Direct Healthcare Professional Communication

December 2022

Ceftriaxone – 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 Ceftriaxone 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 ceftriaxone must be discontinued immediately and adequate emergency measures must be initiated.
- Before therapy with ceftriaxone is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to ceftriaxone, cephalosporins, penicillins, or other drugs
- Ceftriaxone 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 Ceftriaxone 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 severe hypersensitivity reactions to ceftriaxone, to other cephalosporins or to any other type of beta-lactam agent (penicillin, monobactams and carbapenems).
   Caution should be used if ceftriaxone is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.
2. Intramuscular administration should be considered when the intravenous route is not possible or less appropriate for the patient. For doses greater than 2 g intravenous administration should be used.

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3. Before beginning treatment, Sensitivity test should be done; to ceftriaxone, 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 Ceftriaxone dose.
   – The negative result for Ceftriaxone sensitivity test doesn't guarantee negative hypersensitivity reaction as the ceftriaxone sensitivity test has low sensitivity, however it is useful as it exclude those develop positive sensitivity test result.
   – It is recommended to be administrated in hospital settings for emergency measures.
4. This product may contain inactive ingredients, which can cause allergic reactions or other problems.
5. 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.
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. **Sensitivity testing Method:**
   The diagnosis of beta-lactam 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 beta-lactams 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
8. **For IV injection:**
   - Ceftriaxone can be administered by intravenous infusion over at least 30 minutes (preferred route) or by slow intravenous injection over 5 minutes (preferably in larger veins).
   - 1 g ceftriaxone is dissolved in 10 ml of water for injections. The injection should be administered over 5 minutes, directly into the vein or via the tubing of an intravenous infusion

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- For doses greater than 2 g intravenous administration should be used.
- For neonates, intravenous doses should be given over 60 minutes to reduce the potential risk of bilirubin encephalopathy.
- In infants and children up to 12 years of age, Doses of 50mg/kg or over should be given by slow intravenous infusion over at least 30 minutes. Doses greater than 80mg/kg body weight should be avoided because of the increased risk of biliary precipitates.

9. **For IM injection:**
   - Intramuscular administration (IM): should be considered when the intravenous route is not possible or less appropriate for the patient.
   - 1g ceftriaxone should be dissolved in 3.5ml of 1% Lidocaine Injection. The solution should be administered by deep intramuscular injection.
   - Intramuscular injections should be injected well within the bulk of a relatively large muscle and not more than 1 g should be injected at one site.
   - Dosages greater than 1g should be divided and injected at more than one site.
   - As the solvent used is lidocaine, the resulting solution should never be administered intravenously
10. Diluents containing **calcium**, (e.g. Ringer's solution or Hartmann's solution), should not be used to reconstitute ceftriaxone vials or to further dilute a reconstituted vial for intravenous administration because a precipitate can form.
    Precipitation of ceftriaxone-calcium can also occur when ceftriaxone is mixed with calcium-containing solutions in the same IV administration line. Therefore, ceftriaxone and calcium-containing solutions must not be mixed or administered simultaneously.
11. For pre-operative prophylaxis of surgical site infections, ceftriaxone should be administered 30-90 minutes prior to surgery.
12. Ceftriaxone is contraindicated in premature neonates up to a postmenstrual age of 41 weeks (gestational age+chronological age) and full-term neonates at risk of developing bilirubin encephalopathy.

References

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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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