccines (Inactivated/Non-Replicating), Vaccines (Live).
Pregnancy and Lactation	**Pregnancy:** No adequate human reproductive studies for Methylprednisolone. Corticosteroids are associated with congenital abnormalities in animals, but no evidence in humans. Incidence of low birth weights is dose related. Intra-uterine growth retardation and cataract occurred with long use of corticosteroids. Corticosteroids have been shown to impair fertility in animal studies. **Lactation**: Doses up to 40 mg daily of Methylprednisolone are unlikely to cause systemic effects in the infant. Benefit risk ratio should be evaluated.
Administration	**Administration: IM** IM (acetate, succinate): Avoid injection into the deltoid muscle due to a high incidence of subcutaneous atrophy. Avoid injection or leakage into the dermis. Do not inject into areas that have evidence of acute local infection. **Administration: IV** **Preparation of administration** • For intravenous infusion dilute with 5% dextrose, isotonic saline solution, or 5% dextrose in isotonic saline solution. • To avoid compatibility problems with other drugs should be administered separately. • Formulations containing benzyl alcohol should not be used in neonates. • Do not administer acetate form IV. **Rate of administration** • Doses up to 250 mg, should be given IV over a period of at least 5 minutes. • Doses >250 mg should be given over at least 30 minutes to avoid severe adverse effects, including hypotension, cardiac arrhythmia, and sudden death. **Administration: Oral** Administer tablets after meals or with food or milk to decrease GI upset. If prescribed once daily, administer in the morning. In alternate-day therapy, the minimum daily corticoid requirement is doubled and administered as a single dose every other day at 8.00 am. **N.B**. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hepatic effects:** High doses of methylprednisolone IV (usually doses of 1 g/day in adults) may induce a toxic form of acute hepatitis (rare); may be reversible after discontinuation. • **Immunosuppressant Effects:** Increased Susceptibility to Infections and may mask symptoms of infection. • **Following intra-articular injection:** Septic arthritis may occur with symptoms of marked pain increase, local swelling, further restriction of joint motion, fever, and malaise. Appropriate antimicrobial therapy should be used. • **Endocrine Effects:** Prolonged therapy may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree

and duration of adrenocortical insufficiency produced is variable and depends on dose, frequency, time of administration, and duration of glucocorticoid therapy. This effect may be minimized by use of alternate-day therapy. Abrupt withdrawal may lead to a fatal outcome.

• **Diabetes mellitus**: Corticosteroids can increase blood glucose level and worsen pre-existing diabetes. Long term use may predispose to diabetes mellitus.

• **Psychiatric Effects:** systemic treatment may lead to severe psychiatric adverse reactions that emerge within a few days or weeks of starting treatment. Most reactions are reversible on dose reduction or withdrawal,

• **Cardiovascular disease:** Use with caution in patients with heart failure or hypertension; use has been associated with fluid retention, electrolyte disturbances, and hypertension.

• **Gastrointestinal disease**: Use with caution in patients with GI diseases (diverticulitis, fresh intestinal anastomosis, active or latent peptic ulcer, ulcerative colitis, abscess or other pyogenic infection) due to perforation risk. Acute pancreatitis may occur with high doses.

• **Hepatic impairment**: Use with caution. There is an enhanced effect due to decreased metabolism of corticosteroids in patients with cirrhosis.

• **Musculoskeletal Effects:** Use may cause transient worsening of myasthenia gravis; monitor for worsening of case. Acute myopathy is reported with high doses. Clinical improvement after discontinuation may require weeks to years. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. Osteoporosis is associated with long term, large dose use of glucocorticoids.

• **Ocular disease**: Prolonged use of corticosteroids may enhance eye disorders or eye infections. Use with caution in patients with a history of ocular herpes simplex; corneal perforation has occurred; do not use it in active ocular herpes simplex.

• **Renal impairment**: Use with caution in patients with renal impairment; fluid retention may occur.

• **Seizure disorders**: Use corticosteroids with caution in patients with a history of seizure disorder; seizures have been reported with adrenal crisis.

• **Septic shock or sepsis syndrome**: should not be used in the treatment of septic syndrome or septic shock. Corticosteroids have shown benefit in patients with established septic shock who exhibit adrenal insufficiency. Course of 5-11 days of low-dose corticosteroids might reduce mortality. Use may increase mortality in some populations (eg, patients with elevated serum creatinine, patients who develop secondary infections after use).

• **Systemic sclerosis (scleroderma**): Use of higher dose therapy in patients with systemic sclerosis may increase the risk of scleroderma renal crisis; avoid use when possible.

• **Thyroid disease**: Changes in thyroid status may necessitate dosage adjustments; metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid ones.

• **Withdrawal of systemic treatment:** Abrupt withdrawal of doses up to 32 mg daily of Methylprednisolone for 3 weeks unlikely to lead to clinically relevant HPA-axis suppression in the majority of patients. Otherwise gradual decrease is recommended. Symptoms of abrupt withdrawal include: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight

	loss, and/or hypotension
Storage	• Methylprednisolone injection and tablets: Store between 20°C to 25°C. • Protect from light. Do not autoclave. • Powder: After reconstitution with Sterile Water, use immediately for Injection, discard any remainder. **N.B**. Refer to manufacturer PIL if there are specific considerations.

Mometasone

Generic Name	Mometasone
Dosage form/strengths	Metered Nasal Spray: 50 mcg/actuation. Topical Ointment: 1mg/gm (0.1%) (10gm, 15gm, 20gm, 25gm, 30gm). Topical Lotion: 1mg/gm (15ml, 20ml, 60ml). Topical Cream: 1mg/gm (15gm, 20gm, 25gm, 30gm, 40gm, 45gm). And in combinations as topical or inhalation forms.
Route of Administration	Nasal, Topical, Inhalation
Pharmacologic Category	Corticosteroid ATC: Topical (single agent): D07AC13, Nasal: R01AD09
Indications	**Nasal spray** - Treatment of symptoms of seasonal or perennial allergic rhinitis in adults. - Relieve symptoms of hay fever and other upper respiratory allergies. **Topical** - Ointment or cream: Treatment of inflammatory and pruritic manifestations of psoriasis (excluding widespread plaque psoriasis), atopic dermatitis in patients ≥2 years. - Lotion is indicated for the treatment of inflammatory and pruritic manifestations of psoriasis, atopic dermatitis and seborrhoeic dermatitis of the scalp.
Dosage Regimen	**Nasal spray** *Upper respiratory allergies:* **Dosing for Adults and children 12 years and older:** **Intranasal**: 2 sprays in each nostril once daily (total daily dose: 200 mcg). **N.B.** Full benefit of treatment may not be achieved in the first 48 hours. **N.B.** Treatment may need to be initiated some days before the expected pollen season in patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis. **Dosing for children 2-12 years of age:** **Intranasal**: 1 spray in each nostril once daily (total daily dose: 100 mcg). **N.B**. The growth rate of children may be slower while using this product. **N.B**. Children should only use it for the shortest time necessary to achieve symptom relief. **Topical** **Adults, the elderly and children** • Cream or ointment: A thin film should be applied to the affected areas of the skin once daily. • Lotion: Apply a few drops on affected areas of skin or scalp sites once daily; massage gently and thoroughly until the medication disappears. **N.B.** Use for face or in children should be limited to the least effective amount and duration of treatment should be no more than 5 days.

Dosage Adjustment	**Dosing: Renal Impairment: Adult, Pediatrics** There are no dosage adjustments available, not studied. **Dosing: Hepatic Impairment: Adults, Pediatrics** There are no dosage adjustments available. Drug accumulation may increase with severity of hepatic impairment.
Contra-indications	• Hypersensitivity to Mometasone or any component of the formulation. **Nasal**: • Untreated localized infection involving the nasal mucosa, such as herpes simplex. • Recent nasal surgery or trauma. **Topical**: • Bacterial, viral, parasitical and fungal infections, varicella, tuberculosis, syphilis or post-vaccine reactions, facial rosacea, acne vulgaris, skin atrophy, perioral dermatitis, perianal and genital pruritis or napkin eruptions. • Not be used on wounds or ulcerated skin.
Adverse Drug Reactions	Nasal **>10%** • **Infection**: Viral infection (nasal spray: 14%). • **Nervous system**: Headache (nasal spray: 26%). • **Respiratory**: Blood in nasal mucosa (nasal spray: ≤11%), epistaxis (nasal spray: ≤13%), pharyngitis (nasal spray: 12%). **1% to 10%** • **Cardiovascular**: Chest pain (nasal spray: 2% to 5%). • **Gastrointestinal**: Diarrhea (nasal spray: 2% to 5%), dyspepsia (nasal spray: 2% to 5%), nausea (nasal spray: 2% to 5%). • **Genitourinary**: Dysmenorrhea (nasal spray: 5%). • **Hypersensitivity**: Hypersensitivity reaction (implant: 4%). • **Neuromuscular & skeletal**: Arthralgia (nasal spray: 2% to 5%), musculoskeletal pain (nasal spray: 5%), myalgia (nasal spray: 2% to 5%) • **Ophthalmic**: Conjunctivitis (nasal spray: 2% to 5%). • **Otic**: Otalgia (nasal spray: 2% to 5%). • **Respiratory**: Asthma (nasal spray: 2% to 5%), bronchitis (nasal spray: 2% to 5%), cough (nasal spray: 7%), flu-like symptoms (nasal spray: 2% to 5%), upper respiratory tract infection (nasal spray: 6% to 8%). Topical **1% to 10%** • **Central nervous system**: Paresthesia (lotion, infants & children: ≤3%, cream, children: 1%) • **Dermatologic**: Dyschromia (loss of normal skin markings: ≤6%), taut and shiny skin (≤6%), folliculitis (lotion: 3%; cream, children: <1%), telangiectasia (≤3%), dermatologic disorders (2%), bacterial skin infection (infants & children: ≤2%), epidermal thinning (≤2%) • **Endocrine & metabolic**: Decreased cortisol (infants & children: lotion:

	≤6%, cream and ointment: ≤2%), endocrine disease (lotion: 2%). • **Gastrointestinal**: Xerostomia (infants & children: 2%). • **Hematologic & oncologic**: Bruise (1%). • **Local**: Application site burning (2%), application site pruritus (≤2%).
Monitoring Parameters	**Nasal** • Growth rate in pediatrics. • Ophthalmic examination. • Monitor patients periodically for signs of adverse effects: Epistaxis, nasal septal perforation, nasal ulceration, infection, impaired wound healing. • HPA axis suppression, adrenal insufficiency or hypercortisolism. • Risk of infection. **Topical** • At large surface areas or longer periods: HPA axis suppression (urinary free cortisol, ACTH stimulation tests).
Drug Interactions	***Nasal*** ***Risk D: Consider therapy modification*** Esketamine -CYP3A inhibitors**:** is expected to increase the risk of systemic side-effects. Avoid unless the benefit outweighs the risk.
Pregnancy and Lactation	**Pregnancy**: No or limited amount of human data. Animal studies have shown reproductive toxicity in nasal form. Use only if benefit outweighs potential risk. Observe infants for hypoadrenalism. **Lactation**: No human data. Decisions should be made either to discontinue breastfeeding or treatment with this therapy.
Administration	**Nasal sprays**: For intranasal administration only; do not spray into eyes or mouth. Shake the container well before each use. Prime pump (press 10 times or until fine spray appears) prior to first use. If the pump is not used for 14 days or longer, reprime with 2 actuations until a uniform spray is observed. **Topical**: Apply sparingly; avoid contact with eyes. Limit use to face or in children to the least amount and duration (not exceeding 5 days). **N.B**. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Immunosuppressant Effects:** Increased Susceptibility to Infections and may mask symptoms of infection. Caution in immunosuppressed patients. • **Systemic effects** may be associated with high doses or prolonged use which include: Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma, and more rarely, a range of psychological or behavioral effects including psychomotor hyperactivity, sleep disorders, anxiety, depression, or aggression (particularly in children). • **Ocular disorders**: Prolonged use of corticosteroids (nasal, topical or

	systemic) may enhance eye disorders including cataract, glaucoma, increased intraocular pressure, rare diseases such as central serous chorioretinopathy (CSCR) or eye infections. Use with caution. Monitor for visual disturbances. Corticosteroids should not be used in active ocular herpes simplex. • **Withdrawal symptoms:** Avoid sudden discontinuation of treatment**.** Long term continuous or inappropriate use of topical steroids can result in the development of rebound flares after stopping treatment. Symptoms include dermatitis with intense redness, stinging and burning that can spread beyond the initial treatment area. Reapplication should be with caution or consider other treatment options. • **Topical steroids use in psoriasis may be hazardous** due to: Rebound relapses following development of tolerance, risk of pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin. If used in psoriasis careful patient supervision is important**.**
Storage	• Topical: Store below 30°C. • Nasal spray: Store below 30°C. Use within 2 months of first use. Do not freeze. **N.B**. Refer to manufacturer PIL if there are specific considerations.

Prednisolone

Generic Name	Prednisolone
Dosage form/strengths	Orally disintegrating Tablets: 5mg, 15mg, 30mg Oro-dispersible tablet: 5mg, 20mg Oral Solution: 5mg/5ml, 15mg/5ml Tablet: 5mg. Ophthalmic Suspension: 10 mg/ml (1%) Ophthalmic gel: 5mg/ml
Route of Administration	Oral, Ophthalmic
Pharmacologic Category	Corticosteroid, systemic, ophthalmic **ATC** code: Local oral treatment: A01AC04. Systemic: H02AB06. Eye preparations: S01CB02.
Indications	**Systemic** Anti-inflammatory or immunosuppressant agent in the treatment of a variety of diseases, including: • Allergic states • Autoimmune diseases • Dermatologic diseases • Edematous States • Endocrine disorders • GI diseases: During acute episodes of Crohn's disease or ulcerative colitis. • Hematologic disorders • Neoplastic diseases • Nervous system • Ophthalmic diseases • Respiratory diseases • Rheumatic disorders • Solid organ rejection (acute/chronic). **Ophthalmic** • Treatment of steroid-responsive, ocular inflammatory conditions after excluding the presence of viral, fungal and bacterial infections in adults. • Corneal injury, or penetration of foreign bodies.
Dosage Regimen	**Systemic** **Adult dosing** • Dosing depends upon the condition being treated and the response of the patient. • The dose should be gradually decreased till the lowest dose that will maintain an adequate clinical response. • Abrupt withdrawal is not recommended particularly with doses 40 mg or more or 3 weeks of treatment or more.

	Oral: Usual Initial doses: 5 to 60 mg/day given in a single daily dose or in 2 to 4 divided doses. An example of a tapered-dosage regimen - Day 1: 30 mg administered as 10 mg at breakfast, 5 mg at lunch, 5 mg at dinner, and 10 mg at bedtime. - Day 2: 25 mg administered as 5 mg at breakfast, 5 mg at lunch, 5 mg at dinner, and 10 mg at bedtime. - Day 3: 20 mg administered as 5 mg at breakfast, 5 mg at lunch, 5 mg at dinner, and 5 mg at bedtime. - Day 4: 15 mg administered as 5 mg at breakfast, 5 mg at lunch, and 5 mg at bedtime. - Day 5: 10 mg administered as 5 mg at breakfast and 5 mg at bedtime. - Day 6: 5 mg administered as 5 mg at breakfast. **Dosing: Pediatric** **Notes:** • Dosing depends upon the condition being treated and the response of the patient. • The lowest possible dose should be used to control the condition; when dose reduction is possible, the dose should be reduced gradually. • Consider alternate day therapy for long-term therapy. • Fractions of the adult dosage may be used (e.g. 75% at 12 years, 50% at 7 years and 25% at 1 year) but clinical factors must be given due weight. **General dosing, anti-inflammatory or immunosuppressive:** Infants, Children, and Adolescents: Oral: initial: 0.1 to 2 mg/kg/day (4 to 60 mg/m^2 BSA/day), in divided doses 1 to 4 times daily. **Ophthalmic:** **N.B.** Acetate suspension demonstrates greater bioavailability than the sodium phosphate solution. - Instill 1 to 2 drops in the affected eye(s) 2 to 4 times daily. - During initial 24 - 48 hours: Frequency of dosing may be as high as 2 drops every hour. - Do not discontinue therapy prematurely; withdraw therapy with gradual tapering of dose in chronic conditions.
Dosage Adjustment	**Dosing: Altered Kidney Function:** No dosage adjustment is necessary. Caution. **Dosing: Hepatic Impairment:** No dosage adjustment is necessary. Caution.
Contra-indications	**Systemic** • Hypersensitivity to Prednisolone or any component of the formulation. • Systemic infections. **Ophthalmic** • Hypersensitivity to Prednisolone or any component of the formulation.

	• Eye infections:
	  ○ Viral diseases of the cornea and conjunctiva, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella,
	  ○ Mycobacterial infection of the eye.
	  ○ Fungal diseases of the eye.

Adverse Drug Reactions	**Systemic: Frequency not defined** • Cardiovascular: Bradycardia, cardiomegaly, cholesterol embolus syndrome, circulatory shock, edema, heart failure, hypertrophic cardiomyopathy (premature infants), myocardial rupture (after recent myocardial infarction), syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis • Dermatologic: Acne vulgaris, allergic dermatitis, atrophic striae, diaphoresis, dry scalp, ecchymoses, facial erythema, hyperpigmentation, hypopigmentation, inadvertent suppression of skin test reaction, skin atrophy, skin rash, thinning hair (scalp), urticaria • Endocrine & metabolic: Decreased serum potassium, fluid retention, growth retardation (children), hirsutism, HPA-axis suppression, hypokalemic alkalosis, impaired glucose tolerance, menstrual disease, negative nitrogen balance (due to protein catabolism), sodium retention, weight gain • Gastrointestinal: Hiccups, impaired intestinal carbohydrate absorption, increased appetite, nausea, pancreatitis • Genitourinary: Asthenospermia, oligospermia • Hematologic & oncologic: Petechia • Hepatic: Hepatomegaly, increased liver enzymes • Hypersensitivity: Nonimmune anaphylaxis • Infection: Sterile abscess • Nervous system: Abnormal sensory symptoms, amyotrophy, arachnoiditis, headache, increased intracranial pressure (with papilledema), insomnia, malaise, meningitis, myasthenia, neuritis, neuropathy, paraplegia, paresis (paraparesis), paresthesia, seizure, vertigo • Neuromuscular & skeletal: Aseptic necrosis of femoral head, aseptic necrosis of humeral head, Charcot arthropathy, rupture of tendon • Ophthalmic: Exophthalmos • Respiratory: Pulmonary edema • Miscellaneous: Wound healing impairment **Ophthalmic** • Infection: Secondary ocular infection. • Ophthalmic: Glaucoma, increased intraocular pressure, optic nerve damage, subcapsular posterior cataract. • Miscellaneous: Wound healing impairment.
Monitoring Parameters	**Systemic** • Blood pressure • Blood glucose

	• Ophthalmic examinations • Serum Potassium (at high doses) • Growth rate in pediatrics • Renal function (s-creatinine) routinely in patients with systemic sclerosis. • HPA axis suppression, adrenal insufficiency, or hypercortisolism. • Risk of infection **Frequent patient monitoring is necessary in patients with the following conditions:** • Osteoporosis (post-menopausal females are particularly at risk). • Hypertension or congestive heart failure. • Existing or previous history of severe affective disorders (especially previous steroid psychosis). • Diabetes mellitus (or a family history of diabetes). • History of tuberculosis. • Glaucoma (or a family history of glaucoma). • Previous corticosteroid-induced myopathy. • Liver failure - blood levels of corticosteroid may be increased, (as with other drugs which are metabolized in the liver). • Renal insufficiency. • Epilepsy. • Peptic ulceration.
Drug Interactions	***Risk X: Avoid combination*** Aldesleukin, BCG Products, Brivudine, Cladribine, Dengue, Tetravalent Vaccine (Live), Desmopressin, Macimorelin, Mifamurtide, Mifepristone, Mumps- Rubella- or Varicella-Containing Live Vaccines, Natalizumab, Pimecrolimus Poliovirus Vaccine (Live/Trivalent/Oral), Ritlecitinib, Ruxolitinib (Topical), Tacrolimus (Topical), Talimogene, Laherparepvec, Tertomotide, Typhoid Vaccine, Yellow Fever Vaccine ***Risk D: Consider therapy modification:*** Abrocitinib, Antacids, Baricitinib, CAR-T Cell Immunotherapy, Coccidioides immitis Skin Test, COVID-19 Vaccine (Adenovirus Vector), COVID-19 Vaccine (mRNA) ,Denosumab, Desirudin, Deucravacitinib, Filgotinib, Hyaluronidase, Corticosteroids (Systemic), Immune Checkpoint Inhibitors (Anti-PD-1, -PD-L1, and -CTLA4 Therapies), Influenza Virus Vaccines, Leflunomide, Lutetium Lu 177, Dotatate, Metyrapone, Neuromuscular-Blocking Agents (Nondepolarizing), Polymethylmethacrylate, Rabies Vaccine, Sipuleucel-T, Corticosteroids (Systemic), Tofacitinib, Upadacitinib, Vaccines (Inactivated/Non-Replicating).
Pregnancy and Lactation	**Pregnancy**: Prednisolone is a preferred oral corticosteroid for the treatment of maternal conditions during pregnancy due to limited placental transfer. Monitor pregnant women, and babies after birth. Corticosteroids may cause harm to the fetus as shown in animal studies. Use only when benefit outweighs the risk. **Lactation**: Corticosteroids are generally considered acceptable in patients who are breastfeeding when used in usual doses (up to 40mg); however, monitoring of the infant is recommended.

Administration	**Administration: Oral** • Preferably be taken as a single dose in the morning. However, divided daily doses may be employed if required. • Administer after meals or with food or milk to decrease GI upset. • Oro-dispersible tablets: Do not break, cut, split, or use partial tablets. Remove the tablet from the blister pack just before use. May swallow whole or allow to dissolve on the tongue. **Administration: Ophthalmic** • Shake suspension well before use. Avoid eye injury or contamination, by not touching dropper tip to eyelids or other surfaces. • To decrease systemic absorption, apply finger pressure to the lacrimal sac during and for 1 to 2 minutes after instillation. • Wait at least 15 minutes after instilling solution before inserting soft contact lenses. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Immunosuppressant Effects:** Increased Susceptibility to Infections and may mask symptoms of infection. Caution in immunosuppressant agents. • **Endocrine Effects:** Prolonged, high dose therapy may result in hypothalamic-pituitary-adrenal (HPA) suppression particularly in children and hepatic patients. HPA axis suppression may lead to adrenal crisis. Discontinuation of a corticosteroid should be done slowly and carefully. • **Diabetes mellitus**: Corticosteroids can increase blood glucose level and worsen pre-existing diabetes. • **Psychiatric Effects:** May appear with corticosteroids use. Symptoms include euphoria, insomnia, mood swings, personality changes, severe depression and frank psychotic manifestations. • **Cardiovascular disease:** Use has been associated with fluid retention, electrolyte disturbances, and hypertension. Use with caution in patients with heart failure, hypertension or renal insufficiency. • **Gastrointestinal disease**: Use with caution in patients with GI diseases (diverticulitis, fresh intestinal anastomosis, active or latent peptic ulcer, ulcerative colitis, abscess or other pyogenic infection) due to perforation risk. • **Musculoskeletal Effects:** Osteoporosis is associated with long term and large dose uses of glucocorticoids. Use may cause transient worsening of myasthenia gravis; monitor for worsening of case. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. Acute myopathy is reported with high doses. Clinical improvement after discontinuation may require weeks to years. • **Ocular disorders**: Prolonged use of corticosteroids may enhance eye disorders including cataract, glaucoma, or eye infections. Monitor for visual disturbances. Do not use in active ocular herpes simplex. • **Renal impairment**: Use with caution in patients with renal impairment; fluid retention may occur. • **Thyroid disease**: Changes in thyroid status may necessitate dosage adjustments; metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid ones. • **Withdrawal of systemic treatment:** Abrupt withdrawal is not

	recommended after long-term use. Withdraw therapy with gradual tapering of dose. Symptoms of abrupt withdrawal include anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss, and/or hypotension. • **Kaposi sarcoma**: Prolonged treatment with corticosteroids has been associated with the development of Kaposi's sarcoma (case reports); if noted, discontinuation of therapy should be considered. • **Anaphylactoid reactions:** Rare cases of anaphylactoid reactions have been observed in patients receiving corticosteroids. • **Elderly:** Use cautiously in older adults with the smallest possible effective dose for the shortest duration. • **Pediatrics**: May slow growth rate; growth should be routinely monitored in pediatric patients.
Storage	Store between 15°C to 30°C. Protect solid oral dosage forms from moisture. **N.B** Refer to manufacturer PIL if there are specific considerations.

Triamcinolone

Generic Name	Triamcinolone
Dosage form/strengths	Suspension for injection IM or Intra-articular: 40 mg/ml Suspension for Intralesional or intra-articular Injection: 10 mg/ml. Tablets: 4 mg. Nasal spray: 55 mcg/dose. Oral paste: 1 mg/g. Topical cream: 1 mg/g.
Route of Administration	Intra-muscular, Intra-articular, Intralesional, Oral, Nasal, Topical
Pharmacologic Category	**Corticosteroid** ATC code: Systemic: A01AC01, H02AB08 ATC code: Nasal: R01AD11 ATC code: Topical: C05AA12, D07AB09, D07XB02
Indications	**Intra-articular use** As short-term administration for acute episode or exacerbation symptoms associated with rheumatoid arthritis and osteoarthritis, also for bursitis, epicondylitis, and tenosynovitis for adults and children over 6 years. **Intramuscular use** • **Allergic states**: Bronchial asthma. • **Endocrine disorders:** e.g. primary or secondary adrenocortical insufficiency. • **Collagen disorders**: e.g. during an exacerbation of maintenance therapy of selected cases of SLE or acute rheumatic carditis. • **Dermatological diseases**: e.g. pemphigus, severe dermatitis and Stevens Johnson Syndrome. • **Rheumatic, Gastrointestinal or Respiratory disorders**: as an adjunctive, short-term therapy. • **Haematological disorders**: e.g. acquired (autoimmune) haemolytic anaemia. • **Neoplastic diseases:** e.g. palliative management of leukaemia and lymphomas. • **Renal disease:** such as acute interstitial nephritis, minimal change nephrotic syndrome or lupus nephritis. **Intralesional use** For adults and children over 6 years. Alopecia areata; discoid lupus erythematosus; keloids; localized hypertrophic, infiltrated, inflammatory lesions of granuloma annulare, lichen planus, lichen simplex chronicus (neurodermatitis), and psoriatic plaques; necrobiosis lipoidica diabeticorum. Also, may be useful in cystic tumors of an aponeurosis or tendon (ganglia). **Intranasal use**

	Treatment of the symptoms of seasonal and perennial allergic rhinitis. It relieves symptoms such as sneezing, itchy and runny nose, itchy, red or watery eyes, nasal congestion or associated sinus discomfort in adults and children 2 years of age and older. **Topical use** For the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. **Oral:** Treatment of diseases requiring systemic glucocorticoid therapy. **Oral paste:** Acute and chronic lesions of the oral mucosa.
Dosage Regimen	• Dose depends upon the condition being treated, severity and response of the patient. **Intra-Articular Injection** Injection into tendon sheaths and bursae: (depending on disease) • Smaller joints: 2.5-15 mg • Larger joints: up to 40mg. • Single injections into several sites for multiple joint involvement: up to a total of 80 mg. **Intramuscular Injection:** **Adults and Children over 6 Years** • Initial dose: 40 mg. • Subsequent dosage depends on the patient's response and period of relief. • When favorable response is observed, reduce in small decrements at appropriate time intervals until reaching the lowest dosage that will maintain an adequate clinical response. • Withdraw treatment, when needed, gradually rather than abruptly in case of more than an injection during three weeks periods or doses more than 40 mg. **Intralesional** • 2-3 mg up to 5mg at one site. • If several sites are injected the total dosage should not exceed 30 mg. The site of injection and volume of injection should be carefully considered due to the potential for cutaneous atrophy. Intranasal • **Adults and adolescents > 12 years:** 220 micrograms total as 2 sprays in each nostril once daily. Once symptoms are controlled patients can be maintained on 110 micrograms (1 spray in each nostril once daily). • **Children 6 to 12 years of age**: Starting dose is 110 mcg/day (one spray in each nostril once daily). Maximum dose is 220 mcg/day (two sprays per nostril once daily). • **Children 2 to 5 years of age:** Starting and maximum dose 110 mcg/day (one spray in each nostril once daily) **Topical:** Apply to the affected area two to three times daily. Rub it gently. **Oral paste:** Use only enough to coat the lesion with a thin film. Do not rub in. apply

	the preparation 2 or 3 times a day, preferably after meals. **Oral:** **Adult doses:** 4 - 48 mg daily, up to 64 mg in some respiratory conditions. **Children under 27 kg body weight**: 4 - 16 mg daily. Gradually reduction of dose by 2 - 4 mg every two or three days until the maintenance dose is reached after improvement has occurred.
Dosage Adjustment	**Dosing Kidney Impairment** Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed. **Dosing Hepatic Impairment** Systemic dosage may need adjustment depending on the degree of hepatic insufficiency, but quantitative recommendations are not available.
Contra-indications	• Hypersensitivity to Triamcinolone or any component of the formulation. • Systemic infections. • Idiopathic thrombocytopenic purpura (IM administration only). • Administration by intravenous, intrathecal, epidural, or intraocular injection. • Infections of the mouth or throat (Oral topical formulations only).
Adverse Drug Reactions	**Systemic** **1% to 10%** • Hematologic & oncologic: Bruise • Neuromuscular & skeletal: Joint swelling • Respiratory: Cough, sinusitis **Post-marketing** • Dermatologic: Excoriation of skin, skin rash • Endocrine & metabolic: Weight gain • Gastrointestinal: Diarrhea, nausea, oral candidiasis, upper abdominal pain, vomiting. • Infection: Fungal infection (nasal), viral infection. • Local: Application-site reaction (including application-site pain, blood in the nasal mucosa, burning sensation of the nose, epistaxis, nasal mucosa irritation, sneezing, and stinging sensation of the nose). • Nervous system: Bitter taste, headache, insomnia. • Ophthalmic: Retinopathy (central serous chorioretinopathy. • Respiratory: Asthma, cough, dry nose, nasal cavity pain, nasal discomfort, nasopharyngitis, pharyngitis, pharyngolaryngeal pain, rhinitis, sinusitis, upper respiratory tract infection.
Monitoring Parameters	**Systemic** • Blood pressure • Blood glucose • Ophthalmic examinations • Electrolytes, Serum Potassium • Growth rate in pediatrics • HPA axis suppression, adrenal insufficiency or hypercortisolism. • Risk of infection

	Frequent patient monitoring is necessary in patients with the following conditions: • Osteoporosis (post-menopausal females are particularly at risk). • Hypertension, dyslipidemia or congestive heart failure. • Existing or previous history of severe affective disorders (especially previous steroid psychosis). • Diabetes mellitus (or a family history of diabetes). • History of tuberculosis. • Glaucoma (or a family history of glaucoma). • Myasthenia gravis or previous corticosteroid-induced myopathy. myasthenia gravis. • Liver failure - blood levels of corticosteroid may be increased. • Renal insufficiency. • Epilepsy. • Peptic ulceration. • Hypothyroidism. **Nasal** • Growth rate in pediatrics. • Ophthalmic examination. • Monitor patients periodically for signs of adverse effects: Epistaxis, nasal septal perforation, Candida albicans infection, impaired wound healing. • HPA axis suppression, adrenal insufficiency or hypercortisolism. • Risk of infection. **Topical** • At large surface areas or longer periods: HPA axis suppression (urinary free cortisol, ACTH stimulation tests).
Drug Interactions	**Risk X: Avoid combination** Aldesleukin, BCG, Brivudine, Cladribine, Dengue Tetravalent Vaccine (Live), Desmopressin, Indium 111, Capromab, Pendetide, Macimorelin, Mifamurtide, Mifepristone, Mumps, Rubella, and Varicella Virus Vaccine, Nadofaragene Firadenovec, Natalizumab, Pimecrolimus Poliovirus Vaccine (Live/Trivalent/Oral), Ruxolitinib, Tacrolimus (Topical), Talimogene Laherparepvec, Yellow Fever Vaccine. **Risk D: Consider therapy modification** Abrocitinib, Baricitinib, CAR-T Cell, Immunotherapy, Coccidioides immitis Skin Test, CYP3A4 Inhibitors (Strong), Denosumab, Desirudin, Deucravacitinib, Echinacea, Esketamine, Filgotinib, Hyaluronidase, Immune Checkpoint Inhibitors (Anti-PD-1, -PD-L1, and -CTLA4 Therapies), Influenza Virus Vaccines, Leflunomide, Metyrapone, Neuromuscular-Blocking Agents (Nondepolarizing), Rabies Vaccine, Sipuleucel-T, Tofacitinib, Upadacitinib, Vaccines (Inactivated), Vaccines (Live).
Pregnancy and Lactation	**Pregnancy**

	No or limited amount of human data. Animal studies have shown reproductive toxicity in nasal form. Use only if benefit outweighs potential risk. Observe infants for hypoadrenalism. **Lactation** Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Decisions should be made either to discontinue breastfeeding or treatment with this therapy.
Administration	**Administration** **Parenteral** Shake well before use to ensure suspension is uniform. Inspect visually to ensure no clumping; administer immediately after withdrawal so settling does not occur in the syringe. Strict aseptic precautions should be observed. Do **not** administer any product IV or via the epidural or intrathecal route. **Intra-articular** • Prior use of a local anesthetic may often be desirable e.g. Lidocaine. • In treating acute nonspecific tenosynovitis, care should be taken to ensure that the injection is made into the tendon sheath rather than the tendon substance. **Intralesional** • Inject directly into the lesion, ie, intradermally or subcutaneously. For accuracy of dosage measurement and ease of administration, it is preferable to employ a tuberculin syringe and a small-bore needle (23-25 gauge). • Ethyl chloride spray may be used to alleviate the discomfort of the injection. **Intramuscular** When administered IM, inject deep into the gluteal muscle. Alternate sites for subsequent injections. Avoid IM injections into the deltoid area. **Intranasal** Shake well prior to use. Avoid spraying into mouth or eyes and do not blow nose for 15 minutes after use. Prime prior to first use by shaking contents well and releasing several sprays into the air. If product is not used for more than 2 weeks, reprime with 1 spray. **Oral/dental paste**: Apply small amounts into the oral cavity until thin, smooth film develops; do not rub in; apply at bedtime to allow contact of the medication with the lesion overnight; if more frequent application necessary, apply after meals. **Topical products**: Apply to the affected area two to three times daily. Rub it gently. Do not use it on open skin; avoid contact with eyes; wash hands after use.

	N.B. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Immunosuppressant Effects:** Increased Susceptibility to Infections and may mask symptoms of infection. Caution in immunosuppressant agents. • **Endocrine Effects:** Prolonged, high dose therapy may result in hypothalamic-pituitary-adrenal (HPA) suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. HPA axis suppression may lead to adrenal crisis. Discontinuation of a corticosteroid should be done slowly and carefully. • **Diabetes mellitus**: Corticosteroids can increase blood glucose level and worsen pre-existing diabetes. • **Psychiatric Effects:** May appear with corticosteroids use. Symptoms include euphoria, insomnia, mood swings, personality changes, severe depression and frank psychotic manifestations. • **Cardiovascular disease:** Use has been associated with fluid retention, electrolyte disturbances, and hypertension. Use with caution in patients with heart failure, hypertension or renal insufficiency. • **Gastrointestinal disease**: Use with caution in patients with GI diseases (diverticulitis, fresh intestinal anastomosis, active or latent peptic ulcer, ulcerative colitis, abscess or other pyogenic infection) due to perforation risk. • **Musculoskeletal Effects:** Osteoporosis is associated with long term and large dose uses of glucocorticoids. All corticosteroids increase calcium excretion. Use may cause transient worsening of myasthenia gravis; monitor for worsening of case. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. Acute myopathy is reported with high doses. Clinical improvement after discontinuation may require weeks to years. • **Ocular disorders**: Prolonged use of corticosteroids may enhance eye disorders including cataract, glaucoma, or eye infections. Monitor for visual disturbances. Do not use in active ocular herpes simplex. • **Thyroid disease**: Changes in thyroid status may necessitate dosage adjustments; metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid ones. • **Withdrawal of systemic treatment:** Abrupt withdrawal is not recommended after long term use. Withdraw therapy with gradual tapering of dose. Symptoms of abrupt withdrawal include: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss, and/or hypotension. • **Kaposi sarcoma**: Prolonged treatment with corticosteroids has been associated with the development of Kaposi's sarcoma (case reports); if noted, discontinuation of therapy should be considered. • Menstrual irregularities may occur and in postmenopausal women vaginal bleeding has been observed. • **Anaphylactoid reactions:** Rare cases of anaphylactoid reactions have been observed in patients receiving corticosteroids. Cases of serious anaphylaxis, including death, have been reported with Triamcinolone acetonide. • **Elderly:** Use cautiously in older adults with the smallest possible effective dose for the shortest duration.

	• **Pediatrics**: May slow growth rate; growth should be routinely monitored in pediatric patients. • **Benzyl alcohol:** Injection products may contain benzyl alcohol. Benzyl Alcohol may cause toxic reactions and anaphylactoid reactions in infants and children up to 3 years old. Refer to product labeling. • **Intra-Articular Injection:** Corticosteroids should not be injected into unstable joints. Severe joint destruction with necrosis of bone may occur if repeated intra-articular injections are given over a long period of time. Caution when given into tendon sheaths to avoid injection into the tendon itself. Repeated injection into inflamed tendons should be avoided as it has been shown to cause tendon rupture. • **Septic arthritis:** May occur as a complication to intra-articular or soft tissue administration. Local swelling, further restriction of joint motion, fever, and malaise are suggestive of septic arthritis. institute appropriate antimicrobial therapy as required. • **Local nasal effects:** Nasal septal perforation, nasal ulceration, epistaxis, and localized Candida albicans infections of the nose and/or pharynx may occur. Monitor patients periodically for adverse nasal effects. • **Sensitization:** Topical use has been associated with local sensitization (redness, irritation); discontinue if sensitization is noted. • **Systemic effects** may be associated with high doses or prolonged topical use which include: Cushing's syndrome, Cushingoid features, adrenal suppression, hyperglycemia. Absorption is increased by the use of occlusive dressings, or application to large surface areas. • **Appropriate administration:** Administer products only via recommended route (depending on product used). Do not administer any Triamcinolone product via the intrathecal route; serious adverse events, including fatalities, have been reported following intrathecal administration of corticosteroids.
Storage	• Injectable suspension: Store between 15°C to 30°C; avoid freezing. Protect from light. • Intranasal, topical oral forms: Store between 15°C to 30°. **N.B**. Refer to manufacturer PIL if there are specific considerations.

Dopamine-receptor agonists

Bromocriptine

Generic Name	Bromocriptine
Dosage form/strengths	Tablet: 2.5mg Vaginal suppositories: 2.5mg
Route of Administration	Oral, Vaginal
Pharmacologic Category	Dopamine (D2) Agonist: Anti-Parkinson Agent, Antidiabetic Agent, Ergot Derivative; Hyperprolactinemia Agent ATC: G02CB01, N04BC01
Indications	• Inhibition of lactation for medical reasons • Hyperprolactinemia-Associated Dysfunctions • Acromegaly • Parkinson disease • Prolactinomas • Menstrual cycle disorders and female infertility • Premenstrual symptoms and benign breast disease
Dosage Regimen	**Hyperprolactinemic disorders** **Oral:** Initial: 1.25 mg once daily at bedtime; increase dose to 2.5 mg/day then 2.5mg twice daily after 2 to 3 days intervals. Usual dose: 2.5mg 2-3 times daily. N.B. Daily doses should not exceed 30 mg. **Suppression of Lactation for Medical Reasons** **Oral**: 2.5mg on the first day, increasing after 2 to 3 days to 2.5mg twice daily for 14 days. **Prolactinomas, Acromegaly** **Oral**: Dose increased gradually by 2.5mg daily at 2 to 3 days intervals, until 5 mg 4 times daily. Daily doses should not exceed 30 mg. **Parkinson's disease** **Note:** Agents other than bromocriptine are recommended for treatment of patients with **Oral:** Week 1: 1.25mg at bedtime. Week 2: 2.5mg at bedtime. Week 3: 2.5mg twice daily. Week 4: 2.5mg three times daily. then increase by 2.5mg every 3 to 14 days, depending on the patient's response. Usual dose: 10 mg to 30mg daily taken as 3 divided doses. In patients already receiving Levodopa the dosage of this drug may gradually be decreased, while the dosage of Bromocriptine is increased until the optimum balance is determined. **Pediatric dosing** Oral: 1.25 mg twice daily, gradually increased. **Prolactinoma** Maximum daily dose recommended in children aged 7 to 12 years is 5 mg.

	Maximum daily dose recommended in adolescent patients (13-17 years) is 20 mg. **Acromegaly** Maximum daily dose recommended in children ages 7 to 12 years is 10 mg. Maximum daily dose recommended in adolescent patients (13-17 years) is 20 mg.
Dosage Adjustment	**Dosing: Altered Kidney Function** No dose adjustment is recommended. **Dosage: Hepatic Impairment** Dosing decrease may be necessary due to extensive hepatic metabolism.

Contra-indications	• Hypersensitivity to bromocriptine, ergot alkaloids, or any component of the formulation.
	• Uncontrolled hypertension.
	• Hypertensive disorders of pregnancy (including eclampsia, preeclampsia, or pregnancy-induced hypertension).
	• For treatment of non-life-threatening indications:
	  ○ History of coronary artery disease, or other severe cardiovascular conditions.
	  ○ Symptoms/history of severe psychiatric disorders.

Adverse Drug Reactions	**>10%** • Gastrointestinal: Constipation (11% to 14%), nausea (18% to 33%). • Nervous system: Dizziness (≤13%), headache (≤13%). • Neuromuscular & skeletal: Asthenia (13%). • Respiratory: Rhinitis (14%). **1% to 10%** • Cardiovascular: Orthostatic hypotension (6%), Raynaud's disease (<2%), syncope (<2%), vasospasm (digits: 3%). • Endocrine & metabolic: Hypoglycemia (4%). • Gastrointestinal: Abdominal cramps, abdominal distress, anorexia (4% to 5%), diarrhea (9%), dyspepsia (4% to 8%), gastrointestinal hemorrhage (<2%), vomiting (2% to 6%), xerostomia (≤4%). • Infection: Infection (6%). • Nervous system: Drowsiness (3%). • Ophthalmic: Amblyopia (8%). • Respiratory: Nasal congestion (≤4%), sinusitis (10%).
Monitoring Parameters	• Blood pressure and heart rate (baseline and periodically thereafter) especially during the first days of therapy. • Visual fields (prolactinoma; periodic) • Monitor for melanomas: Periodic skin examinations by qualified individuals (e.g. dermatologists). • Monitor for tumor expansion. • Monitor for GI bleeding (patients with history of peptic ulcer).
Drug Interactions	***Risk X: Avoid combination*** Alizapride, Amisulpride, Bromperidol, Ergot Derivatives, Fusidic Acid (Systemic), Fexinidazole, Fusidic Acid (Systemic), Lisuride, Lorcaserin,

	Methotrimeprazine, Methysergide, Metoclopramide, Sulpiride. ***Risk D: Consider therapy modification*** Alpha-/Beta-Agonists, Alpha1-Agonists, Amifostine, Antipsychotic Agents, CYP3A4 Inhibitors, Nefazodone, Obinutuzumab, Serotonin 5-HT1D Receptor Agonists (Triptans).
Pregnancy and Lactation	**Pregnancy**: If pregnancy occurs it is generally advisable to withdraw Bromocriptine after the first missed menstrual period. If Bromocriptine is needed, monitor closely for hypertensive disorders during pregnancy and immediately postpartum. **Lactation**: Bromocriptine is known to inhibit lactation. Do not use it for lactating women.
Administration	Administer with food to decrease GI distress. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	***Concerns related to adverse effects*** • Cardiac valvular fibrosis: usually associated with long-term, chronic use. • **Cardiovascular effects:** Hypotension, including orthostatic hypotension and syncope, may occur, particularly upon initiation of therapy and dose escalation. In addition, hypertension, seizures, MI, and stroke have been reported. Monitor closely the first days of therapy. particular care should be exercised when driving or operating machinery. • **Hallucinations**: Visual or auditory hallucinations may occur when administered alone or concomitantly with levodopa. Hallucinations usually resolve with dosage reduction. symptoms may persist for several weeks following discontinuation of high doses. • **Impulse control disorders**: symptoms include pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating. Dose reduction or tapered discontinuation should be considered if such symptoms develop. • Pleural and pericardial effusions, as well as pleural and pulmonary fibrosis: Discontinue therapy if fibrotic changes are suspected. ***Disease-related concerns*** • **Cardiovascular disease**: Use with caution in patients with cardiovascular disease (myocardial infarction; residual atrial, nodal, or ventricular arrhythmia). • **Dementia**: Use with caution in patients with dementia; high doses may be associated with confusion and mental disturbances. • **Galactose intolerance**: Avoid use in patients with rare hereditary problems. • **Hepatic impairment**: Use with caution in patients with hepatic impairment. • **Macroadenomas**: Discontinuation of therapy in patients with macroadenomas has been associated with rapid regrowth of tumor and increased prolactin serum levels. • **Peptic ulcer disease**: Use with caution in patients with peptic ulcer disease; severe gastrointestinal bleeding has been reported (some fatal). • **Prolactin-secreting adenomas**: Cerebrospinal fluid rhinorrhea has been observed in some of these patients. • **Psychosis**: Use with caution in patients with psychosis; dopamine agonists may exacerbate the disorder or diminish the effectiveness of drugs used to

	treat the disorder. Use in patients with severe psychotic disorder is not recommended. ***Other warnings/precautions*** • **Discontinuation of therapy:** associated with a neuroleptic malignant syndrome on abrupt withdrawal or significant dosage reduction after long-term use; gradual dosage reduction is recommended. Educate patients on potential withdrawal symptoms; consider readministration of a dopamine agonist at the lowest effective dose in patients experiencing symptoms. • **Visual monitoring**: Rapidly progressing visual field loss requires neurosurgical consultation. **Overdose management**: activated charcoal can be used. The management of acute intoxication is symptomatic; Metoclopramide may be indicated for the treatment of emesis or hallucinations.
Storage	Store between 15°C to 25°C **N.B** Refer to manufacturer PIL if there are specific considerations.

Cabergoline

Generic Name	Cabergoline
Dosage form/strengths	Tablets: 0.5mg, 1 mg, 2 mg
Route of Administration	Oral
Pharmacologic Category	Ergot Derivative; Hyperprolactinemia Agent, Dopamine (D2) Agonist ATC: As Prolactin inhibitors: G02CB03 **As** dopaminergic Agents antiparkinsonism: N04BC06
Indications	• Hyperprolactinemic disorders: either idiopathic or caused by pituitary adenomas. • Inhibition of lactation for medical reasons.
Dosage Regimen	**Hyperprolactinemic disorders** **Adult dosing** **Initial**: 0.5 mg/week administered in 1 or 2 divided weekly doses, may increase dose by 0.5 mg/week no sooner than every 4 weeks if needed based on serum prolactin levels. **Usual dosage**: 0. 5 to 2 mg/week administered in 1 or 2 divided weekly doses. **Maximum dose**: Doses of up to 4.5 mg cabergoline per week have been used in hyperprolactinaemic patients, and may be divided into two or more doses weekly. **Duration of therapy**: After a normal serum prolactin level has been maintained for 6 months, Cabergoline may be discontinued, with periodic monitoring of the serum prolactin level. Use beyond 24 months has not been established. **For inhibition of lactation** The recommended therapeutic dosage is 1 mg cabergoline given as a single dose or the more tolerable dose regimen 0.25 mg (one-half 0.5 mg tablet) every 12 hours for two days i.e. 1 mg total dose. Cabergoline should be administered within the first 24 hours post-partum.
Dosage Adjustment	**Dosing Kidney Function** There are no dosage adjustments needed. **Dosing Hepatic Impairment** Mild and moderate hepatic impairment: There are no dosage adjustments available. Severe hepatic impairment (Child-Pugh class C): Lower doses should be considered. (extensive hepatic metabolism).
Contra-indications	• Hypersensitivity to the active substance, any ergot alkaloid, or to any excipient. • Pre-eclampsia, eclampsia. • Post-partum hypertension or uncontrolled hypertension. • Severe impairment of liver function. • History of pulmonary, pericardial, and retroperitoneal fibrotic disorders. • History of psychosis or risk of post-partum psychosis. • **For long-term treatment**: Evidence of cardiac valvulopathy as determined by pre-treatment echocardiography.

Adverse Drug Reactions	**>10%** **Gastrointestinal**: Nausea (27% to 29%). **Nervous system**: Dizziness (15% to 17%), headache (26%). **1% to 10%** **Cardiovascular**: Dependent edema (1%), hypotension (≤1%), orthostatic hypotension (4%), palpitations (≤1%), peripheral edema (1%), syncope (≤1%) **Dermatologic**: Acne vulgaris (≤1%), pruritus (≤1%). **Endocrine & metabolic**: Hot flash (3%). **Gastrointestinal**: Abdominal pain (5%), anorexia (≤1%), constipation (7% to 10%), diarrhea (≤2%), dyspepsia (2% to 5%), flatulence (≤2%), toothache (1%), vomiting (2% to 4%), xerostomia (≤2%). **Genitourinary**: Dysmenorrhea (≤1%), mastalgia (1% to 2%). **Nervous system**: Anxiety (≤1%), asthenia (6%), depression (3%), drowsiness (≤2%), fatigue (5% to 7%), insomnia (≤1%), lack of concentration (1%), malaise (≤1%), nervousness (≤2%), pain (2%), paresthesia (≤2%), vertigo (1% to 4%). **Neuromuscular & skeletal**: Arthralgia (1%). **Ophthalmic**: Periorbital edema (1%), visual disturbance (≤1%). **Respiratory**: Flu-like symptoms (≤1%), rhinitis (1%), throat irritation (1%).
Monitoring Parameters	• **As baseline and as necessary in long term use:** - Cardiovascular evaluation, including echocardiogram, to assess the potential presence of asymptomatic valvular disease. First echocardiogram after initiation must occur within 3-6 months, and at least every 6 to 12 months thereafter. - Erythrocyte sedimentation rate. - Lung function/chest x-ray. - Renal function. **During long-term treatment** monitor for Signs and symptoms of: - Pleuro-pulmonary disease, such as dyspnoea, shortness of breath, persistent cough, or chest pain. - Renal insufficiency or ureteral, abdominal vascular obstructions as well as any possible abdominal masses or tenderness that may indicate retroperitoneal fibrosis. - Cardiac failure • **Serum prolactin levels (monthly).**
Drug Interactions	***Risk X: Avoid combination*** Antipsychotic Agents, Bromocriptine, Dihydroergotamine, Lisuride, Lorcaserin, Methysergide, Metoclopramide, Pipamperone, Sulpiride.
Pregnancy and Lactation	**Pregnancy** Limited data. It is recommended that dopamine agonist therapy be discontinued once pregnancy is discovered. **Lactation** No data. A decision should be made whether to discontinue nursing or to discontinue the drug due to the potential for serious adverse reactions in nursing infants from Cabergoline.
Administration	Administer with meals to reduce the risk of gastrointestinal undesirable effects. **N.B** Refer to manufacturer PIL if there are specific considerations.

Warnings/ Precautions	• **Cardiac valvulopathy**: Risk is increased with use of high doses (e.g. >2 mg/day). If valvular disease is detected by echocardiogram, the patient should not be treated with Cabergoline. use the lowest effective dose. Clinical and diagnostic monitoring (for example, chest x-ray, CT scan and cardiac echocardiogram) should be conducted to assess the risk of cardiac valvulopathy. • **Extracardiac Fibrotic Reactions:** Pleural, pericardial, and retroperitoneal fibrosis have been reported. Should not be used in patients with a history of cardiac or extracardiac fibrotic disorder. Following diagnosis of pleural effusion or pulmonary fibrosis, the discontinuation of therapy results in improvement of signs and symptoms. • **Cardiovascular effects:** Initial doses >1 mg may cause orthostatic hypotension; use with caution in patients with cardiovascular disease; hypertension, stroke, and seizure have been reported with other dopamine agonists. • **Psychiatric disorders**: Pathological gambling, increased libido, and hypersexuality, generally reversible with dose reduction or discontinuation of treatment. • **CNS depression**: Patients must be cautioned about performing tasks that require mental alertness (e.g., operating machinery or driving). • **Peptic ulcer disease:** Use with caution in patients with peptic ulcer disease (PUD) or GI bleeding. • **Raynaud syndrome**: Use with caution in patients with Raynaud syndrome.
Storage	- Store between 15-30°C **N.B**. Refer to manufacturer PIL if there are specific considerations.

Estrogens

Estradiol

Generic Name	Estradiol
Dosage form/strengths	Tablets: 1 mg, 2 mg estradiol valerate And in combinations.
Route of Administration	Oral
Pharmacologic Category	Estrogen derivative ATC code: G03CA03
Indications	• Hormone replacement therapy (HRT) for estrogen deficiency symptoms in peri- and postmenopausal women. • Prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or contraindicated for, other medicinal products approved for the prevention of osteoporosis.
Dosage Regimen	**Hormone replacement therapy for estrogen deficiency symptoms in peri- and postmenopausal women, Menopausal symptoms:** **Oral**: 1mg daily continuously without break. May be increased to 2 mg. Once treatment is established the lowest effective dose and shortest duration necessary for relief of symptoms should be used. **Note:** In women with an intact uterus, a progestogen should be added to Estradiol for at least 12 - 14 days each month/28-day cycle, starting on the first day of menstruation bleeding or may start any day if the menstrual periods are very infrequent or there is amenorrhea. (unless there is endometriosis).
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** No dosage adjustment. Not studied. **Dosing: Hepatic Impairment: Adult** Use is contraindicated with active hepatic dysfunction.
Contra-indications	• Anaphylactic reaction or hypersensitivity to estradiol or any of the excipients. • Untreated endometrial hyperplasia • Undiagnosed abnormal genital bleeding. • Known or suspected cancer of the breast. • Known or suspected estrogen-dependent neoplasia • Active deep vein thrombosis, pulmonary embolism, or history of these conditions. • Active or recent (e.g., within the past year) arterial thromboembolic disease (e.g., stroke, myocardial infarction).

	• Known thrombophilic disorders (e.g. protein C, Protein S, or antithrombin Deficiency). • Active liver dysfunction. • Porphyria
Adverse Drug Reactions	**Frequency not defined:** **Neoplasms benign or malignant**: Breast cancer, Endometrial cancer, Ovarian cancer. **Immune system disorders:** Hypersensitivity reaction, Exacerbation of hereditary angioedema. **Metabolism and nutrition disorder:** Porphyria aggravated, Increased or decreased weight, Increased appetite, Carbohydrate tolerance decreased. **Psychiatric disorders:** Anxiety/depressive symptoms, Decreased or increased libido. **Nervous system disorders:** Migraine, Headache, Dizziness, Fatigue, Chorea, Stroke, Dementia (in patients over 65 years). **Eye disorders:** Visual disturbances, Intolerance to contact lenses **Cardiac disorders:** Palpitations, Myocardial infarction. **Vascular disorders:** Hypertension, Thrombophlebitis, Venous Thromboembolism. **Respiratory, thoracic and mediastinal disorders:** Epistaxis **Gastrointestinal disorders:** Dyspepsia, Abdominal pain, Vomiting, Nausea, Bloating, Flatulence. **Hepatobiliary disorders:** Gallbladder disease including Cholestasis **Skin and subcutaneous tissue disorders:** Rashes, various Skin disorders (including Pruritus, Eczema, Urticaria, Acne, Hirsutism, Hair loss, Erythema nodosum, Erythema multiforme, Rash hemorrhagic, Chloasma. **Musculoskeletal and connective tissue disorders:** Muscle cramps, Leg pain. **Renal and urinary disorders:** Cystitis-like symptom. **Reproductive system and breast disorders:** Increased size of uterine fibroids, Vaginal candidiasis, Uterine cervical erosions, Changes in vaginal bleeding pattern and abnormal bleeding or flow, Breakthrough bleeding, Spotting (bleeding irregularities usually subside during continued treatment), Dysmenorrhoea, Changes in vaginal secretion, Premenstrual-like syndrome, Breast secretion, Breast tenderness, enlargement or pain**.** **General disorders and administration site conditions**: Edema.
Monitoring Parameters	• Before therapy: Complete patient history including baseline risk for breast cancer and CVD. • During therapy, age-appropriate breast and pelvic exams • Blood pressure.
Drug Interactions	***Risk X: Avoid combination*** Anastrozole, Dehydroepiandrosterone, Exemestane, Fexinidazole, Fezolinetant, Fusidic Acid (Systemic), Hemin, Indium 111 Capromab Pendetide, Ospemifene, Raloxifene, Tranexamic Acid.

	Risk D: Consider therapy modification Cosyntropin, Growth Hormone Analogs, Metyrapone, Tizanidine.
Pregnancy and Lactation	**Pregnancy** Contraindicated. Not indicated for use during pregnancy. If pregnancy occurs during medication treatment should be withdrawn immediately. **Lactation** Estrogens have been shown to decrease the quantity and quality of human milk; therefore, it is not recommended.
Administration	**Oral:** • The tablets can be taken with or without food. The tablets should be swallowed whole with a glass of water or milk. May administer with food or after a meal to reduce GI upset. • Once a woman has selected a particular time for administration, she should keep to it every day. • If missed dose, the tablet can be taken as long as it is within 12 hours of the usual time. Otherwise take the next dose in its usual time. In the case of a missed or delayed dose the likelihood of breakthrough bleeding or spotting may be increased. **N.B**. Refer to product PIL for other considerations.
Warnings/ Precautions	• **Breast cancer:** an increased risk of invasive breast cancer was observed in patients who are postmenopausal using estrogens in combination with progesterone. The level of risk is dependent on the duration of use**.** • **Endometrial cancer:** The use of estrogen-only HRT in patients with a uterus is associated with an increased risk of endometrial cancer. Adding a progestogen to estrogen therapy for at least 12 days per cycle can prevent this increased risk. • **Ovarian cancer:** Slightly increase in incidence of ovarian cancer with estrogen replacement therapy. • **Cardiovascular disease** - The use of estrogen-only and estrogen-progestogen therapy is associated with an up to 1.5-fold increased relative risk of ischemic stroke. - The risk of coronary artery disease is slightly increased in users of combined estrogen-progestogen HRT over the age of 60. - HRT is associated with a 1.3- to 3-fold risk of developing venous thromboembolism (VTE), i.e. deep vein thrombosis or pulmonary embolism. The occurrence of such an event is more likely in the first year

	of HRT than later. Risk factors include use of estrogens, older age, major surgery, prolonged immobilization, obesity (BMI > 30kg/m^2) pregnancy/post-partum period, systemic lupus erythematosus (SLE) and cancer. • **Continuation of therapy**: a careful appraisal of the risks and benefits should be undertaken at least annually and HRT should only be continued as long as the benefit outweighs the risk. • **Caution**: Conditions may recur or be aggravated during treatment, and need close supervision: - Leiomyoma (uterine fibroids) or endometriosis. - Thromboembolic disorders. - Estrogen dependent tumors, risk factor is 1st degree heredity for breast cancer. - Hypertension. - Liver disorders (e.g. liver adenoma). - Diabetes mellitus with or without vascular involvement - Cholelithiasis. - Migraine or (severe) headache. - Systemic lupus erythematosus. - A history of endometrial hyperplasia. - Epilepsy. - Asthma. - Otosclerosis. - Hereditary angioedema. • **Immediate withdraw therapy in the following situations** - Jaundice or deterioration in liver function. - Significant increase in blood pressure. - New onset of migraine-type headache. - Pregnancy. • **Fluid retention**: Estrogens may cause fluid retention, and therefore patients with cardiac or renal dysfunction should be carefully observed. • **Lipid effects:** Estrogen compounds are generally associated with lipid effects such as increased triglycerides. Monitor closely for pre-existing hypertriglyceridemia women. • **Thyroid hormones**: Estrogens increase thyroid binding globulin (TBG), leading to increased circulating total thyroid hormone. The level of free T3 and T4 remains unchanged. • **Hepatic dysfunction:** Estrogens are poorly metabolized in patients with hepatic dysfunction.
Storage	Store between 15 ^{0}C and 30^{0}C. **N.B**. Refer to product PIL for other considerations.

Glycogenolytic hormones

Glucagon

Generic Name	Glucagon
Dosage form/strengths	Lyophilized Powder: 1 mg/ml.
Route of Administration	IV, IM, SC
Pharmacologic Category	Antidote, Hypoglycemia; Diagnostic Agent ATC: H04AA01
Indications	• Treatment of severe hypoglycemia in pediatric and adult patients with diabetes. • As a diagnostic aid for use during radiologic examinations to temporarily inhibit movement of the gastrointestinal tract in adult patients.
Dosage Regimen	**Hypoglycemia** • *Adult dosing and pediatric weighing ≥20 kg:* **IM, SC, IV:** 1 mg; may repeat in 15 minutes as needed. • *Pediatric weighing <20 kg:* **IM, SC, IV:** 0.5 mg; may repeat in 15 minutes as needed. **Diagnostic aid, radiologic examinations for adults** • *Relaxation of duodenum and small bowel:* **IM:** Usual dose: 1 mg. **IV:** Usual dose: 0.25 to 0.5 mg. • *Relaxation of colon:* **IM:** 2 mg given 10 minutes before the procedure. • *Relaxation of stomach:* ***IM:*** *2 mg.* ***IV:*** *0.5 mg.*
Dosage Adjustment	**Dosing: Kidney Function** There are no dosage adjustments needed. **Dosing: Hepatic Impairment** There are no dosage adjustments needed.
Contra-indications	• Hypersensitivity to Glucagon or any component of the formulation. • Glucagonoma when used as a diagnostic aid. • Insulinoma. • Pheochromocytoma.
Adverse Drug Reactions	**>10%** Gastrointestinal: Nausea (IV: 26% to 30%), vomiting (IV: 15% to 16%). Nervous system: Headache (IV: 5% to 18%). **1% to 10%** Immunologic: Antibody development (2%). Local: Pain at the injection site (1%), swelling at the injection site (7%).

Monitoring Parameters	• Blood glucose levels. • Blood Pressure, ECG, heart rate (when used as a diagnostic aid). • Signs or symptoms of a hypersensitivity reaction.
Drug Interactions	There is no Consideration therapy modification or avoid combination interactions.
Pregnancy and Lactation	**Pregnancy**: Use has not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. **Lactation**: Glucagon is not absorbed from the GI tract. Therefore, even if the infant ingested glucagon it would be unlikely to to cause harm to an exposed infant.
Administration	**Preparation for administration:** • Reconstitute in 1ml diluent. Dissolve well until a clear colorless solution. The formed solution is 1mg/ml. • Inject the proper dose immediately. Discard any unused portion. ***As a diagnostic agent*** May administer IM or IV over 1 minute. After the diagnostic procedure, administer oral carbohydrates to patients who have been fasting, if this is compatible with the diagnostic procedure applied. ***For severe hypoglycemia*** Inject the solution subcutaneously or intramuscularly in the upper arm, thigh, or buttocks. In addition, healthcare providers may administer intravenously. When the patient has responded to the treatment and is able to swallow, give oral carbohydrates to restore the liver glycogen and prevent recurrence of hypoglycemia. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Pheochromocytoma:** Glucagon may cause the release of catecholamines, resulting in an increase in blood pressure. The use of glucagon is contraindicated in patients with this condition. If the patient develops a substantial increase in blood pressure and a previously undiagnosed pheochromocytoma is suspected, 5 to 10 mg of phentolamine mesylate, administered intravenously, has been shown to be effective in lowering blood pressure. • **Insulinoma:** Exogenous Glucagon may cause an initial rise in blood glucose followed by rebound hypoglycemia. The use of glucagon is contraindicated in patients with this condition. If a patient develops symptoms of hypoglycemia after a dose of Glucagon for Injection, give glucose orally or intravenously. • **Glucagonoma**: Glucagon administered to patients with glucagonoma may cause secondary hypoglycemia. Test patients suspected of having glucagonoma for blood levels of glucagon prior to use as a diagnostic aid as Glucagon is contraindicated in this condition. • **Hypersensitivity Reactions**: Allergic reactions have been reported with glucagon, these include generalized rash, and in some cases anaphylactic

	shock with breathing difficulties and hypotension. • **Lack of Efficacy in Patients with Decreased Hepatic Glycogen:** Patients in states of starvation, with adrenal insufficiency or chronic hypoglycemia may not have adequate levels of hepatic glycogen for Glucagon to be effective. Patients with these conditions should be treated with glucose. • **Necrolytic migratory erythema**: Necrolytic migratory erythema (NME), a skin rash associated with glucagonomas (glucagon-producing tumors) and characterized by scaly, pruritic, erythematous plaques, bullae, and erosions, has been reported (rarely) following continuous glucagon infusion. Rash may occur on face, groin, perineum, and legs or may be more wide spread; rash generally resolves with discontinuation of treatment. Consider the risks versus benefits of continuing the glucagon infusion if NME occurs. • **Cardiac disease**: Use with caution in patients with cardiac disease when Used as a Diagnostic Aid. Blood Pressure and Heart Rate may Increase in cardiac disease patients. • **Diabetes**: Use caution if using as diagnostic aid in patients with diabetes on insulin; may cause hyperglycemia.
Storage	• Before reconstitution, store between (2°C to 8°C). Do not freeze. Protect from light. • Use a reconstituted solution immediately; discard unused portions. **N.B** Refer to manufacturer PIL if there are specific considerations.

Insulins

Degludec Long acting Insulin

Generic Name	Degludec Long acting Insulin
Dosage Form/Strengths	Solution for SC injection (prefilled pen): 100 units/ml.
Route of Administration	*SC*
Pharmacologic Category	Insulin, Long-Acting ATC code: A10AE06
Indications	To improve glycemic control of diabetes mellitus, types 1 and 2 in adults and children of age more than 1 year.
Dosage Regimen	**Basal insulin Dosing:** Once daily at any time of the day, preferably at the same time every day, the dose is determined according to the individual patient's needs. - **Type 2 diabetes mellitus**: To be taken alone or in combination with bolus insulin or other antidiabetic agents. The initial dose is 10 units then adjust dose. **Type 1 diabetes mellitus**: Must be combined with short or rapid-acting insulin to cover mealtime insulin requirements.
Dosage Adjustment	**Dosing: Renal or Hepatic Impairment** Glucose monitoring is to be intensified and the insulin dose adjusted on an individual basis. Dosage reduction may be needed. **Transferring between types of insulins or in additions of other antidiabetics**: An initial dose reduction of 20% should be considered in order to minimize the risk of hypoglycemia, then adjust the dose according to patient needs.
Contra-Indications	• Hypersensitivity to the active substance or any of the excipients. • Hypoglycemia.
Adverse Drug Reactions	**>10%** • Endocrine & metabolic: Severe hypoglycemia. • Immunologic: Antibody development. • Nervous system: Headache. • Respiratory: Nasopharyngitis, upper respiratory tract infection. **1% to 10%** • Cardiovascular: Peripheral edema. • Gastrointestinal: Diarrhea. • Local: Injection site reaction. • Respiratory: Sinusitis.
Monitoring Parameters	• Blood glucose, Glycosylated hemoglobin levels. • May need to monitor: electrolytes; renal function; hepatic function; weight.
Drug Interactions	***Risk X: Avoid combination*** Macimorelin, Rosiglitazone. ***Risk D: Consider therapy modification***

	Alpha-Glucosidase Inhibitors, Dipeptidyl Peptidase-IV Inhibitors, Glucagon-Like Peptide-1 Agonists, Liraglutide, Metreleptin, Pioglitazone, Pramlintide, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors. **Insulin dose reduction may be needed with** Oral antidiabetic medicinal products, GLP-1 receptor agonists, monoamine oxidase inhibitors (MAOI), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, and sulfonamides. **Insulin dose increase may be needed with** Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol. **Antiadrenergic Drugs** (e.g., beta-blockers) may mask the symptoms of hypoglycemia.
Pregnancy and Lactation	**Pregnancy**: Animal Data Suggest Low Risk. Insulin requirements usually decrease in the first trimester and increase subsequently during the second and third trimesters. Close monitoring is required throughout pregnancy. **Lactation**: Adverse events have not been reported in breastfeeding infants. Close monitoring of mothers treated with insulin is recommended as dose adjustments may be required.
Administration	**Subcutaneous administration**: Injection in the thigh, the upper arm, or the abdominal wall. Injection sites should always be rotated within the same region to reduce the risk of lipodystrophy and cutaneous amyloidosis. New needles should always be used to avoid the risk of blocked needles. **N.B**. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hyperglycaemia**: May occur at inadequate dosing or unplanned discontinuation of treatment. Symptoms include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as acetone odour of breath. • **Hypoglycemia:** May occur with omission of a meal or unplanned physical exercise. • **Concomitant illness**, especially infections and fever, usually increases the patient's insulin requirement. Kidney, liver, or adrenal diseases, pituitary or thyroid gland may require changes in the insulin dose by reduction. • **Skin and subcutaneous tissue disorders**: Continuous rotation of the injection site is needed. Potential risk of delayed absorption and worsened glycemic control occur following insulin injections at sites with lipodystrophy and cutaneous amyloidosis. • **Combination of Pioglitazone and insulin medicinal products:** If the combination is used, patients should be observed for symptoms of heart failure, weight gain and edema. Discontinue Pioglitazone if any deterioration in cardiac symptoms occurs. • **Metabolism and nutrition disorder**: Hypokalemia may occur with insulin therapy. Monitor. Insulin therapy may lead to weight gain.

	• **Hypersensitivity**: Hypersensitivity reactions (serious, life-threatening and anaphylaxis) may occur. If occurred, discontinue administration and initiate supportive care measures. • **Multiple dose injection pens**: pen-shaped injection devices should never be used for more than one person (even when the needle is changed) because of the risk of infection. The injection device should be clearly labeled with individual patient information to ensure that the correct pen is used. • **Administration**: Insulin Degludec is NOT intended for IV, IM administration or in insulin infusion pumps. • **Diabetic ketoacidosis**: Should not be used in patients with diabetic ketoacidosis; use of a rapid-acting or short-acting insulin is required. **Insulin antibodies:** In rare cases, Insulin antibodies may form which necessitate adjustment of the insulin dose.
Storage	• Store at 2-8 ^{0}C. protect from freezing. • After opening: store up to 8 weeks at 2-30 ^{0}C. keep the cap on to protect from light. **N.B**. Refer to manufacturer PIL if there are specific considerations.

Detemir Long-acting Insulin

Generic Name	Detemir Long-acting Insulin
Dosage Form/Strengths	Solution for injection in Pre-filled Syringe: 100 I.U./ml.
Route of Administration	SC
Pharmacologic Category	Insulin, Long-Acting ATC: A10AE05
Indications	Improvement of glycemic control of diabetes mellitus (type 1 and 2) in adults, adolescents and children aged 1 year and above.
Dosage Regimen	**Type 1 diabetes mellitus**: Initial: SC: One-third to one-half of the total daily insulin dose. The remainder of the total daily insulin dose should be administered as rapid or short-acting insulin before meals. Adjust dose individually. **Type 2 diabetes mellitus**: Initial: SC: 10 units (or 0.1-0.2 unit/kg) in adults taken once daily in the evening or divided into a twice daily regimen. When used in combination with oral antidiabetics or GLP-1 receptor agonists, it is recommended to use detemir once daily. Adjust dose according to patients' needs. N.B. Adjustment of dose may be necessary if patients undergo increased physical activity, change their usual diet or during concomitant illness.
Dosage Adjustment	**Renal, hepatic impairment, elderly and pediatrics** Glucose monitoring is to be intensified and the insulin dose adjusted on an individual basis. Dosage reduction may be needed.
Contra-Indications	• Hypersensitivity to the active substance or to any of the excipients. • Hypoglycemia.
Adverse Drug Reactions	**>10%** **Endocrine & metabolic**: Hypoglycemia (Type 1 combination regimens: adults: 82% to 88%; children and adolescents: 93% to 95%; Type 2 combination regimens: adults: 9% to 41%), severe hypoglycemia (Type 1 combination regimens: adults: 5% to 9%; children and adolescents: 2% to 16%; Type 2 combination regimens: adults: ≤2%). **Gastrointestinal**: Abdominal pain (6% to 13%), gastroenteritis (6% to 17%) Nervous system: Headache (14% to 31%). **Respiratory**: Flu-like symptoms (6% to 14%), pharyngitis (10% to 17%), upper respiratory tract infection (26% to 36%). **1% to 10%** **Gastrointestinal**: Nausea (children and adolescents: 7%), vomiting (children and adolescents: 7%). **Infection**: Viral infection (children and adolescents: 7%).

	Neuromuscular & skeletal: Back pain (adults: 8%). **Respiratory**: Bronchitis (adults: 5%), cough (children and adolescents: 8%), rhinitis (children and adolescents: 7%). **Miscellaneous**: Fever (children and adolescents: 10%).
Monitoring Parameters	• Blood glucose, gGlycosylated hemoglobin levels. • May need to monitor: electrolytes; renal function; hepatic function; weight.
Drug Interactions	***Risk X: Avoid combination*** Macimorelin, Rosiglitazone ***Risk D: Consider therapy modification*** Alpha-Glucosidase Inhibitors (Acarbose), Dipeptidyl Peptidase-IV Inhibitors (gliptins), Glucagon-Like Peptide-1 Agonists, Liraglutide, Metreleptin, Pioglitazone, Pramlintide, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors (eg. canagliflozin, dapagliflozin, and empagliflozin),. **Insulin dose reduction may be needed with** Oral antidiabetic medicinal products, GLP-1 receptor agonists, monoamine oxidase inhibitors (MAOI), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, and sulfonamides. **Insulin dose increase may be needed with** Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol. **Antiadrenergic Drugs** (e.g., beta-blockers) may mask the symptoms of hypoglycemia.
Pregnancy and Lactation	**Pregnancy**: Insulin is the preferred treatment of type 1 and type 2 diabetes mellitus in pregnancy, and gestational diabetes mellitus. Close monitoring is required throughout pregnancy. **Lactation** Adverse events have not been reported in breastfeeding infants. Close monitoring of the mother treated with insulin is recommended as dose adjustments may be required.
Administration	**Subcutaneous**: Inject into the thigh, upper arm, or abdomen. Rotate injection sites to decrease risk of lipodystrophy and localized cutaneous amyloidosis. For patients who require twice daily dosing, the evening dose can be administered in the evening or at bedtime. **N.B**. Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hyperglycaemia**: May occur at inadequate dosing or unplanned discontinuation of treatment. Symptoms include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as acetone odour of breath. • **Hypoglycemia:** Omission of a meal or physical exercise may lead to hypoglycemia. • **Concomitant illness**, especially infections and fever, usually increases

	the patient's insulin requirement. Kidney, liver, or adrenal diseases, pituitary or thyroid gland may require changes in the insulin dose by reduction. • **Skin and subcutaneous tissue disorders**: Continuous rotation of the injection site is needed. Potential risk of delayed absorption and worsened glycemic control occur following insulin injections at sites with lipodystrophy and cutaneous amyloidosis. • **Combination of Pioglitazone and insulin medicinal products:** If the combination is used, patients should be observed for symptoms of heart failure, weight gain and edema. Discontinue Pioglitazone if any deterioration in cardiac symptoms occurs. • **Metabolism and nutrition disorder**: Hypokalemia may occur with insulin therapy. Monitor. Insulin therapy may lead to weight gain. • **Hypersensitivity**: Hypersensitivity reactions (serious, life-threatening and anaphylaxis) may occur. If occurred, discontinue administration and initiate supportive care measures. • **Multiple dose injection pens**: Devices should never be used for more than one person (even when the needle is changed) because of the risk of infection. The injection device should be clearly labeled with individual patient information to ensure that the correct pen is used. • **Diabetic ketoacidosis**: Should not be used in patients with diabetic ketoacidosis; use of a rapid-acting or short-acting insulin is required.
Storage	• Store at 2-8 ^{0}C. Protect from freezing. Unopened vials should be thrown away after 6 weeks, if they are stored at room temperature up to 30 ^{0}C. • After opening: store up to 6 weeks at 2-30 ^{0}C. • Keep away from heat or light. Keep the pen cap on the pen in order to protect it from light. **N.B**. Refer to manufacturer PIL if there are specific considerations.

Glargine Long-acting Insulin

Generic Name	Glargine Long-acting Insulin
Dosage Form/Strengths	Solution for SC injection: 100 I.U./ml
Route of Administration	SC
Pharmacologic Category	Insulin, Long-Acting ATC: A10AE04
Indications	To improve glycemic control of diabetes mellitus (types 1 and 2) in adults, adolescents, and children aged 2 years and above.
Dosage Regimen	**Dosing** Once-daily at any time of the day, preferably at the same time every day, dose is determined according to individual patient's needs. - **Type 2 diabetes mellitus**: To be taken alone or in combination with other antidiabetic agents. - **Type 1 diabetes mellitus**: Must be combined with short or rapid-acting insulin to cover mealtime insulin requirements. **Note:** Insulin glargine is a long-acting insulin. Insulin requirements vary dramatically between patients, and therapy requires dosage adjustments with careful medical supervision.
Dosage Adjustment	**Dosing: Renal or Hepatic Impairment** Glucose monitoring is to be intensified and the insulin dose adjusted on an individual basis. Dosage reduction may be needed. **Transferring between types of insulins or in additions of other antidiabetics**: An initial dose reduction of 20% should be considered in order to minimize the risk of hypoglycemia, then adjust dose according to patient needs.
Contra-Indications	• Hypersensitivity to insulin glargine or any component of the formulation. • Hypoglycemia
Adverse Drug Reactions	**>10%** • Cardiovascular: Hypertension (20%), peripheral edema (≤20%). • Endocrine & metabolic: Severe hypoglycemia (Type I on combination regimens: 4% to 69%; Type II on combination regimens: ≤37%; monotherapy in adults ≥50 years old: 6%. • Gastrointestinal: Diarrhea (11%). • Genitourinary: Urinary tract infection (11%). • Immunologic: Antibody development (12% to 44%). • Infection: Infection (9% to 24%), influenza (19%). • Nervous system: Depression (11%). • Neuromuscular & skeletal: Arthralgia (14%), back pain (13%), limb pain (13%). • Ophthalmic: Cataract (18%).

	• Respiratory: Bronchitis (15%), cough (12%), nasopharyngitis (6% to 16%), sinusitis (19%), upper respiratory tract infection (5% to 29%). **1% to 10%** • Local: Pain at injection site (3%). • Nervous system: Headache (6% to 10%). • Ophthalmic: Retinal vascular disease (6%). • Respiratory: Pharyngitis (children and adolescents: 8%), rhinitis (children and adolescents: 5%). • Miscellaneous: Accidental injury (6%). **Frequency not defined** • Dermatologic: Urticaria at injection site. • Endocrine & metabolic: Sodium retention, weight gain. • Hypersensitivity: Anaphylaxis, angioedema, hypersensitivity reaction. • Local: Erythema at the injection site, hypertrophy at the injection site, inflammation at the injection site, itching at the injection site, lipoatrophy at the injection site, localized edema, and swelling at the injection site.
Monitoring Parameters	• Blood glucose, Glycosylated hemoglobin levels. • May need to monitor: electrolytes; renal function; hepatic function; weight.
Drug Interactions	***Risk X: Avoid combination*** Macimorelin, Rosiglitazone. ***Risk D: Consider therapy modification*** Dipeptidyl Peptidase-IV Inhibitors, Glucagon-Like Peptide-1 Agonists, Liraglutide, Metreleptin, Pioglitazone, Pramlintide, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors. **Insulin dose reduction may be needed with** Oral antidiabetic medicinal products, GLP-1 receptor agonists, monoamine oxidase inhibitors (MAOI), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, and sulfonamides. **Insulin dose increase may be needed with** Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol. **Antiadrenergic Drugs** (e.g., beta-blockers) may mask the symptoms of hypoglycemia.
Pregnancy and Lactation	**Pregnancy**: Insulin is the preferred treatment of type 1 and type 2 diabetes mellitus in pregnancy, and gestational diabetes mellitus. Close monitoring is required throughout pregnancy. **Lactation** Adverse events have not been reported in breastfeeding infants. Close monitoring of the mother treated with insulin is recommended as dose adjustments may be required.
Administration	**Subcutaneous administration**: Injection in the thigh, the upper arm, or the abdominal wall.

	• Do not use if the solution is viscous or cloudy; use only if clear and colorless with no visible particles. Administer consistently at the same time each day. Cold injections should be avoided. • Injection sites should always be rotated within the same region to reduce the risk of lipodystrophy and cutaneous amyloidosis. • Rotating from an injection site where lipodystrophy/cutaneous amyloidosis is present to an unaffected site may increase the risk of hypoglycemia. • Do not mix with any other insulin or solution. • Do not administer IV or in an insulin pump. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hyperglycaemia**: May occur at inadequate dosing or unplanned discontinuation of treatment. Symptoms include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as acetone odour of breath. • **Hypoglycemia:** May occur with omission of a meal or unplanned physical exercise. • **Concomitant illness**, especially infections and fever, usually increases the patient's insulin requirement. Kidney, liver, or adrenal diseases, pituitary or thyroid gland may require changes in the insulin dose by reduction. • **Skin and subcutaneous tissue disorders**: Continuous rotation of the injection site is needed. Potential risk of delayed absorption and worsened glycemic control occur following insulin injections at sites with lipodystrophy and cutaneous amyloidosis. • **Combination of Pioglitazone and insulin medicinal products:** If the combination is used, patients should be observed for symptoms of heart failure, weight gain and edema. Discontinue Pioglitazone if any deterioration in cardiac symptoms occurs. • **Insulin antibodies:** In rare cases, Insulin antibodies may form which necessitate adjustment of the insulin dose. • **Metabolism and nutrition disorder**: Hypokalemia may occur with insulin therapy. Monitor. Insulin therapy may lead to weight gain. • **Hypersensitivity**: Hypersensitivity reactions (serious, life-threatening and anaphylaxis) may occur. If occurred, discontinue administration and initiate supportive care measures. • **Multiple dose injection pens**: pen-shaped injection devices should never be used for more than one person (even when the needle is changed) because of the risk of infection. The injection device should be clearly labeled with individual patient information to ensure that the correct pen is used. • **Diabetic ketoacidosis**: Should not be used in patients with diabetic ketoacidosis; use of a rapid-acting or short-acting insulin is required. **Administration**: Insulin glargine is a clear solution, but it is not intended for IV or IM administration or via an insulin pump.

Storage	Store unopened vials and prefilled pens refrigerated at 2°C to 8°C. do not freeze. **N.B** Refer to manufacturer PIL if there are specific considerations.

Intermediate-acting insulin

Generic Name	**Neutral Protamine Hagedorn (NPH) insulin**
Dosage Form/Strengths	Cartridge, vial, or penfill: 100 I.U./ml.
Route of Administration	SC
Pharmacologic Category	Insulin, Intermediate-Acting
Indications	**Diabetes mellitus, management** in adults and pediatric patients requiring a depot insulin of intermediate duration.
Dosage Regimen	**Dosing** **Note:** Insulin requirements vary dramatically between patients, and therapy requires dosage adjustments with careful medical supervision. - Onset of action occurs within 2 hours after subcutaneous injection. Maximum effect is exerted between 4-12 hours.
Dosage Adjustment	**Dosing: Renal or Hepatic Impairment** Glucose monitoring is to be intensified and the insulin dose adjusted on an individual basis. Dosage reduction may be needed. **Transferring between types of insulins or in additions of other antidiabetics**: An initial dose reduction of 20% should be considered in order to minimize the risk of hypoglycemia, then adjust dose according to patient needs.
Contra-Indications	• Hypersensitivity to insulin NPH or any component of the formulation. • Hypoglycemia.
Adverse Drug Reactions	**Frequency not defined:** **Cardiovascular**: Peripheral edema **Dermatologic**: Injection site pruritus **Endocrine & metabolic**: Amyloidosis (cutaneous at the injection site), hypoglycemia, hypokalemia, lipodystrophy, lipohypertrophy, weight gain **Hypersensitivity**: Anaphylaxis, hypersensitivity reaction **Immunologic**: Immunogenicity **Local**: Atrophy at the injection site, erythema at the injection site, hypertrophy at injection site, injection site reaction, swelling at injection site **Neuromuscular & skeletal:** Swelling of extremities **Ophthalmic**: Visual disturbance
Monitoring Parameters	• Blood glucose, Glycosylated hemoglobin levels. • May need to monitor: electrolytes; renal function; hepatic function; weight.
Drug Interactions	***Risk X: Avoid combination*** Macimorelin, Rosiglitazone.

	Risk D: Consider therapy modification Alpha-Glucosidase Inhibitors, Dipeptidyl Peptidase-IV Inhibitors, Glucagon-Like Peptide-1 Agonists, Liraglutide, Metreleptin, Pioglitazone, Pramlintide, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors. **Insulin dose reduction may be needed with** Oral antidiabetic medicinal products, GLP-1 receptor agonists, monoamine oxidase inhibitors (MAOI), beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, salicylates, and sulfonamides. **Insulin dose increase may be needed with** Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol. **Antiadrenergic Drugs** (e.g., beta-blockers) may mask the symptoms of hypoglycemia.
Pregnancy and Lactation	**Pregnancy** Human regular insulin remains the standard treatment for pregnant patients with diabetes or gestational diabetes. Close monitoring is required throughout pregnancy. **Lactation** Adverse events have not been reported in breastfeeding infants. Close monitoring of the mother treated with insulin is recommended as dose adjustments may be required.
Administration	**Administration: Subcutaneous** • For subcutaneous administration into the thigh, upper arm, buttocks, or abdomen; do not administer IM or IV, or in an insulin pump. • Injection sites should always be rotated within the same region to reduce the risk of lipodystrophy and cutaneous amyloidosis. • Rotating from an injection site where lipodystrophy/cutaneous amyloidosis is present to an unaffected site may increase risk of hypoglycemia. • Prior to use the vial should be gently rolled between the palms or inverted several times. The vial must not be used if the contents have been frozen or it contains lumps that do not disperse on mixing. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hyperglycaemia**: May occur at inadequate dosing or unplanned discontinuation of treatment. Symptoms include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as acetone odour of breath. • **Hypoglycemia:** May occur with omission of a meal or unplanned physical exercise. • **Concomitant illness**, especially infections and fever, usually increases the patient's insulin requirement. Kidney, liver, or adrenal diseases, pituitary or thyroid gland may require changes in the insulin dose by reduction. • **Skin and subcutaneous tissue disorders**: Continuous rotation of the injection site is needed. Potential risks of delayed absorption and worsened glycemic control occur following insulin injections at sites with lipodystrophy and cutaneous amyloidosis. • **Combination of Pioglitazone and insulin medicinal products:** If the combination is used, patients should be observed for symptoms of heart

	failure, weight gain, and edema. Discontinue Pioglitazone if any deterioration in cardiac symptoms occurs. • **Insulin antibodies:** In rare cases, Insulin antibodies may form which necessitate adjustment of the insulin dose. • **Metabolism and nutrition disorder**: Hypokalemia may occur with insulin therapy. Monitor. Insulin therapy may lead to weight gain. • **Hypersensitivity**: Hypersensitivity reactions (serious, life-threatening and anaphylaxis) may occur. If occurred, discontinue administration and initiate supportive care measures. • **Multiple dose injection pens**: pen-shaped injection devices should never be used for more than one person (even when the needle is changed) because of the risk of infection. The injection device should be clearly labeled with individual patient information to ensure that the correct pen is used. • **Administration**: Insulin NPH is NOT intended for IV or IM administration.
Storage	Store unopened vials in the refrigerator between 2°C and 8°C. Do not freeze. **N.B** Refer to manufacturer PIL if there are specific considerations.

Short-acting Insulin injection (soluble)

Generic Name	Short-acting Insulin (soluble, neutral, or regular)
Dosage Form/Strengths	Solution for injection: 40 I.U./ml, 100 I.U./ml
Route of Administration	SC, IM, IV
Pharmacologic Category	Insulin, Short-Acting
Indications	Glycemic control in management of diabetes mellitus.
Dosage Regimen	**Dosing** - The individual insulin requirement is usually between 0.3 and 1.0 international units/kg/day. Adjustment of dose may be necessary if patients undertake increased physical activity, change their usual diet or during concomitant illness. - It can be used alone or in combination with intermediate-acting or long-acting insulin before a meal or a snack. **Note:** Regular insulin is a short-acting insulin. Insulin requirements vary dramatically between patients, and therapy requires dosage adjustments with careful medical supervision.
Dosage Adjustment	**Dosing: Renal or Hepatic Impairment** Glucose monitoring is to be intensified and the insulin dose adjusted on an individual basis. Dosage reduction may be needed. **Transferring between types of insulins or in additions of other antidiabetics** An initial dose reduction of 20% should be considered in order to minimize the risk of hypoglycemia, then adjust dose according to patient needs.
Contra-Indications	• Hypersensitivity to regular Insulin or any component of the formulation. • Hypoglycemia.
Adverse Drug Reactions	**Frequency not defined** **Cardiovascular**: Peripheral edema. **Dermatologic**: Injection site pruritus. **Endocrine & metabolic**: Amyloidosis (localized at injection site), hypoglycemia, hypokalemia, weight gain. **Hypersensitivity**: Anaphylaxis, hypersensitivity reaction. **Immunologic**: Immunogenicity. **Local**: Erythema at the injection site, hypertrophy at the injection site, lipoatrophy at the injection site, swelling at the injection site.
Monitoring Parameters	• Blood glucose, Glycosylated hemoglobin levels. • May need to monitor: electrolytes; renal function; hepatic function; weight.
Drug Interactions	***Risk X: Avoid combination*** Macimorelin, Rosiglitazone.

	Risk D: Consider therapy modification Alpha-Glucosidase Inhibitors, Dipeptidyl Peptidase-IV Inhibitors, Glucagon-Like Peptide-1 Agonists, Liraglutide, Metreleptin, Pioglitazone, Pramlintide, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors. **Antiadrenergic Drugs** (e.g., beta-blockers) may mask the symptoms of hypoglycemia.
Pregnancy and Lactation	**Pregnancy**: Human regular insulin remains the standard treatment for pregnant patients with diabetes or gestational diabetes. Close monitoring is required throughout pregnancy. **Lactation** Adverse events have not been reported in breastfeeding infants. Close monitoring of the mother treated with insulin is recommended as dose adjustments may be required.
Administration	**Administration: IV** Regular insulin may be administered IV with close monitoring of blood glucose and serum potassium; appropriate medical supervision is required. Do not use if the solution is viscous or cloudy; use only if clear and colorless **Usual Infusion Concentrations:** **IV infusion:** 0.05-1 unit/mL of NS 0.9% or dextrose 5%. **Administration: Subcutaneous** Do not use if the solution is viscous or cloudy; use only if clear and colorless. Regular insulin should be administered approximately 30 minutes before a meal. Cold injections should be avoided. Subcutaneous injection into the abdominal wall ensures a faster absorption than from other injection sites. Injection into a lifted skin fold minimizes the risk of intramuscular injection. Injection sites should be rotated within the same region. As with all insulin, the duration of action will vary according to the dose, injection site, blood flow, temperature, and level of physical activity. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	• **Hyperglycaemia**: May occur at inadequate dosing or unplanned discontinuation of treatment. Symptoms include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as acetone odour of breath. • **Hypoglycemia:** May occur with omission of a meal or unplanned physical exercise. • **Concomitant illness**, especially infections and fever, usually increases the patient's insulin requirement. Kidney, liver, or adrenal diseases, pituitary or thyroid gland may require changes in the insulin dose by reduction. • **Skin and subcutaneous tissue disorders**: Continuous rotation of the injection site is needed. Potential risks of delayed absorption and worsened glycemic control occur following insulin injections at sites with lipodystrophy and cutaneous amyloidosis. • **Combination of Pioglitazone and insulin medicinal products:** If the combination is used, patients should be observed for symptoms of heart

	failure, weight gain, and edema. Discontinue Pioglitazone if any deterioration in cardiac symptoms occurs. • **Metabolism and nutrition disorder**: Hypokalemia may occur with insulin therapy. Monitor. Insulin therapy may lead to weight gain. • **Hypersensitivity**: Hypersensitivity reactions (serious, life-threatening and anaphylaxis) may occur. If this occurs, discontinue administration and initiate supportive care measures. **Multiple dose injection pens**: pen-shaped injection devices should never be used for more than one person (even when the needle is changed) because of the risk of infection. The injection device should be clearly labeled with individual patient information to ensure that the correct pen is used.
Storage	• Store unopened vials in refrigerator between 2°C and 8°C until expiration date; do not freeze; keep away from heat and sunlight. • Once punctured (in use), vials may be stored for ≤1 month in the refrigerator between 2°C and 8°C or at ≤30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Ovulation Stimulants

Clomiphene

Generic Name	Clomiphene
Dosage form/strengths	Tablets: 50mg.
Route of Administration	Oral.
Pharmacologic Category	Ovulation Stimulator; Selective Estrogen Receptor Modulator (SERM). ATC: G03GB02.
Indications	**Treatment of ovulatory dysfunction** in women desiring pregnancy. Causes of infertility other than Clomiphene must be excluded or adequately treated before giving Clomiphene.
Dosage Regimen	**Oral**: 50 mg once daily for 5 days, to be started at any time if no recent uterine bleeding, or on or around the fifth day of cycle. • If progestin-induced bleeding is planned, or if spontaneous uterine bleeding occurs prior to therapy, the regimen of 50 mg daily for 5 days should be started on or about the 5th day of the cycle. • If ovulation does not appear to occur after the first course of therapy, a second course of 100 mg daily (two 50 mg tablets given as a single daily dose) for 5 days should be given. This course may be started as early as 30 days after the previous one. **N.B.** Efficacy and safety of clomiphene for more than 6 treatment cycles have not been demonstrated. If ovulatory menses have not occurred after 3 courses, the diagnosis should be re-evaluated.
Dosage Adjustment	**Dosing: Altered Kidney Function** No dosage adjustments are needed. **Dosing: Hepatic Impairment** Use is contraindicated in patients with liver disease or a history of liver dysfunction.
Contra-indications	• Hypersensitivity. • Abnormal uterine bleeding. • Hepatic disease or history hepatic disease. • Ovarian cyst not due to polycystic ovarian syndrome. • Hormone dependent tumors (e.g. Pituitary tumor). • Pregnancy (Category X). • Uncontrolled thyroid or adrenal dysfunction.
Adverse Drug Reactions	**>10%:** Endocrine & metabolic: Ovary enlargement (14%). **1% to 10%** Central nervous system: Headache (1%). Endocrine & metabolic: Hot flash (10%). Gastrointestinal: Abdominal distention (≤6%), abdominal distress (≤6%), bloating (≤6%), nausea (≤2%), vomiting (≤2%). Genitourinary: Breast disease (discomfort: 2%), abnormal uterine bleeding (1%) Ophthalmic: Visual disturbance (2%).

Monitoring Parameters	**Before therapy** • Serum estrogen. • Rule out primary pituitary or ovarian failure, endometriosis/endometrial carcinoma, adrenal disorders, thyroid disorders, hyperprolactinemia, and male infertility. • Pelvic exam prior to each course of therapy. • Pregnancy test prior to repeat courses. • Ovulation. • Serum triglycerides in patients with family history of hyperlipidemia and use of higher than recommended dose and/or longer duration of treatment.
Drug Interactions	***Risk X: Avoid combination:*** Ospemifene. ***Risk D: Consider therapy modification*** Fluoroestradiol F18.
Pregnancy and Lactation	**Pregnancy**: Use is contraindicated in females who are already pregnant. Potential risks to the fetus if used during pregnancy. **Lactation**: No data. Caution should be used. Clomiphene may decrease lactation.
Administration	The total daily dose should be taken at one time to maximize effectiveness. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	**Concerns related to adverse effects:** • **Hyperlipidemia**: Women with, or a family history of, hyperlipidemia may be at increased risk of hypertriglyceridemia. High doses of clomiphene or long durations of therapy may increase this risk. Pancreatitis has been reported. Pretreatment screening of triglycerides is recommended. • **Ovarian enlargement**: May be accompanied by abdominal distention or abdominal pain and generally regresses without treatment within a few days or weeks after therapy discontinuation. If ovaries are abnormally enlarged, withhold therapy until ovaries return to pretreatment size; reduce clomiphene dose and duration of future cycles. • **Ovarian hyperstimulation syndrome (OHSS):** is an ovarian enlargement case marked by increasing degree of severity, high serum sex steroids, and an accumulation of fluid in the peritoneal and pleural cavities. And in severe cases: abdominal pain, abdominal distension, weight gain, dyspnoea, oliguria, and gastrointestinal symptoms, may be complicated rarely by ovarian torsion or thromboembolic events such as pulmonary embolism, ischaemic stroke, or myocardial infarction. Stop gonadotropins in severe cases and hospitalize the patient if needed. Treatment is primarily symptomatic and includes fluid and electrolyte management, analgesics, and prevention of thromboembolic complications. Monitoring of stimulation cycles by ultrasound scans as well as estradiol measurements are recommended to identify risk factors. Transient liver function test abnormalities have been reported in association with OHSS. • **Visual disturbances**: Blurring or other visual symptoms can occur; in some cases, may be irreversible. These visual disturbances may render some activities to be more hazardous than normal (eg, operating machinery or driving). Patients with visual disturbances should discontinue therapy and receive prompt ophthalmic evaluation.

	• **Hypersensitivity reactions:** Hypersensitivity reactions including anaphylaxis and angioedema have been reported with Clomiphene use. In case of allergic reactions, discontinue therapy and appropriate symptomatic treatment initiated • **Ectopic pregnancy:** There is an increased chance of ectopic pregnancy (including tubal and ovarian sites). Multiple pregnancies, including simultaneous extrauterine and intrauterine pregnancies, have been reported. • **Ovarian cancer**: Prolonged use may increase the risk of ovarian cancer. Clomiphene should not normally be used for longer than 6 cycles (possible increased risk of ovarian cancer). • **Polycystic ovarian syndrome:** Use with caution in patients unusually sensitive to pituitary gonadotropins; a lower dose may be necessary. • **Uterine fibroids:** Use caution in patients with uterine fibroids, may cause further enlargement. • **Appropriate use**: To minimize risks, use only at the lowest effective dose for the shortest duration of therapy. • **Appropriate use**: Patients most likely to achieve success with clomiphene therapy include: patients with polycystic ovary syndrome, amenorrhea-galactorrhea syndrome, psychogenic amenorrhea, post-oral-contraceptive amenorrhea, and certain cases of secondary amenorrhea of undetermined etiology. • **Multiple births:** May result from the use of this medication; advise patients of the potential risk of multiple births before starting the treatment.
Storage	• Store between 15°C to 30°C. • Protect from light, heat, and excessive humidity. **N.B** Refer to manufacturer PIL if there are specific considerations.

Follitropin Alfa

Generic Name	Follitropin Alfa
Dosage Form/Strengths	**Powder and solvent for injection:** 75 I.U/VIAL, 150 I.U/VIAL **Solution for injection in Pre-Filled Syringe:** 150 I.U., 225 I.U., 300 I.U. **Solution for injection in prefilled pen:** 300 IU / 0.5 ml, 900 IU/ 1.5ml
Route of Administration	SC
Pharmacologic Category	Gonadotropin; Ovulation Stimulator ATC: G03GA05
Indications	Biological medicines must be prescribed and dispensed by brand name. • **Induction of ovulation** and pregnancy in oligo-anovulatory infertile women for whom the cause of infertility is functional and not due to primary ovarian failure. • **Development of multiple follicles** in ovulatory infertile women as part of Assisted Reproductive Technology (ART)(such as in vitro fertilization). • **Spermatogenesis induction:** Induction of spermatogenesis in men with azoospermia and primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure.
Dosage Regimen	**Ovulation induction** **SC:** Initial: 75 units daily for 14 days in the first cycle; dose increased according to ovarian response with increments of up to 37.5 units every 7 days (maximum dose: 300 units daily). **Multifollicular development during assisted reproductive technology** **SC** • Initiate therapy with Follitropin alfa in the early follicular phase (cycle day 2 or day 3) at a dose of 150 units daily, until sufficient follicular development is attained. • In patients whose endogenous gonadotropin levels are suppressed, initiate Follitropin alfa at a dose of 225 units daily. • Consider dose adjustments after 5 days based on the patient's response; adjust subsequent dosage every 3 to 5 days by ≤75 to 150 units additionally at each adjustment. • Maximum dose: 450 International Units per day. **Spermatogenesis induction** **SC:** After normalization of serum testosterone, administer 150 International Units subcutaneously three times a week in conjunction with hCG.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** There are no dosage adjustments necessary. **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments necessary.

Contra-indications	• Prior hypersensitivity to recombinant FSH products or one of their excipients. • High levels of FSH indicating primary testicular failure. • Uncontrolled thyroid, pituitary, or adrenal dysfunction. • Sex hormone-dependent tumors of the reproductive tract and accessory organs (breast, ovaries, prostate, uterus). • Tumors of the pituitary gland or hypothalamus. • Abnormal uterine bleeding of undetermined origin. • Ovarian cyst or enlargement of undetermined origin.
Adverse Drug Reactions	**Significant Adverse reactions** • Hypersensitivity Reactions and Anaphylaxis. • Ovarian Hyperstimulation Syndrome. • Pulmonary and Vascular Complications. • Ovarian Torsion. • Abnormal Ovarian Enlargement. • Multi-fetal Gestation and Birth. • Embryofetal Toxicity. • Ectopic Pregnancy. • Spontaneous Abortion. • Ovarian Neoplasms. • Serum testosterone levels and sperm count. **>10%** **Dermatologic**: Acne vulgaris (males: 27%). **Endocrine & metabolic:** Ovarian cyst (4% to 15%). **Gastrointestinal**: Abdominal pain (5% to 23%), enlargement of abdomen (14%) **Local**: Pain at the injection site (males: 11%; females: 5% to 6%). **Nervous system:** Headache (10% to 27%). **1% to 10%** **Dermatologic**: Seborrhea (males: 5%). **Endocrine & metaboli**c: Decreased libido (males: 3%), gynecomastia (males: 6%), intermenstrual bleeding (5%), ovarian hyperstimulation syndrome (5% to 7%). **Gastrointestinal**: Diarrhea (4%), flatulence (4% to 6%), nausea (4% to 8%). **Genitourinary**: Pelvic pain (7%). **Local**: Bruising at injection site (10%), inflammation at injection site (2% to 4%), injection site reaction (4%), swelling at injection site (3%). **Nervous system:** Fatigue (males: 10%), pain (5%).
Monitoring Parameters	• Pelvic exam, Pelvic ultrasound. • Pregnancy testing. • Serum concentrations of estradiol, gonadotropin, progesterone and/or testosterone. • Thyroid function tests (TFTs). • Ovulation. • Weight

	• Semen analysis 4 to 6 months after the beginning of treatment as part of the assessment of the response.
Drug Interactions	• Medicinal products used to stimulate ovulation (e.g. hCG, Clomiphene citrate) may potentiate the follicular response. • GnRH agonist or antagonist may increase the needed dose of Follitropin alf to induce the required ovarian effect.
Pregnancy and Lactation	**Pregnancy**: No data. No indication during pregnancy. **Lactation**: Not indicated during breast-feeding.
Administration	Administer subcutaneously in the abdomen, upper arm, or upper leg. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Pulmonary and Vascular Complications:** Serious pulmonary conditions (for example, atelectasis, acute respiratory distress syndrome and exacerbation of asthma) have been reported in women treated with gonadotropins. • **Thromboembolism**: Patients with risk factors for thromboembolic events, such as personal or family history, obesity or thrombophilia may have an increased risk of venous or arterial thromboembolic events, during or following treatment with gonadotrophins. Consider the benefit risk ratio. • **Hypersensitivity Reactions and Anaphylaxis**: If occurs, discontinue treatment and initiate appropriate therapy including supportive measures. **Abnormal Ovarian Enlargement: T**o minimize the hazards associated with this case, individualize treatment and use the lowest effective dose. Use of ultrasound monitoring of ovarian response and/or measurement of serum estradiol levels is important to minimize the risk of ovarian stimulation. • **Ovarian Hyperstimulation Syndrome OHSS:** is an ovarian enlargement case marked by increasing degree of severity, high serum sex steroids, and an accumulation of fluid in the peritoneal and pleural cavities. And in severe cases: abdominal pain, abdominal distension, weight gain, dyspnoea, oliguria, and gastrointestinal symptoms, may be complicated rarely by ovarian torsion or thromboembolic events such as pulmonary embolism, ischaemic stroke, or myocardial infarction. Stop gonadotropins in severe cases and hospitalize the patient if needed. Treatment is primarily symptomatic and includes fluid and electrolyte management, analgesics, and prevention of thromboembolic complications. Monitoring of stimulation cycles by ultrasound scans as well as estradiol measurements are recommended to identify risk factors. Transient liver function test abnormalities have been reported in association with OHSS. • **Ovarian Torsion:** Ovarian torsion has been reported after treatment with gonadotropins. Early diagnosis and immediate detorsion limit damage to the ovary due to reduced blood supply • **Multi-fetal pregnancy**: Advise the woman and her partner of the potential risk before beginning therapy. • **Congenital malformation**: The prevalence of congenital malformations after ART may be slightly higher than after spontaneous conceptions. This is thought to be due to differences in parental characteristics (e.g. maternal age, sperm characteristics) and multiple pregnancies.

	• **Ectopic Pregnancy**: Women with a history of tubal disease are at risk of ectopic pregnancy. The prevalence of ectopic pregnancy after ART was reported to be higher than in the general population. • **Spontaneous Abortion**: The risk of spontaneous abortion (miscarriage) is increased with gonadotropin products. • **Ovarian Neoplasm**: Both benign and malignant ovarian neoplasms are reported in women who have had multiple drug therapy for infertility treatment, however, causality has not been established. • **Porphyria:** Patients with porphyria or a family history of porphyria should be closely monitored during treatment with Follitropin alfa. Deterioration or a first appearance of this condition may require cessation of treatment.
Storage	• Store vials refrigerated or at room temperature between 2°C to 25°C. • Store prefilled pen in a refrigerator (2°C-8°C). Do not freeze. • Protect from light. • Following reconstitution, multidose vials may be stored under refrigeration or at room temperature for a period according to the product. **N.B** Refer to manufacturer PIL if there are specific considerations.

Human Chorionic Gonadotropin HCG

Generic Name	Human Chorionic Gonadotropin
Dosage form/strengths	**Powder and Solvent for Solution for injection:** 5000 I.U. **Lyophilized Powder:** 1500 I.U., 5000 I.U. **Solution for injection in a prefilled syringe:** 250 mcg/0.5ml (Recombinant)
Route of Administration	IM, SC.
Pharmacologic Category	Gonadotropin; Ovulation Stimulator ATC: G03GA01
Indications	Biological medicines must be prescribed and dispensed by brand name. **Ovulation induction:** In anovulatory or oligo-ovulatory women to trigger ovulation and luteinization induction after stimulation of follicle growth. **For Assisted Reproductive Technology (ART) programs** such as in vitro fertilization: triggering of final follicular maturation and luteinization after stimulation of follicle growth. **Prepubertal cryptorchidism** (undescended testes) in Pediatric population: which is not caused by anatomic obstruction. **Selected cases of hypogonadotropic hypogonadism** (hypogonadism secondary to a pituitary deficiency) in males.
Dosage Regimen	**Ovulation induction, Assisted Reproductive Technology programs** **IM**: 5000 IU to 10000 IU are administered 24 to 48 hours after the last administration of an FSH- or hMG preparation, i.e. when optimal stimulation of follicular growth is achieved. **SC**, Recombinant: 250 mcg administered 24 to 48 hours after optimal stimulation of follicular growth is achieved. **Prepubertal cryptorchidism** not due to anatomical obstruction: **IM**: 5000 units every second day for 4 injections. **IM**: Young infants: 250 IU/dose (0.17 ml of the 1500 IU vial) twice a week for five weeks. **Selected cases of hypogonadotropic hypogonadism in males.** **IM**: 500 to 1000 USP units 3 times a week for 3 weeks, followed by the same dose twice a week for 3 weeks.
Dosage Adjustment	**Dosing: Altered Kidney Function** Safety and efficacy have not been established. Use with caution. **Dosing: Hepatic Impairment** Safety and efficacy have not been established.
Contra-indications	• Hypersensitivity to active substances or any of the excipients. • Uncontrolled non-gonadal endocrinopathies (e.g. thyroid, adrenal, or pituitary disorders). • Breast, uterine, and ovarian tumors. • Abnormal (not menstrual) vaginal bleeding of unknown etiology. **N.B** Should not be used when response cannot be achieved, as in case of

	primary ovarian failure, malformations of the reproductive organs, fibroid tumors of the uterus incompatible with pregnancy. **Paediatric population and andrology**: Not to be used in case of sex hormone dependent tumors, not for the treatment of undescended testes known to be of organic origin.
Adverse Drug Reactions	**0.1-1%:** Local hypersensitivity reaction, Abdominal pain, nausea, vomiting and diarrhea, Bruising, pain, redness, swelling and itching at the injection site, oedema, Headache, Mood changes, Mild or moderate OHSS, painful breasts, ovarian cysts.
Monitoring Parameters	• Ultrasonography. • Estradiol levels. • Monitor for signs and symptoms of OHSS for at least 2 weeks following hCG administration.
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	**Pregnancy**: No human data. May cause fetal harm. Not indicated during pregnancy. **Lactation**: No human data. Not indicated during breastfeeding.
Administration	**Human chorionic gonadotropin:** **IM or SC**: Reconstitute powder with the provided solvent, dissolve completely. The final solution should be given immediately. Any unused solution should be discarded. **Recombinant chorionic gonadotropin** For SC use only; inject into the stomach area. • Use immediately after reconstitution or within ≤60 days in the refrigerator (product dependent). **Administration: Subcutaneous for Recombinant chorionic gonadotropin** • For SC use only; inject into stomach area. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Thromboembolism**: Patients with risk factors for thromboembolic events, such as personal or family history, obesity, or thrombophilia may have an increased risk of venous or arterial thromboembolic events, during or following treatment with gonadotropins. Consider the benefit-risk ratio. • **Hypersensitivity Reactions and Anaphylaxis**: If occurs, discontinue treatment and initiate appropriate therapy including supportive measures • **Ovarian hyperstimulation syndrome (OHSS):** is an ovarian enlargement case marked by an increasing degree of severity, high serum sex steroids, and an accumulation of fluid in the peritoneal and pleural cavities. In severe cases: abdominal pain, abdominal distension, weight gain, dyspnoea, oliguria, and gastrointestinal symptoms, may be complicated rarely by ovarian torsion or thromboembolic events such as pulmonary embolism, ischaemic stroke, or myocardial infarction. Stop gonadotropins in severe cases and hospitalize the patient if needed. Treatment is primarily symptomatic and includes fluid and electrolyte management, analgesics, and prevention of thromboembolic

	complications. Monitoring of stimulation cycles by ultrasound scans as well as estradiol measurements are recommended to identify risk factors. Transient liver function test abnormalities have been reported in association with OHSS. • **Multi-fetal pregnancy**: Advise the woman and her partner of the potential risk before beginning therapy. • **Congenital malformation:** The prevalence of congenital malformations after ART may be slightly higher than after spontaneous conceptions. This is thought to be due to differences in parental characteristics (e.g. maternal age, sperm characteristics) and multiple pregnancies. • **Ectopic Pregnancy:** Women with a history of tubal disease are at risk of ectopic pregnancy. The prevalence of ectopic pregnancy after ART was reported to be higher than in the general population. • **Abortion**: The risk of spontaneous abortion (miscarriage) is increased with gonadotropin products. • **Ovarian Neoplasm**: Both benign and malignant ovarian neoplasms are reported in women who have had multiple drug therapy for infertility treatment, however, causality has not been established. • **Medical examinations**: For up to ten days after administration, a pregnancy test may give a false-positive result. • **Cryptorchidism:** May induce precocious puberty in children being treated for cryptorchidism; discontinue if signs of precocious puberty occur. • **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. • **Caution:** Since androgens may cause fluid retention, HCG should be used with caution in patients with cardiac or renal disease, epilepsy, migraine or asthma
Storage	• ***Human chorionic gonadotropin*** Store at intact vials at 15°C to 30°C. Protect from light. • ***Recombinant chorionic gonadotropin Prefilled syringe:*** Before dispensing, store at 2°C to 8°C. Patients may store at 25°C for up to 30 days. Protect from light. **N.B** Refer to manufacturer PIL if there are specific considerations.

Urofollitropin

Generic Name	Urofollitropin
Dosage form/strengths	Powder and solvent for injection: 75 I.U., 150 I.U.
Route of Administration	IM. SC.
Pharmacologic Category	Gonadotropin; Ovulation Stimulator **ATC:** G03GA04
Indications	Biological medicines must be prescribed and dispensed by brand name. Therapeutic indications Sterility in women: • **Induction of ovulation in anovulation cases** (including polycystic ovarian syndrome, PCOS) in women who have been unresponsive to treatment with clomiphene citrate. • **Development of multiple follicles** in ovulatory infertile women as part of Assisted Reproductive Technology (such as in vitro fertilization).
Dosage Regimen	Biological medicines must be prescribed and dispensed by brand name. **Induction of ovulation**: • **IM. or SC:** Initial dose: 75-150 IU daily is administered within the first seven days of menstrual cycle. • **IM. or SC**: Increase dose by (37.5 to 75 IU) gradually, in order to achieve an adequate but not excessive response. • Maximum daily dosages should generally not exceed 450 IU. • Once the ideal response is obtained, an injection of hCG should be administered 24 to 48 hours after the last Urofollitropin injection. **Controlled ovarian hyperstimulation during ART:** • **SC**: 225 IU are administered daily starting on the 2nd or 3rd day of the cycle. The dose is then adjusted according to the patient's ovarian response. The treatment is continued until sufficient follicular development has been achieved. Usually achieved around the 10th day of treatment. ▪ Refer to used protocols in literature. ▪ Response is assessed by measuring the follicle size by ultrasonography and/or oestrogen levels.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** There are no dosage adjustments **Dosing: Hepatic Impairment: Adult** There are no dosage adjustments
Contra-indications	• Hypersensitivity to any of the excipients. • Ovarian enlargement or cysts not related to polycystic ovarian syndrome. • Gynaecological bleeding of unknown cause. • Ovarian, uterine, or breast carcinoma. • Uncontrolled thyroid, pituitary, or adrenal dysfunction.

	• Tumors of the hypothalamus or pituitary gland. Pregnancy. **N.B** Not to be used when an effective response cannot be achieved, for example: • Primary ovarian failure. • Malformations of sexual organs incompatible with pregnancy. • Fibroid tumours of the uterus incompatible with pregnancy.
Adverse Drug Reactions	**≥1%:** Headache, hot flashes, Ovarian Hyperstimulation Syndrome, pain, respiratory disorder, abdominal cramps, abdominal fullness or enlargement, headache and nausea
Monitoring Parameters	• Ultrasonography • Estradiol levels. • Monitor for signs and symptoms of OHSS for at least 2 weeks following administration.
Drug Interactions	• There are no known significant interactions. • It is expected that the concomitant use of clomiphene citrate may enhance the follicular response.
Pregnancy and Lactation	Not indicated during pregnancy and lactation. No human data. Avoid.
Administration	**Preparation for administration** The powder should be reconstituted immediately prior to use with the solvent provided. **Administration: Subcutaneous** Administer SC to alternating sites on the lower abdomen. The subcutaneous injection site should be alternated to prevent lipo-atrophy **Administration: IM** IM administration should be given slowly to minimize pain and leakage. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Thromboembolism**: Patients with risk factors for thromboembolic events, such as personal or family history, obesity, or thrombophilia may have an increased risk of venous or arterial thromboembolic events, during or following treatment with gonadotropins. Consider the benefit risk ratio. • **Hypersensitivity Reactions and Anaphylaxis**: If occurs, discontinue treatment and initiate appropriate therapy including supportive measures • **Ovarian Hyperstimulation Syndrome OHSS:** is an ovarian enlargement case marked by increasing degree of severity, high serum sex steroids, and an accumulation of fluid in the peritoneal and pleural cavities. And in severe cases: abdominal pain, abdominal distension, weight gain, dyspnoea, oliguria, and gastrointestinal symptoms, may be complicated rarely by ovarian torsion or thromboembolic events such as pulmonary embolism, ischaemic stroke, or myocardial infarction. Stop gonadotropins in severe cases and hospitalize the patient if needed. Treatment is primarily symptomatic and includes fluid and electrolyte management, analgesics, and prevention of thromboembolic complications. Monitoring of stimulation cycles by ultrasound scans as well as

	estradiol measurements are recommended to identify risk factors. Transient liver function test abnormalities have been reported in association with OHSS. • **Multi-fetal pregnancy**: Advise the woman and her partner of the potential risk before beginning therapy. • **Congenital malformation:** The prevalence of congenital malformations after ART may be slightly higher than after spontaneous conceptions. This is thought to be due to differences in parental characteristics (e.g. maternal age, sperm characteristics) and multiple pregnancies. • **Ectopic Pregnancy:** Women with a history of tubal disease are at risk of ectopic pregnancy. The prevalence of ectopic pregnancy after ART was reported to be higher than in the general population. • **Abortion**: The risk of spontaneous abortion (miscarriage) is increased with gonadotropin products. • **Ovarian Neoplasm**: Both benign and malignant ovarian neoplasms are reported in women who have had multiple drug therapy for infertility treatment, however, causality has not been established.
Storage	Do not store above 25°C. Protect from light. After reconstitution, immediate use is recommended. **N.B** Refer to manufacturer PIL if there are specific considerations.

Oxytocics

Carbetocin

Generic name	Carbetocin
Dosage form/strengths	Solution for I.M or slow I.V Injection: 100 mcg/ml
Route of Administration	IM, IV
Pharmacologic Category	Oxytocic Agent ATC: H01BB03
Indications	Prevention of postpartum hemorrhage by controlling uterine atony.
Dosage Regimen	**Prevention of postpartum hemorrhage:** Following vaginal delivery: IM or IV: 100 mcg (single dose only). Following cesarean section: IV: 100 mcg (single dose only). IV is to be given slowly over 1 minute, administered as soon as possible after delivery, preferably before removal of placenta.
Dosage Adjustment	**Dosing: Altered Kidney Function:** Avoid in cases of renal disease. **Dosing: Hepatic Impairment:** Avoid in cases of hepatic disease.
Contra-indications	• Hypersensitivity to Carbetocin, Oxytocin, or any component of the formulation • For labor induction or augmentation • During pregnancy or labor (i.e. at any time before the baby is born) • Serious cardiovascular disorders • Liver or kidney disease • Epilepsy • Use in children
Adverse Drug Reactions	**>10%** • Cardiovascular: Flushing (2% to 25%), hypotension (2% to 21%) • Gastrointestinal: Abdominal pain (40%), nausea (3% to 27%) • Hematologic: Anemia (23%) • Nervous system: Headache (13% to 26%), localized warm feeling (19%) • Neuromuscular & skeletal: Tremor (1% to 12%) **1% to 10%** • Cardiovascular: Chest pain (4%), tachycardia (1%) • Dermatologic: Diaphoresis (1%), pruritus (10%) • Gastrointestinal: Metallic taste (1% to 6%), vomiting (3% to 8%) • Nervous system: Anxiety, chills, dizziness (1% to 4%), pain (4%)

	• Neuromuscular & skeletal: Back pain (4%) • Respiratory: Dyspnea (1% to 10%) • Miscellaneous: Fever (9%)
Monitoring Parameters	• Blood pressure • Persistent postpartum bleeding • Heart rate
Drug Interactions	***Risk X: Avoid combination*** Bromperidol, Carboprost Tromethamine, Dinoprostone, Levoketoconazole, Misoprostol Pimozide, Sertindole ***Risk D: Consider therapy modification*** Amifostine, Domperidone, Levoketoconazole, Obinutuzumab, QT-prolonging Agents (Highest Risk)
Pregnancy and Lactation	**Pregnancy**: Use in pregnancy prior to delivery is contraindicated. **Lactation**: Exposure to the breastfeeding infant is expected to be minimal and not expected to pose significant health risks as Carbetocin in breast milk is rapidly degraded in the GI tract of a breastfeeding infant.
Administration	**Administration: IM** IM administration may also be used following vaginal delivery only. **Administration: IV** Administer undiluted as slow bolus IV injection over 1 minute. - Following vaginal delivery, administer as soon as possible after delivery of the infant, preferably before delivery of the placenta. - Following cesarean section, administer only after delivery of infant has been completed by cesarean section; may administer before or after delivery of placenta. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	**High alert medication:** A drug with high risk of causing significant patient harm when used in error. ***Concerns related to adverse effects*** • Antidiuretic effect: May produce antidiuretic effect; risk of water intoxication. • Bleeding: Persistent bleeding warrants further evaluation to rule out coagulopathy, genital tract trauma, or the presence of retained placental fragments.

	• Monitor carefully Patients that use prostaglandins concomitantly with Carbetocin (Prostaglandins may potentiate effect). • Monitor patients with eclampsia and pre-eclampsia as no data on the use of Carbetocin in patients with eclampsia. ***Disease-related concerns*** • Asthma: Use with caution in patients with asthma. • Cardiovascular disease: Use has not been studied in patients with a history of hypertension or known coagulopathy; use with extreme caution in patients with cardiovascular disease (contraindicated in serious cardiovascular disorders), especially coronary artery disease. • Migraines: Use with caution in patients with migraines. ***Other warnings/precautions*** • Appropriate use: Carbetocin induced contractions are of a longer duration than those observed with Oxytocin and are not stopped by discontinuation of therapy. Improper use during pregnancy may produce symptoms similar to those observed with Oxytocin overdose (eg, hyperstimulation of uterus with strong or prolonged contractions, tumultuous labor, uterine rupture, cervical and vaginal lacerations, postpartum hemorrhage, utero-placental hypoperfusion and variable deceleration of fetal heart rate, fetal hypoxia, hypercapnia, or death). Therapy should not be repeated if response to initial dose is inadequate; aggressive therapy with alternative agents (eg, Oxytocin) should be utilized. Monitor patients with eclampsia and pre-eclampsia closely.
Storage	• Refer to Product label. Recommendations of storage may differ. • Do not freeze. Protect from light. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Oxytocin

Generic name	Oxytocin
Dosage form/strengths	Solution for slow I.V injection or infusion: 5 I.U./ml, 10 I.U./ml Concentrate for solution for IM injection/ I.V. infusion or short infusion: 25 mg/ml (5 I.U), 50 mg/ml (10 I.U)
Route of Administration	IV, IM
Pharmacologic Category	Oxytocic Agent ATC: H01BB02
Indications	• **Prevention** and treatment of **postpartum hemorrhage after delivery of placenta.** • **Incomplete, inevitable, or missed miscarriage.** • **Induction of labour for medical reasons, Stimulation of labour in hypotonic uterine inertia.**
Dosage Regimen	**N.B**. Dosage is individualized for each patient using the lowest effective dose, determined by uterine response (ie, contractions and fetal heart rate). Protocol for dosing rate and interval should be standardized and followed to prevent errors. **Induction of labour for medical reasons, Stimulation of labour in hypotonic uterine inertia:** IV drip Infusion: initial: 1 to 4mU/min (2 to 8 drops/min of a 5 IU in 500ml solution)). It may be gradually increased at intervals of 20 min or more, until a pattern of contraction similar to that of normal labour. For prevention of postpartum uterine haemorrhage, infusion should be continued at an increased rate during the third stage of labour and for the next few hours thereafter. **In pregnancy near term**: Maximum recommended rate is 20mU/min (40 drops/min). **For earlier stages of pregnancy**: Use a more concentrated Oxytocin solution, e.g., 10 IU in 500ml. **Caesarean section**: 5 IU immediately after delivery by slow IV injection. **Prevention of postpartum uterine hemorrhage** **IV:** Usual dose: 5 IU slowly after delivery of the placenta. **IM:** 10 units after delivery of the placenta.

	Treatment of postpartum uterine hemorrhage: IV: 5 IU slowly, followed in severe cases by IV infusion of a solution containing 5 to 20 IU of Oxytocin in 500ml of a diluent, at the rate necessary to control uterine atony. **Incomplete, inevitable, or missed abortion**: 5 IU slowly iv, if necessarily followed by IV infusion at a rate of 20 to 40mU/min or higher of solution of 10U in 500ml.
Dosage Adjustment	**Dosing: Altered Kidney Function** No dosage adjustments are needed. **Dosing: Hepatic Impairment:** No dosage adjustments are needed.
Contra-indications	• Inadvisable Spontaneous Labour or vaginal delivery. • Avoid Intravenous Injection During Labour. • Prolonged use in uterine inertia. • Fetal Distress (Discontinue Immediately If This Occurs). • Hypertonic Uterine Contractions (Discontinue Immediately If This Occurs). • Severe cardiovascular disease. • Severe preeclamptic toxaemia. • Significant cephalopelvic disproportion. • Fragility or overdistension of the uterus. • Predisposition to amniotic fluid embolism (foetal death in utero, retroplacentar hematoma)
Adverse Drug Reactions	**Frequency not defined** **Cardiovascular**: Cardiac arrhythmia, hypertensive crisis, subarachnoid hemorrhage, ventricular premature contractions **Endocrine & metabolic**: Water intoxication (severe water intoxication with seizure and coma is associated with a slow oxytocin infusion over 24 hours). **Gastrointestinal**: Nausea, vomiting **Genitourinary**: Postpartum hemorrhage, uterine rupture **Hematologic & oncologic**: Pelvic hematoma **Hypersensitivity**: Anaphylaxis
Monitoring Parameters	• Fluid intake and output during administration (due to antidiuretic effect). • Maternal blood pressure. • In Induction of Labor: Continuous monitoring of fetal heart rate and uterine motility.
Drug Interactions	***Risk X: Avoid combination*** Carboprost Tromethamine, Gemeprost, Levoketoconazole, Pimozide, Sertindole. ***Risk D: Consider therapy modification*** Dinoprostone, Domperidone, Misoprostol, QT-prolonging Agents (Highest Risk).

Pregnancy and Lactation	**Pregnancy**: Small amounts of exogenous Oxytocin are expected to reach the fetal circulation. When used as indicated, teratogenic effects would not be expected. Nonteratogenic adverse reactions are reported in the neonate as well as the mother. **Lactation**: Oxytocin is not expected to cause harmful effects in the newborn because it passes into the alimentary tract where it undergoes rapid inactivation. Endogenous Oxytocin mediates milk ejection. Administration of exogenous Oxytocin may negatively impact breastfeeding. However, available studies have inconsistent results.
Administration	**Administration: IM** Postpartum uterine bleeding: IM administration may be used when IV access is not available. **Administration: IV** **Induction or augmentation of labor:** IV administration requires the use of an infusion pump that allows minute-to-minute adjustments. Direct IM or IV injection should be avoided. **Incomplete or inevitable abortion:** Administer by IV infusion. **Postpartum uterine bleeding:** Administer by IV or IM. IM administration may be used when IV access is not available. **Rate of Administration** IV push is not recommended as it's associated with cardiovascular collapse. Slow IV injections (5 or 10 units over 1 minute) are preferred for patients without cardiovascular risk factors; very slow injections (>5 minutes) are preferred for patients with cardiovascular risk factors. **Preparation for Administration** Compatible with NS solution or D5W. For drip infusion: Oxytocin added to 500-1000 ml of a physiological electrolyte solution (NS or 5% Dextrose). **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hazardous agent** (NIOSH 2016 [group 3]): Due to Developmental toxicity – third trimester. • **Antidiuretic effect**: Oxytocin may produce an intrinsic antidiuretic effect. Avoid large infusion volumes and restrict fluid intake by mouth (risk of hyponatraemia and water-intoxication).

	• **Cardiovascular effects**: Tachycardia, bradycardia or QT interval prolongation has been observed after oxytocin administration. Therefore, it should be administered with caution in patients with conditions such as congenital or documented acquired QT prolongation. • **Rapid intravenous injection**: may transiently reduce blood pressure. • **Uterine hyperstimulation** -usually with excessive doses—may cause fetal distress, asphyxia, and death, or may lead to hypertonicity, tetanic contractions, soft-tissue damage or uterine rupture. Overdose Placental abruption and amniotic fluid embolism reported on overdose. • **Appropriate use:** Abortion: For the adjunctive management of abortion in the first trimester, curettage is generally considered primary therapy. Oxytocin infusion in second trimester abortion will often be effective; however, other therapy may be required. • **Trained personnel:** IV preparations should be administered by adequately trained individuals familiar with its use and able to identify complications; continuous observation is necessary for all patients. • **Risk of postpartum disseminated intravascular coagulation:** The pharmacological labour induction itself and not a particular agent is linked rarely to such a risk. Risk factors include being 35 years of age or over, complications during pregnancy and gestational age more than 40 weeks. In these women, Oxytocin or any other alternative drug should be used with care, and the practitioner should be alerted by signs of DIC (fibrinolysis).
Storage	Store between 2-8°C. To be used immediately afer dilution. Protect from light. **N.B** Refer to manufacturer PIL if there are specific considerations.

Methylergometrine

Generic name	Methylergometrine
Dosage form/strengths	Solution for I.M or slow I.V Injection: 0.2 mg/ml Tablets: 0.125 mg
Route of Administration	IM, IV, Oral
Pharmacologic Category	Ergot Derivative ATC: G02AB01
Indications	**Postpartum hemorrhage**: Following delivery of the placenta, for management of uterine atony, hemorrhage and sub-involution of the uterus. For control of uterine hemorrhage in labor following delivery of the anterior shoulder.
Dosage Regimen	**Postpartum hemorrhage:** **Oral:** 0.2 mg 3 to 4 times daily for up to 7 days. **Maximum Dosage Limits:** 0.8 mg/day oral for up to 7 days. **IM:** 0.2 mg after delivery of anterior shoulder, after delivery of placenta, or during puerperium; may be repeated every 2 to 4 hours as needed. **IV:** 0.2 mg, administered slowly over a period of no less than 60 seconds **Note:** This drug should not be administered I.V. routinely because of the possibility of inducing sudden hypertensive and cerebrovascular accidents. IV should be administered slowly over at least 1 minute.
Dosage Adjustment	**Dosing: Altered Kidney Function: Adult** No dosage adjustment available; use with caution. **Dosing: Hepatic Impairment: Adult** No dosage adjustment available; use with caution.
Contra-indications	• Hypersensitivity to methylergonovine or any component of the formulation. • Hypertension. • Toxemia. • Pregnancy.
Adverse Drug Reactions	**Frequency not defined.** **Cardiovascular**: bradycardia, cerebrovascular accident, chest pain, hypertension, hypotension, local thrombophlebitis, myocardial infarction, palpitations, paresthesia, tachycardia. **Central nervous system**: Dizziness, hallucination, headache, seizure

	Dermatologic: Diaphoresis, skin rash **Endocrine & metabolic**: Water intoxication **Gastrointestinal**: Abdominal pain, diarrhea, nausea, unpleasant taste, vomiting **Genitourinary**: Hematuria **Hypersensitivity**: Anaphylaxis **Neuromuscular & skeletal**: Leg cramps **Otic**: Tinnitus **Respiratory**: Dyspnea, nasal congestion
Monitoring Parameters	• Blood pressure • Heart rate
Drug Interactions	***Risk X: Avoid combination*** Alpha-/Beta-Agonists, Alpha1-Agonists, Bromocriptine, CYP3A4 Inhibitors (Strong), Delavirdine, Dihydroergotamine, Erythromycin (Systemic), Fexinidazole, Fosamprenavir, Fusidic Acid (Systemic), Lenacapavir, Letermovir, Lisuride, Lorcaserin, Methysergide, Nefazodone, Roxithromycin, Serotonin 5-HT1D Receptor Agonists (Triptans), Tipranavir. ***Risk D: Consider therapy modification*** Nitroglycerin.
Pregnancy and Lactation	**Pregnancy**: Use is contraindicated during pregnancy. **Lactation**: Methylergonovine maleate may be administered orally for a maximum of 1 week postpartum to control uterine bleeding. Mothers should not breast-feed during treatment with Methergine and at least 12 hours after administration of the last dose. Recommended dosage is 1 tablet (0.2 mg) 3 or 4 times daily. At this dosage level a small quantity of drug appears in mothers' milk. Caution should be exercised when methylergonovine maleate is administered to a nursing woman.
Administration	**Administration: IV, IM, Oral** **IV**: Administer slowly over a period of no less than 60 seconds with careful monitoring of blood pressure. Do not routinely administer IV because of the possibility of inducing sudden hypertension and cerebrovascular accidents; only consider IV administration during life-threatening situations. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	• **Hazardous agent** (NIOSH 2016 [group 3]): due to Developmental toxicity – third trimester ***Concerns related to adverse effects*** • Coronary artery disease: Patients with coronary artery disease (CAD) or risk factors for CAD may be more likely to develop myocardial ischemia and infarction. ***Disease-related concerns***

	• Labor: Use with caution in the second stage of labor. • Sepsis: Use with caution in patients with sepsis. • Vascular disease: Use with caution in patients with obliterative vascular disease. ***Other warnings/precautions*** • IV administration: Not for routine IV administration due to risk of inducing sudden hypertensive and cerebrovascular accidents. IV administration should only be considered during life-threatening situations given slowly over a period of no less than 60 seconds with careful monitoring of blood pressure.
Storage	• Injection: 2-8 °C, Protect from light. Use a carton to protect contents until used. • Tablets: Store below 30°C. **N.B** Refer to manufacturer PIL if there are specific considerations**.**

Posterior pituitary hormone analogue

Desmopressin Acetate

Generic Name	Desmopressin Acetate
Dosage form/strengths	Solution for injection: 4mcg/ml. Tablets: 0.1 mg, 0.2 mg. Sublingual Tablet: 240 mcg. Oral lyophilisate Tablet: 60 mcg, 120 mcg. Nasal Spray: 0.1 mg/ml.
Route of Administration	*Subcutaneous, Intramuscular, Intravenous, Oral, Sublingual, Nasal*
Pharmacologic Category	Antihemophilic Agent; Hemostatic Agent; Hormone, Posterior Pituitary; Vasopressin Analog, Synthetic. ATC: H01BA02.
Indications	***Injection*** Diagnosis and treatment of cranial diabetes insipidus. Mild to moderate hemophilia or von Willebrand's disease undergoing surgery or following trauma to increase Factor VIII: C and Factor VIII: Ag. To establish renal concentration capacity. To treat a headache resulting from a lumbar puncture. To test for fibrinolytic response. ***Oral*** Vasopressin sensitive cranial diabetes insipidus. Post-hypophysectomy polyuria/polydipsia Oral lyophilisate Tablet Vasopressin sensitive cranial diabetes insipidus. Post-hypophysectomy polyuria/polydipsia ***Sublingual*** Vasopressin sensitive cranial diabetes insipidus. Primary nocturnal enuresis. Post-hypophysectomy polyuria/polydipsia. ***Intranasal*** Diagnosis and treatment of vasopressin-sensitive cranial diabetes insipidus. Treatment of Nocturia. Establishing renal concentration capacity.
Dosage Regimen	**Injection:** • ***Treatment of Cranial Diabetes Insipidus:*** Adults: IM, SC, IV: The usual dose is 1 to 4 mcg given once daily.

Children and infants: IM, SC, IV: Doses from 0.4 mcg may be used.

- ***Diagnosis of Cranial Diabetes Insipidus:***

Adults and children: IM, SC: 2 mcg.

- ***Mild to moderate hemophilia and von Willebrand's disease:***

Adults, children and infants**:** IV infusion: 0.3-0.4 mcg per kg body weight. Up to 20 mcg.

Further doses may be administered at 12 hourly intervals so long as cover is required.

- ***Renal Function Testing***

Adults and children: IM, SC: 2 mcg, it is expected to achieve urine concentrations above 700mOsm/kg in the period of 5 to 9 Hours following this dose. It is recommended that the bladder should be emptied at the time of administration.

Infants: 0.4 mcg, a urine concentration of 600mOsm/kg should be achieved in the 5 hours period following this dose. The fluid intake at the two meals following the administration should be restricted to 50% of the ordinary intake to avoid water overload.

- ***Post Lumbar Puncture Headache***

Adult: IM, SC: 4mcg. which may be repeated 24 hours later if necessary. Alternatively, a prophylactic dose of 4 micrograms can be given immediately prior to the lumbar puncture and repeated 24 hours later

- ***Fibrinolytic Response Testing***

Adults and children: IV infusion: 0.4 mcg per kilogram body weight. A sample of venous blood should be taken 20 minutes after the infusion. In patients with a normal response the sample should show fibrinolytic activity of euglobulin clot precipitate on fibrin plates of at least 240mm^2.

Oral tablet

- ***Treatment of Diabetes Insipidus***

Adults and children: sublingual: initially: 0.1mg three times daily. Adjust dose according to patient's response.

Total daily oral dose normally lies in the range of 0.2 to 1.2mg.

Usual maintenance dose is 0.1mg to 0.2mg three times daily.

- ***Post-hypophysectomy polyuria/polydipsia***

The dose should be controlled by measurement of urine osmolality.

Oral lyophilisate Tablet, Sublingual

- ***Treatment of diabetes insipidus***

Adults and children: initially: 60 mcg three times daily. Adjust dose according to patient's response.

Total daily dose normally lies in the range of 120 mcg to 720 mcg.

Usual maintenance dose is 60 mcg - 120 mcg three times daily.

- ***Post-hypophysectomy polyuria/polydipsia***

The dose should be controlled by measurement of urine osmolality.

- ***Primary nocturnal enuresis***

Children (from 5 years of age) and adults (up to 65 years of age): Initially: 120 mcg at bedtime. If no sufficient effectiveness, the dose may be increased up to 240 mcg.

Fluid restriction should be observed.

Duration of treatment may be up to 3 months. Reassess the need for treatment continuation by means of a period of at least 1 week without Desmopressin sublingual tablets. If inadequate clinical effect within 4 weeks following appropriate dose titration, discontinue the medication.

Nasal Spray

- ***Treatment of Nocturia in multiple sclerosis patients***

Patients up to 65 years age: Intranasal: 1-2 sprays (10 to 20 mcg) once at bedtime. If a dose of two sprays is required, this should be as one spray into each nostril.

- ***Treatment of Diabetes Insipidus***

Adults and children: Average maintenance dose is 1-2 sprays (10 to 20 mcg) once or twice daily. If a dose of two sprays is required, this should be as one spray into each nostril.

- ***Diagnosis of Diabetes Insipidus***

Adults and children: Intranasal: Two sprays (20 micrograms).

Failure to elaborate a concentrated urine after water deprivation, followed by the ability to do so after the administration of Desmopressin confirms the diagnosis of cranial diabetes insipidus. Failure to concentrate after the administration suggests nephrogenic diabetes insipidus.

- ***Renal Function Testing***

Adults: Two sprays into each nostril (a total of 40 mcg)

Children: (1-15 years): One spray into each nostril (a total of 20 mcg).

	Infants (to 1 year): One spray (10 mcg). Adults and children with normal renal function can be expected to achieve concentrations above 700mOsm/kg in the period of 5-9 hours following administration. It is recommended that the bladder should be emptied at the time of administration. In normal infants a urine concentration of 600mOsm/kg should be achieved in the 5-hour period following the administration. The fluid intake at the two meals following the administration should be restricted to 50% of the ordinary intake in order to avoid water overload.
Dosage Adjustment	**Dosing: Renal Impairment** CrCl ≥50 mL/minute: No dosage adjustment necessary. Caution. CrCl <50 mL/minute: Use is contraindicated. **Dosing: Hepatic Impairment** There are no dosage adjustments needed.
Contra-indications	• Known hypersensitivity to desmopressin acetate or to any of the excipients. • Moderate to severe renal impairment defined as a creatinine clearance below 50 mL/min. • Hyponatremia or a history of hyponatremia. • Known or suspected syndrome of inappropriate antidiuretic hormone (SIADH) secretion. • Polydipsia. Concomitant use with loop diuretics or systemic or inhaled glucocorticoids. • During illnesses that can cause fluid or electrolyte imbalance. • Heart failure or uncontrolled hypertension. • Desmopressin should not be prescribed to patients over the age of 65 for the treatment of nocturia associated with multiple sclerosis.
Adverse Drug Reactions	**>10%** • Endocrine & metabolic: Hyponatremia (intranasal: 2% to 12%; sublingual: 3% to 4%). • Gastrointestinal: Xerostomia (sublingual: 12% to 14%). **1% to 10%** • Cardiovascular: Hypertension (2% to 3%). • Gastrointestinal: Abdominal pain (2%), nausea (2%). • Nervous system: Asthenia (2%), chills (2%), dizziness (intranasal, sublingual: 2% to 3%), headache (intranasal, oral, sublingual: 2% to 5%).

	• Neuromuscular & skeletal: Back pain (1% to 2%). • Ophthalmic: Abnormal lacrimation (2%), conjunctivitis (2%), ocular edema (2%). • Respiratory: Bronchitis (2%), epistaxis (2% to 3%), nasal congestion (3%), nasal discomfort (6%), nasopharyngitis (4%), nostril pain (2%), rhinitis (3% to 8%), sneezing (2% to 3%).
Monitoring Parameters	***General monitoring parameters*** • Blood Pressure. • Risk for Hyponatremia: Serum sodium within 1 week and approximately 1 month after starting therapy and periodically during treatment. More frequently monitor serum sodium in patients 65 years of age and older and in patients at increased risk of hyponatremia. • Monitor for symptoms of hypersensitivity. • Renal function (particularly in elderly). • Fluid intake, body weight. ***Diabetes Insipidus*** **Before treatment and Intermittently during treatment** Assess urine volume and osmolality. ***Hemophilia A*** **Before treatment** • Verify that factor VIII coagulant activity levels are >5%. • In certain clinical situations, it may be justified to try Desmopressin in patients with factor VIII levels between 2% to 5%; however, these patients should be carefully monitored. • Exclude the presence of factor VIII autoantibodies. • Assess aPTT before treatment. ***Von Willebrand's Disease (Type I)*** **Before treatment** • Verify that factor VIII coagulant activity levels are >5%. • Exclude severe von Willebrand's disease (Type I) and presence of an abnormal molecular form of factor VIII antigen. **During treatment** Assess bleeding time, factor VIII coagulant activity, ristocetin cofactor activity, and von Willebrand antigen to ensure that adequate levels are being achieved.

Drug Interactions	***Risk X: Avoid combination*** Corticosteroids (Orally Inhaled) (Systemic), Loop Diuretics, Tolvaptan.
Pregnancy and Lactation	**Pregnancy** Studies have not identified a drug associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. In addition, in vitro studies with human placenta demonstrate poor placental transfer of Desmopressin. Caution. Monitoring blood pressure is recommended. **Lactation** Amounts of Desmopressin that may be transferred to the child are considerably less than the amounts required to influence diuresis.
Administration	**Administration: IV** **IV push: Central diabetes insipidus:** Administer as direct injection; dilution is not required. **IV infusion; Hemophilia A, von Willebrand disease and Fibrinolytic Response Testing:** Administer over 15 to 30 minutes, half to one hour prior to procedure. Diluent Required: 0.9% sodium chloride. Infants and children ≤10 kg: 10 mL; Children >10 kg and adolescents and adults: 50 mL. **Administration: Intranasal** Ensure that nasal passages are intact, clean, and free of obstruction prior to administration. Nasal pump spray: The spray bottle should be held upright and the protective cap removed from the spray nozzle. The spray should be primed when using it for the first time. This is done by spraying several actuations in the air until a consistent, fine spray is seen. If the pump is not used for ≥1 week, re-prime by pressing down on the pump once. **Administration: Oral** **Oral:** Tablets: May administer with or without food. Food may reduce the intensity and duration of the antidiuretic effect. **Diabetes insipidus:** Fluid restriction should be observed. **Primary nocturnal enuresis:** Fluid intake should be limited a minimum of 1 hour prior to dose until at least 8 hours after administration. **Administration Sublingual**

	Nocturia: Tablet should be kept under the tongue until completely dissolved without water. Administer 1 hour prior to bedtime. Fluid intake should be limited a minimum of 1 hour prior to dose until at least 8 hours after administration. **N.B** Refer to manufacturer PIL if there are specific considerations**.**
Warnings/ Precautions	**Fluid intake** Precautions to prevent fluid overload must be taken in following conditions - Conditions characterized by fluid and/or electrolyte imbalance e.g. renal function and/or cardiovascular disease. - Patients at risk for increased intracranial pressure. Fluid intake restriction: When Desmopressin is used for the treatment of nocturia associated with multiple sclerosis, fluid intake must be limited to a minimum from 1 hour before using the spray at bedtime until the next morning and in any case for a minimum of 8 hours after administration. Fluid accumulation can be readily monitored by weighing the patient or by determining plasma sodium or osmolality. If there is a gradual increase of the body weight, decrease of serum sodium to 130 mmol/L or plasma osmolality to below 270mOsm/kg, the fluid intake must be reduced drastically and the administration interrupted. **Hyponatremia** • In the event of signs or symptoms of water retention and/or hyponatremia (headache, nausea/vomiting, weight gain, and, in severe cases, convulsions) treatment should be interrupted until the patient has fully recovered. When restarting treatment strict fluid restriction should be enforced. Elderly patients and patients with serum sodium levels in the lower range of normal may have an increased risk of hyponatremia. • More frequent monitoring of serum sodium, must be taken in case of concomitant treatment with drugs which are known to induce SIADH e.g. tricyclic antidepressants, selective serotonin reuptake inhibitors, chlorpromazine and carbamazepine, NSAIDs and Loperamide as they may cause an additive antidiuretic effect leading to an increased risk of water retention and/or hyponatremia. **Intranasal** Consider alternative Route of Administration if changes in the nasal mucosa (scarring, edema) occur leading to unreliable absorption. Discontinue in

	patients with concurrent nasal conditions that may increase systemic absorption of desmopressin (e.g., acute or chronic rhinitis, severe atrophic rhinitis, nasal blockage, nasal mucosal atrophy, recent nasal surgery); may resume desmopressin when conditions resolve. **Injection** During infusion of Injection for hemostatic use, it is recommended that the patient's blood pressure is monitored continuously. **Cardiovascular disease** Injection and high-dose intranasal desmopressin may cause a slight increase or transient decrease in blood pressure, and a compensatory increase in heart rate. Use with caution in patients with coronary artery insufficiency and/or hypertensive cardiovascular disease.
Storage	Tablet: Store at 20°C to 25°C. Avoid excessive heat. Protect from light and moisture Solution for injection: Do not store above 25°C. Keep the container tightly closed. Nasal spray: Store at 20°C to 25°C. Keep nasal spray in an upright position. Sublingual: Store in the original blister in order to protect from moisture. Store in the original package. Keep the bottle tightly closed. **N.B** Refer to manufacturer PIL if there are specific considerations.

Thyroid Hormone

Levothyroxine

Generic Name	Levothyroxine
Dosage form/strengths	Tablet 25mcg, 50mcg, 100mcg
Route of Administration	Oral.
Pharmacologic Category	Thyroid Product. ATC: H03AA01.
Indications	• Control of hypothyroidism, congenital hypothyroidism in infants, acquired hypothyroidism in children and juvenile myxoedema. • Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) Suppression: As an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer.
Dosage Regimen	**Adult dosing:** • **Hypothyroidism** **Patients under 50 years age** Initially 50 to 100 mcg daily. Adjust at 3-4week intervals by 50 mcg until normal metabolism is maintained. The final daily dose may be up to 100 to 200 mcg. **Patients over 50 years age** - *Without cardiac disease*: Initially 25-50 mcg daily. The daily dose may be increased by 50 mcg at intervals of every 3-4 weeks, until clinically stable. The final daily dose may be up to 50 to 200 mcg. - *With cardiac disease:* 25 mcg daily or 50 mcg on alternate days is more suitable. In this condition, the daily dosage may be increased by 25 mcg increments at intervals of every 4 weeks, until clinically stable. The final daily dose may be up to 50 to 200 mcg. • **TSH Suppression in Well-differentiated Thyroid Cancer** Initial: 1.6 to 2 mcg/kg/day immediately post surgery; adjust dose as needed in 6 weeks based on TSH suppression goals. • **Pregnancy Pre-existing Hypothyroidism:** For patients with serum TSH above the normal specific range, increase the dose by 12.5 to 25 mcg/day and monitor and adjust every 4 weeks. Reduce dose to pre-pregnancy immediately after delivery. • **Pregnancy New Onset Hypothyroidism**: Normalize thyroid function as rapidly as possible. - Moderate to severe symptoms of hypothyroidism: initially 1.6 mcg per kg body weight per day. - Mild hypothyroidism (TSH < 10 IU per liter): initially 1 mcg per kg body

	weight per day. - Evaluate serum TSH every 4 weeks and adjust dosage until a serum TSH is within the normal trimester specific rang **Pediatric Dosing** - The maintenance dose is generally 100 to 150 micrograms per m^2 body surface area. - The dose for children depends on their age, weight and the condition being treated. - Regular monitoring using serum TSH levels, as in adults, is required to make sure he/she gets the right dose. • **Congenital hypothyroidism in infants** Initially, 10 to 15 mcg per kg BW per day for the first 3 months. Thereafter, dose should be adjusted according to the clinical findings and thyroid hormone and TSH values. • **Acquired hypothyroidism in children** Initially 12.5- 50 mcg per day. The dose should be increased gradually every 2 to 4 weeks according to the clinical findings and thyroid hormone and TSH values until the full replacement dose is reached. Infants should be given the total daily dose at least half an hour before the first meal of the day. • **Juvenile myxoedema in children** Initially 25 mcg daily. The daily dose may be increased by 25 mcg at intervals of every 2 - 4 weeks, until mild symptoms of hyperthyroidism are seen. The dose will then be reduced slightly. **Note**: In children under 5 years of age, the administration of whole tablets is not recommended. It is also not recommended that tablets are crushed and dispersed in water or other liquids, due to limited solubility which could lead to dosing inaccuracy. In this age group it is preferable to administer an approved oral solution of levothyroxine. • **TSH suppression in well differentiated thyroid cancer (papillary)** Oral: Highly individualized; doses >2 mcg/kg/day may be needed to suppress TSH to <0.1 milliunits/L in high-risk tumors; for lower-risk tumors, initial TSH suppression needed may be lower.
Dosage Adjustment	**Dosing: Renal Impairment** There are no dosage adjustments needed. **Dosing: Hepatic Impairment** There are no dosage adjustments needed. **Dosing: Obesity: Adult** Individual T_4 requirements correlate better with lean body weight than total body weight; weight-based dosing may overestimate initial replacement doses in obese patients; as such, dosing in obesity must be individualized.

	Dosing: Adjustment for Toxicity: Adult: Cardiac symptoms (onset or worsening): Reduce dosage or withhold therapy for 7 days and then resume therapy at reduced dosage.
Contra-indications	• Uncorrected adrenal insufficiency. • Subclinical thyrotoxicosis. • Untreated pituitary insufficiency. • Acute myocardial infarction, acute myocarditis, or acute pancarditis.
Adverse Drug Reactions	**Adverse Reactions (Significant): Considerations** **Cardiovascular effects** • Potentially life-threatening cardiovascular effects may occur with levothyroxine. The effects commonly result from overtreatment but can also occur with initiation of levothyroxine, especially in patients with severe hypothyroidism or in patients with a history of cardiovascular disease or arrhythmias. • Effects may include palpitations, tachycardia, exercise intolerance, dyspnea on exertion, widened pulse pressure, and atrial fibrillation; cardiac overload and arrhythmias have been described in infants. **Frequency not defined** • Cardiovascular: Angina pectoris, cardiac arrhythmia, cardiac failure, flushing, increased blood pressure, increased pulse, tachycardia. • Dermatologic: Alopecia, diaphoresis, skin rash. • Endocrine & metabolic: menstrual disease, weight loss. • Gastrointestinal: Abdominal cramps, diarrhea, increased appetite, vomiting. • Genitourinary: Reduced fertility. • Hepatic: Increased liver enzymes. • Nervous system: Anxiety, emotional lability, fatigue, headache, heat intolerance, hyperactive behavior, idiopathic intracranial hypertension (children), insomnia, irritability, myasthenia, nervousness. • Neuromuscular & skeletal: Craniosynostosis (infants; dose-related [i.e., overtreatment]), decreased bone mineral density (dose- and duration-related), muscle spasm, slipped capital femoral epiphysis (children), tremor. • Respiratory: Dyspnea. • Miscellaneous: Fever.
Monitoring Parameters	• Monitor closely for under/overtreatment. • TSH, total or free T4 at 2 and 4 weeks after starting treatment or adjusting dose, then periodically. • Heart rate, Blood pressure • New/worsened cardiac symptoms (e.g., chest pain, palpitations, edema), • Bone mineral density (particularly with long-term use in postmenopausal patients).
Drug	***Risk X: Avoid combination***

Interactions	Sodium Iodide I131. ***Risk D: Consider therapy modification*** Bile Acid Sequestrants, Calcium Polystyrene Sulfonate, Calcium Salts, Iron Preparations, Lanthanum, Magnesium Salts, Multivitamins/Minerals (with ADEK, Folate, Iron), Orlistat, Patiromer, Polaprezinc, Raloxifene, Sevelamer, Sodium Polystyrene Sulfonate, Sucroferric Oxyhydroxide.
Pregnancy and Lactation	• Levothyroxine is the preferred treatment of maternal hypothyroidism; other agents should not be used during pregnancy. • Due to alterations of endogenous maternal thyroid hormones, the dose taken should be increased as soon as pregnancy is confirmed. Close monitoring of pregnant patients is recommended. • The World Health Organization considers levothyroxine to be compatible with breastfeeding. Use of levothyroxine is a preferred agent as thyroid replacement therapy during lactation.
Administration	• Administer consistently in the morning on an empty stomach, at least 30 to 60 minutes before food or caffeine-containing liquids. • Alternatively, may consistently administer at night 3 to 4 hours after the last meal. Do not administer within 4 hours of calcium- or iron-containing products or bile acid sequestrants. **N.B** Refer to manufacturer PIL if there are specific considerations.
Warnings/ Precautions	**Disease-related concerns** • **Adrenal insufficiency**: Use with caution in patients with adrenal insufficiency; symptoms may be exaggerated or aggravated. Treatment with glucocorticoids should precede levothyroxine therapy in patients with adrenal insufficiency. Use is contraindicated in patients with uncorrected adrenal insufficiency. • **Benign thyroid nodules**: Appropriate use: Routine use of T_4 for TSH suppression is not recommended in patients with benign thyroid nodules. Treatment should never be fully suppressive (TSH <0.1 milliunits/L). - Use of T_4 may be considered in association with iodine supplementation only in young patients residing in iodine-deficient areas with small thyroid nodules and no evidence of functional autonomy. - Use should be avoided in postmenopausal patients, older adults, patients with cardiovascular disease, osteoporosis, large thyroid nodules or long-standing goiters, or low-normal TSH levels. • **Cardiovascular disease**: May require lower initial dose and conservative dose titration. Refer to the dosing section. • **Diabetes**: Use with caution in patients with diabetes mellitus (may worsen glycemic control) and diabetes insipidus (thyroid hormone increases glomerular filtration rate and downregulates aquaporin channels in the renal tubules, which could affect urinary output). • **Osteoporosis**: Thyroid hormone overreplacement may result in increased bone resorption and decreased bone mineral density, especially in postmenopausal patients; use the lowest effective dose to achieve therapy goals. • **Subacute thyroiditis**: Transient and mild hypothyroidism during the

	recovery phase of subacute thyroiditis often can be managed without treatment; levothyroxine therapy may be required in patients with overt and clinical hypothyroidism. **Special populations** • **Older adults**: Use with caution; May require lower initial dose and conservative dose titration. Refer to dosing. **Dosage form specific issues** • **Product interchangeability**: Switching between different levothyroxine products may result in variations in the administered dose and altered TSH values and is not generally recommended; if formulations are changed, close monitoring of TSH is recommended. Pediatric patients with congenital hypothyroidism may be more sensitive to changes in formulation. **Other warnings/precautions** • **Hypersensitivity**: Patients with reported hypersensitivity to levothyroxine may be managed with dose reductions and slow titration, by switching formulations or products.
Storage	• Store between 15°C and 30°C. • Protect from heat, light, and moisture. **N.B** Refer to manufacturer PIL if there are specific considerations.

Sources

- The Egyptian Drug Authority database for drugs and pharmaceutical products, available on the official website, https://www.edaegypt.gov.eg/
- The United Kingdom, drug authority, Medicines and Healthcare Products Regulatory Agency (MHRA) https://products.mhra.gov.uk/
- The United States Food and Drug Administration, the federal agency of the Department of Health and Human Services, www.accessdata.fda.gov
- Lexicomp Online, reference handbooks, and desktop software, as a source of drugs full monographs, by Wolters Kluwer Health, www.lexicomp.com
- The searchable version of the complete Anatomical Therapeutic Classification (ATC) index with Defined Daily Dose (DDDs), by the World Health Organization (WHO), www.whocc.no/atc_ddd_index/

Alphabetical List of content