EGYPTIAN DRUG AUTHORITY

هيئة الدواء المصرية

The Egyptian Pharmaceutical Vigilance center

مركز اليقظة الصيدلية المصري

IN THIS ISSUE

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EPVC Mission

Pharmaceutical Vigilance administration is the way through which the processes for authorizing, regulating, monitoring and evaluating the safety of any pharmaceutical product or medical device take place, in addition to disseminating any safety information for public health programs, healthcare professionals, and the Egyptian citizen.

The Pharmaceutical vigilance administration is an integral part of the Central Administration of Pharmaceutical Care that works on the enhancement of the pharmaceutical services to guarantee safe and effective use of medications in Egypt, under the patronage of the Egyptian Drug Authority.

Newsletter

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Local Alert: Sub-standardized and Falsified (SF) Product

Egyptian Drug Authority Alert Regarding Xoraxon (Ceftriaxone) 1 g Vial Counterfeit

The Egyptian Drug Authority (EDA) through the Central Administration of Operations announced an alert regarding the presence of counterfeited Xoraxon 1 gm vials antibiotic packs in the market. EDA started to quarantine the known counterfeited packs with batch numbers 212584-212160-212588-211801-212126 and any other packs with different specifications than the original one.

EDA distributed and published circular with all data concerning the counterfeited product and how to differentiate between the original and counterfeit packs on EDA's website *(Click here)*.

The Egyptian Pharmaceutical Vigilance Center is encouraging public to report any detected packs through *(Click here)*.

ORIGINAL

COUNTERFEIT

The Egyptian Pharmaceutical Vigilance center
مركز اليقظة الصيدلية المصري

Interaction reminder: Bone marrow suppression with methotrexate and trimethoprim or trimethoprim with sulfamethoxazole

Severe bone marrow suppression has been reported in patients on methotrexate who have received trimethoprim or trimethoprim with sulfamethoxazole. Some cases have been fatal.

Trimethoprim and trimethoprim with sulfamethoxazole should be avoided in patients taking methotrexate. If this drug combination cannot be avoided, warn patients about the symptoms of bone marrow suppression. Advise them to seek immediate medical attention should these symptoms occur.

Background:

Trimethoprim and co-trimoxazole have additive bone marrow suppression effects with methotrexate

Trimethoprim or co-trimoxazole (trimethoprim with sulfamethoxazole), when used with methotrexate, increase the risk of bone marrow suppression (also known as myelosuppression).1 The evidence for this interaction consists of case reports of severe bone marrow suppression in patients on methotrexate who have received trimethoprim or co-trimoxazole. Some cases have been fatal.2

Although the mechanism for this interaction is not fully understood, trimethoprim can have additive antifolate effects and when used with methotrexate, lead to increased myelosuppression.3 Additionally, sulfamethoxazole (in co-trimoxazole) may displace methotrexate from protein binding sites and compete with the renal transport of methotrexate, leading to increased free methotrexate levels.4

It is unclear whether increases in free methotrexate levels also occurs with prophylactic doses of co-trimoxazole. Some studies suggest that prophylactic doses might not delay methotrexate clearance. Monitoring of full blood count is recommended.

Recommendations for Healthcare Professionals:

In patients taking methotrexate, avoid trimethoprim and co-trimoxazole. In circumstances where the combination cannot be avoided, healthcare professionals should consider the following:

1. Seek specialist advice for safely prescribing trimethoprim or co-trimoxazole antimicrobial therapy for patients on methotrexate in primary care.
2. Educate patients to seek immediate medical attention if they notice symptoms of bone marrow suppression. These symptoms may include:
   * Mouth ulcers, sore throat, fever or chills
   * New or non-resolving infections
   * Bruising or bleeding more easily than usual
   * Anaemia symptoms such as shortness of breath, dizziness and pallor.
1. Monitor full blood count. If any abnormalities arise, consider this interaction as a possible cause and seek urgent specialist advice. More frequent monitoring of other laboratory tests such as renal function may be required3 – refer to local clinical guidelines and the advice from relevant specialists.
2. Ensure regular folate supplement is continued or started.

References: *Medsafe (Click here)*

Case Report from Alexandria: Anaphylactic shock, Vomiting, and Fainting following Ceftriaxone and Ketorolac Administration due to Missing Product Information and Drug Contraindication

The regional center in Alexandria received a case of a 10 years old female patient who weighing 25 kg, suffering from tonsillitis associated with fever. She was administered intramuscularly firstly Ketorolac tromethamine, then after 10 min 1 g Ceftriaxone without making a skin hypersensitivity test (in her home) on 15/1/2022. After administration of Ceftriaxone and Ketorolac tromethamine by several minutes, the patient experienced an anaphylactic reaction including severe vomiting till fainting.

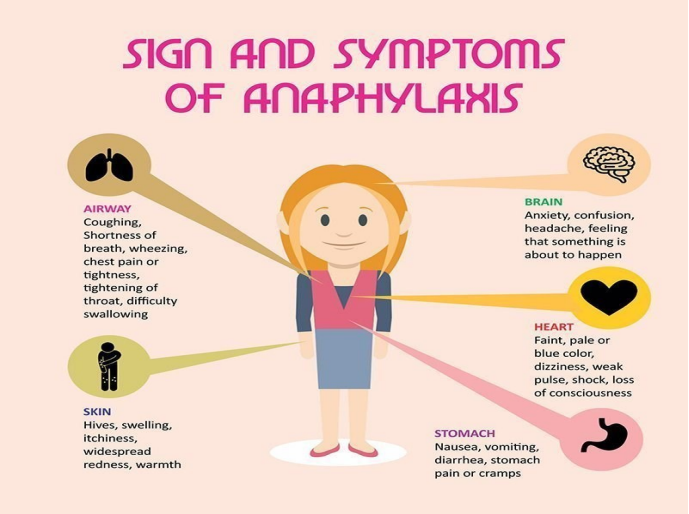
Ketorolac tromethamine was used off-label, prescribed for fever, while it should be prescribed in post-operative pain and it is contraindicated for children less than 16 years old according to the Egyptian leaflet. Both Ceftriaxone 1 g and Ketorolac tromethamine were prescribed by the physician, without informing the patient's relatives to carry out a skin hypersensitivity test for Ceftriaxone before its administration (Product information not provided to the patient).

The patient did not suffer from any other diseases in her medical history

Background:

Ceftriaxone[1]: is a third-generation cephalosporin antibiotic that is used to treat many kinds of bacterial infections, including severe or life-threatening forms such as E. coli, pneumonia, or meningitis. Ceftriaxone is also used to prevent infection in people having certain types of surgery.

Ketorolac tromethamine[2]: is a nonsteroidal anti-inflammatory drug (NSAID) used for the short-term treatment of moderate to severe pain in adults. It is usually used before or after medical procedures or after surgery. It works by blocking your body's production of prostaglandins that cause inflammation. This effect helps to decrease swelling, pain, or fever.



Anaphylaxis[3]: is an acute life-threatening type I hypersensitivity reaction. The signs and symptoms of anaphylaxis typically develop within a few minutes of exposure to the offending agent but can occur as late as 72 hours post-exposure. Anaphylaxis is usually but not always mediated by an immunologic mechanism that results from the sudden systemic release of mediators such as histamine, leukotrienes, prostaglandins from mast cells, and basophils. Anaphylaxis most commonly affects the cutaneous, respiratory, cardiovascular, and gastrointestinal systems. The skin or mucous membranes are involved in 80-90% of cases.

Case Report from Alexandria: Anaphylactic shock, Vomiting, and Fainting following Ceftriaxone and Ketorolac Administration due to Missed Product Information and Drug Contraindication Continued

Labeled information:

Cephalosporins are among the most commonly used antibiotics, and their use is increasing over time. Several types of hypersensitivity reactions have been reported with cephalosporins, ranging from mild, delayed-onset cutaneous reactions to life-threatening anaphylaxis in patients with immunoglobulin E (IgE)-mediated allergy [4]

Hypersensitivity (less than 0.1%): Anaphylaxis/ anaphylactic-type reactions (e.g., bronchospasms), serum sickness

Hypersensitive reactions that occur immediately within the first hour of administration are characterized by urticaria, angioedema, rhinitis, and anaphylactic shock. The incidence of hypersensitivity reactions with cephalosporins is 1-3%. The most common manifestations are the development of maculopapular rash, urticaria, and anaphylaxis. In cases where there is no previous exposure to ceftriaxone or other cephalosporins, an IgE-dependent mechanism could be a possibility for such an occurrence. [5]

Drugs that Interfere with Drug Sensitivity Testing:

⇒ Certain drugs can suppress antibiotic susceptibility testing. They are H1- antihistamines, imipramine, phenothiazines, dopamine, clonidine, montelukast, and corticosteroids.

⇒ Also, the presence of certain diseases like eczema, urticaria, and infectious diseases like leprosy can result in a false positive test

Management of Hypersensitivity Reactions:

Mild-moderate hypersensitivity reactions are managed by antihistamines and corticosteroids. Severe hypersensitivity reactions like anaphylactic shock are usually managed by oxygen therapy, intravenous fluids, vasopressors such as corticosteroids, adrenaline, and chlorpheniramine

Ketorolac tromethamine:

Commonly reported side effects of ketorolac to include: abdominal pain, gastrointestinal pain, dyspepsia, headache, increased liver enzymes, increased serum alanine aminotransferase, increased serum aspartate aminotransferase, and nausea. Other side effects include diarrhea, dizziness, drowsiness, and edema.

A very serious allergic reaction to this drug is rare. However, some serious allergic reactions, including fever, swollen lymph nodes, rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing, need immediate medical attention [6]

Ketorolac tromethamine Injection route Solution):

Ketorolac tromethamine is indicated for short-term use only (up to 5 days total duration, including IV/ IM and oral therapy in adults) for the management of moderately severe acute pain that requires analgesia at the opioid level. Ketorolac tromethamine oral tablets are indicated only as continuation treatment following IV or IM dosing of ketorolac tromethamine if necessary.

Contraindications of Ketorolac tromethamine: [6]

Not for use in pediatric patients and not indicated for minor or chronic pain.

Case Report from Alexandria: Anaphylactic shock, Vomiting, and Fainting following Ceftriaxone and Ketorolac Administration due to Missed Product Information and Drug Contraindication Continued

Recommendations for Healthcare Professionals

1. Before the beginning of Ceftriaxone treatment, a skin hypersensitivity test should be established whether the patient has a history of severe hypersensitivity reactions to any type of beta-lactam agents or not.
2. In case a lidocaine solution is used as a solvent, Ceftriaxone solutions must only be used for intramuscular injection, the lidocaine solution should never be administered intravenously.
3. Diluents containing calcium, (e.g., Ringer's solution, 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 (must not be mixed or administered simultaneously with calcium-containing solutions including total parenteral nutrition).
4. If a patient develops anemia while on Ceftriaxone, the diagnosis of cephalosporin-associated anemia should be considered and Ceftriaxone discontinued until the etiology is determined.
5. During prolonged treatment with Ceftriaxone complete blood count should be performed at regular intervals.
6. If anaphylaxis is suspected, rapidly assess airway, breathing, circulation, and mentation as rapidly as possible, as cardiac arrest and death can occur within several minutes.
7. The lowest effective dose of Ketorolac tromethamine should be administered for the shortest duration (not exceeding 5 days) consistent with individual patient treatment goals.
8. Ketorolac tromethamine should not be used in pediatrics under 16 years old according to Egyptian leaflet.
9. Ketorolac tromethamine has to be used for management of moderately severe acute pain that requires analgesia at the opioid level and is not indicated to be used for mild or long-term painful conditions.

Disclaimer: The method of case handling depends on the evaluation of the treating physician according to individual patient's need.

References:

1. *Drugs.com* (Click here)
2. *Webmed* (Click here)
3. *Journal of Gandaki* (Click here)
4. *UpToDate* (Click here)
5. *Journal of Gandaki* (Click here)
6. *Drugs.com* (Click here)

The Egyptian Pharmaceutical Vigilance Center (EPVC) in Awareness Session "Nurses for Future"

The Egyptian Pharmaceutical Vigilance Center (EPVC) is delighted to continue its awareness among the healthcare professionals by participating in awareness sessions titled" Nurses for Future".

This training is held by Roche in collaboration with the training department in Health Insurance Organization (HIO), aiming to increase the pharmaceutical vigilance awareness among healthcare professionals and strengthening pharmaceutical vigilance practice, and therefore patient safety, throughout Egypt. This is a part of an educational program held to provide the nurses in the Health Insurance sector with several sessions regarding different topics to empower them to provide the best care for patients.

The training sessions included lectures on Pharmacovigilance basics, scope, reporting methods, and medical device safety vigilance.

The training was held over 4 days in the presence of around 140 oncology nurses trainees in a live training sessions as following:

-Two sessions on 19/March and 20/March in Alexandria

-Two sessions on 21/March and 22/March in Mansoura

This comes in accordance with EPVC's believe that nursing is an essential partner in patient safety, as it is the closest healthcare professional attached to the patients.



Middle Medical District Pharmacovigilance Training Held at the Ophthalmologic Hospital

The Egyptian Pharmaceutical Vigilance Center (EPVC) is pleased to continue a series of training events in various health directorates in collaboration with the pharmaceutical sector.

During March, the Middle medical district pharmacovigilance focal points Training was held at the Ophthalmologic Hospital for 4 days.

This event is within the scope of our objective of increasing pharmaceutical vigilance awareness among healthcare professionals and strengthening pharmaceutical vigilance practice, and therefore patient safety, throughout Egypt.

The trainings were launched in order to meet the problems of COVID-19 and the limitations of in-person events, as well as to adhere to the Egyptian Ministry of Health and Population (MoHP) recommendation to maintain physical distance.

One report counts

A call for reporting

What is Pharmacovigilance

Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug- related problem.

What is the Egyptian Pharmaceutical Vigilance Center?

With the increasing demand for patient's safety which is becoming more stringent, . The Egyptian Pharmaceutical Vigilance Center was established to be responsible for the safety monitoring of the pharmaceutical products throughout its lifecycle and it is the regulatory authority regarding Pharmacovigilance and its applications .

EPVC monitors the safety of all types of pharmaceutical products, including human medicines, biological products, supplements, cosmetics, veterinary medicines, medical devices, Biocides and pesticides

Please remember that you can report safety information of medicines to EPVC using the following communication information:

Communication information

The Egyptian Drug Authority (EDA)
Pharmaceutical Care Administration
The Egyptian Pharmaceutical Vigilance Center (EPVC)

The Egyptian Pharmaceutical Vigilance center
مركز اليقظة الصيدلية المصري

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Reporting link: www.edaegypt.gov.eg
https://sites.google.com/view/epvc-reporting/healthcare-professional-public-adverse-drug-event-reporting/reporting-other-adverse-drug-event-cases

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