Direct Healthcare Professional Communication

December 2022

Cefotaxime – Reminder of Precautions to Minimize Severe Hypersensitivity Reactions and Life-threatening Adverse Events

Dear Healthcare Professional,

The General Administration for Pharmaceutical Vigilance of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to inform you of the following:

Summary:

- EPVC has received recently some reports of hypersensitivity, anaphylaxis and life-threatening adverse events which may be linked with Cefotaxime improper administration or administration without doing sensitivity testing.
- As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with cefotaxime must be discontinued immediately and adequate emergency measures must be initiated.
- Before therapy with cefotaxime is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cefotaxime sodium, cephalosporins, penicillin, or other drugs.
- Cefotaxime is strictly contraindicated in subjects with history of immediate-type hypersensitivity to cephalosporins. This product should be given with caution to patients with type 1 hypersensitivity reactions to penicillin. Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs.
- EPVC is reminding Health care professionals (HCPs) with the current precautions; and method of administration for Cefotaxime antibiotic.
- EPVC is reminding HCPs to follow international guidelines for rational and safe use of antibiotics.

Background on the safety concern & recommendations for Health care professionals:

- **<u>Regarding the method of administration take in your consideration the following precautions:</u>**
  1. Before beginning treatment, it should be established whether the patient has a history of hypersensitivity reactions to Cefotaxime, to other cephalosporins or to any other type of beta-lactam agent (penicillins, monobactams and carbapenems).
     Caution should be used if cefotaxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents and penicillin-sensitive subjects.
  2. Cefotaxime is strictly contraindicated in subjects with history of immediate-type hypersensitivity to cephalosporins

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3. Before beginning treatment, Sensitivity test should be done; to Cefotaxime, to other cephalosporins or to any other type of beta-lactam agent, however take in your consideration the followings:
   – The Sensitivity test should be done before each Cefotaxime dose.
   – The negative result for cefotaxime sensitivity test doesn't guarantee negative hypersensitivity reaction as the cefotaxime sensitivity test has low sensitivity, however it is useful as it exclude those who develop positive sensitivity test result.
   – It is recommended to be administrated in hospital settings for emergency measures.
4. An anaphylactic reaction (also called anaphylaxis) is a sudden, severe allergic reaction triggered by the body's disease-fighting system (immune system). It is a potentially fatal condition that must be treated immediately. The following are symptoms of anaphylaxis which require immediate medical care:
   - A feeling of warmth in the face (flare) that may include redness.
   - Itching, redness, and swelling of areas of the skin (urticaria).
   - Swelling of the eyes, lips, face, mouth, tongue, or throat.
   - Difficulty breathing, speaking or swallowing.
   - High-pitched whistling sounds when breathing in, often when exhaling (wheezing).
   - Feeling dizzy, lightheaded or fainting.
   - Abdominal pain or cramps.
   - Vomiting or diarrhea.
5. A potentially life-threatening arrhythmia may occur to patients who receive a rapid (less than 60 seconds) bolus injection of cefotaxime through a central venous catheter. Therefore, cefotaxime should only be administered as instructed.
6. Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.
7. Cefotaxime constituted with lidocaine must never be used in infants under 30 months of age.
8. **Sensitivity testing Method:**
   The diagnosis of betalactam allergic reaction can be determined using the standardized diagnostic procedures of the European Network for Drug Allergy (ENDA). Intradermal testing is done by the injection of 0.02–0.05 ml of the hapten solution, raising a small bleb that is marked initially. It should be performed on the volar forearm, although other skin areas can be used.
   Particular caution and testing, starting with 1000-fold dilutions of the stock reagents, should be used in patients who have experienced severe or life-threatening reactions such as anaphylaxis.
   Skin testing with betalactams should be performed under controlled conditions with emergency treatment available, as systemic side-effects may occur up to 10% of the patients being tested for drug allergy

9. **For IV injection:**

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- Cefotaxime Sodium injection 500 mg is dissolved in at least 2 ml water for injections and 1g in at least 4 ml and subsequently injected directly into the vein over 3 to 5 minutes or after clamping of the infusion tube into distal end of the tube.
- For brief infusion 2g of cefotaxime Sodium injection is dissolved in 100ml isotonic sodium chloride or glucose solution and IV infused over 50 to 60 minutes (another compatible infusion solution could be used).

10. **For IM injection:**
    - Cefotaxime Sodium injection 500 mg is dissolved in at least 2 ml water for injections and 1g in at least 4 ml respectively.
    - Intramuscular injections should be injected deep into the gluteal muscle.
    - It is recommended that no more than 4 ml be injected unilaterally. If the daily dose exceeds 2g cefotaxime or it is injected more than twice daily, the IV route is recommended.
    - As the solvent used is lidocaine, the resulting solution should never be administered intravenously
11. For pre-operative prophylaxis of surgical site infections, cefotaxime should be administered 30-90 minutes prior to surgery.

References

EMC https://www.medicines.org.uk/emc/product/8750/smpc

FDA https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/050547s071,050596s042lbl.pdf

Blackwell Munksgaard Journal https://ferrerpharma.com.au/wp-content/uploads/2018/01/Article-2.-Diagnosis-of-immediate-allergic-reactions-to-beta-lactam-antibiotics.pdf

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

Name: General Administration for Pharmaceutical Vigilance

Email: pv.followup@edaegypt.gov.eg

Online reporting: https://primaryreporting.who-umc.org/EG
QR Code:

Hotline: 15301

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