EGYPTIAN DRUG AUTHORITY

هيئة الدواء المصرية

The Egyptian Pharmaceutical Vigilance center

مركز اليقظة الصيدلية المصري

EPVC

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 Omnevora IM Solution Counterfeit

The Egyptian Drug Authority (EDA) through the Central Administration of Operations announced an alert regarding presence of counterfeited Omnevora IM Solution for injection in the market with batch number 211640. EDA is quarantining the counterfeited batches.

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

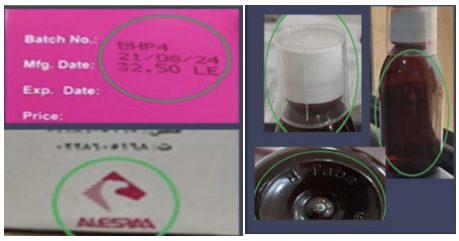
Egyptian Drug Authority Alert Regarding Pedicort Forte Oral Solution Counterfeit

The Egyptian Drug Authority (EDA) through the Central Administration of Operations announced an alert regarding presence of counterfeited Pedicort Forte Oral Solution in the market. EDA is quarantining the counterfeited batches with numbers BCJ6 - BHP4.

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

Direct Healthcare Professional Communication (DHPC): Tixagevimab + Cilgavimab – Updated Dosage Recommendations for Pre-exposure Prophylaxis

EPVC in agreement with marketing authorization holders (MAH) of products containing Tixagevimab + Cilgavimab would like to inform you of the following:

Summary:

* The Evusheld (Tixagevimab and Cilgavimab) dosage recommendations have been updated.
* Specifically, the initial dose for pre-exposure prophylaxis has been increased from 300 mg administered intramuscularly (IM) to 600 mg IM (300 mg of tixagevimab and 300 mg of cilgavimab), and guidance on repeat dosing has also been provided.1
* These updated dose recommendations are based on the totality of the available data including clinical pharmacology, pharmacokinetics, antiviral activity and clinical trial data.
* Tixagevimab + Cilgavimab has been studied for the prophylaxis of COVID-19 at the 300 mg dose2. The clinical safety of 600 mg dose for prophylaxis use is supported by safety data from TACKLE in patients with mild to moderate COVID-19..

Background on safety concern:

The updated dosing recommendations are as follows[1]:

Initial Dosing:

The initial dosage of Evusheld is 600 mg (300 mg of tixagevimab and 300 mg of cilgavimab) administered as two separate, 3.0 mL sequential intramuscular (IM) injections.

Dosing for Individuals Who Initially Received 150 mg of Tixagevimab and 150 mg of Cilgavimab:

- Individuals who initially received 150 mg tixagevimab and 150 mg cilgavimab should receive 300 mg tixagevimab and 300 mg cilgavimab as soon as possible.
- A minimum dosing interval of 3 months should be maintained between administration of the initial (150 mg tixagevimab and 150 mg cilgavimab) dose and second (300 mg tixagevimab and 300 mg cilgavimab) dose.

Repeat Dosing:

For individuals who require repeat dosing for ongoing prevention of COVID-19, subsequent doses of 600 mg (300 mg tixagevimab and 300 mg cilgavimab) should be given once every 6 months.

Healthcare Provider Action:

Each carton of Evusheld contains two vials (one vial of 150 mg/1.5 mL tixagevimab and one vial of 150 mg/1.5 mL cilgavimab); therefore, you will need 2 cartons for a 600 mg dose.

Please note the product preparation of a 600 mg (300 mg tixagevimab and 300 mg cilgavimab) dose as shown in Table 1.1

Healthcare providers should refer to the and stay abreast of any changes to the label implemented by local Health Authorities.

Direct Healthcare Professional Communication (DHPC): Tixagevimab + Cilgavimab – Updated Dosage Recommendations for Pre-exposure Prophylaxis Continued

Table 1. Initial Dosing of 300 mg of Tixagevimab and 300 mg of Cilgavimab

Dose Tixagevimab & Cilgavimab 600 mg (2 cartoons)	Antibody dose	Number of vials needed	Volume to withdraw from vials
	Tixagevimab 300 mg	2 vials	3 mL * (1.5 ml from each vial into the same syringe)
	Cilgavimab 300 mg	2 vials	3 mL * (1.5 ml from each vial into the same syringe)

*Each carton of EVUSHELD contains one vial of tixagevimab 150 mg/1.5 mL and one vial of cilgavimab 150 mg/1.5 mL. The 300 mg of tixagevimab and 300 mg of cilgavimab doses are to be administered as separate, consecutive intramuscular injections. Withdraw the 3 mL of tixagevimab solution and 3 mL of cilgavimab solution into TWO separate syringes. Each vial has overfill to enable withdrawal of 1.5 ml from each vial. **Any leftover product should be discarded.**

References: *FDA (Click here)*

Case Report from Alexandria: Gadoteric Acid - Two Cases of Cardiac Arrest Following Administration

The regional center in Alexandria received the first ICSR concerning a 71-year-old male patient who was admitted to the medical diagnostic imaging center to perform an MRI prostate, and experienced cardiac arrest once injected intravenously with the Gadoteric Acid as a contrast diagnostic agent. The patient was managed with CPR for about 30 minutes, then return of spontaneous circulation (ROSC) occurred and the patient was admitted to CCU immediately on endotracheal intubation and adrenaline infusion was given to the patient until the blood pressure improved.

Next day, the patient was mechanically ventilated and on Nitroglycerin infusion.

Brain and lung CT scans were carried out that showed the following:

- Bilateral basal ganglia attenuation like ischemia
- Subcortical arteriosclerosis leukoencephalopathy with few small bilateral cerebral ischemic foci.
- Right lung lower lobe area of consolidation

Several lab investigations were performed including:

Serum creatinine, Urea, Sodium, Potassium.

A sputum culture was carried out showing MRSA.

The patient was given the following treatments at the ICU:

Enoxaparin sodium 40 mg once daily, Atorvastatin 40 mg once daily, Ipratropium bromide nebulizer three times daily, Vitamin B once daily, Glucose 5% 5 cc/hour, Acetylsalicylic acid 75 mg once daily, hydrocortisone 100 mg twice daily, Cerebrolysin twice daily, Citicoline once daily and Linezolid 300 mg twice daily

The patient had medical history of hypertension, diabetes, IHD (CABG), tetracycline hypersensitivity and underwent stent placement surgeries.

The second ICSR concerned A 66-year-old woman with breast cancer who was admitted to the hospital following a cardiac arrest after being given 10 ml Gadoteric Acid to perform an MRI scan on the breast, where the patient was anesthetized by giving her 25 mg Ketamine, 20 mg Propofol, 2 mg Midazolam, and 20 mg Lidocaine prior to the MRI due to claustrophobia. The patient had a slowing heartbeat right after the examination was finished. She was promptly removed from the MRI machine and given 0.3 mg of atropine twice. The pulseless state was confirmed, and immediate restoration to the supine position was done with chest compression and an Ambu bag mask was immediately initiated. In addition, Adrenaline 1 mg was given intravenously where the pulse started to be improved and reached 120 beats/ min, B.P: 70/40 mmHg then the patient was referred to the ICU, where she arrested and resumed back sinus rhythm after one cycle of CPR, then the case was managed by the hospital.

The patient was in a deep coma (with a consciousness level of 3/15) and suffered from severe hypotension and convulsions. Also, the patient experienced abnormalities in her brain as a result of decreased oxygen owing to cardiac arrest, as well as elevated liver enzymes and metabolic acidosis.

All ADRs were serious life-threatening resulting in the patient's hospitalization.

The patient was given concomitantly 0.4 mg Atro-

Case Report from Alexandria: Gadoteric Acid - Two Cases of Cardiac Arrest Following Administration Continued

pine and 100 mg Hydrocortisone. There was a drug interaction between the administered Ketamine and Midazolam that might contribute to the incidence of cardiac arrest.

The patient underwent an MRI on 6th June 2022 and was given an Gadodiamide and had never had any of these adverse effects before.

The patient took eight sessions of Paclitaxel in her medical history.

The patient has no allergy history or any drug hypersensitivity in her medical history

Background:

Gadoteric Acid : [1] is a gadolinium-based contrast agent indicated for intravenous use with magnetic resonance imaging (MRI) in the brain (intracranial), spine, and associated tissues in adult and pediatric patients (including term neonates) to detect and visualize areas with disruption of the blood-brain barrier (BBB) and/or abnormal vascularity.

Gadolinium-based contrast agent:[2] Gadolinium-Based Contrast Agents (GBCA) are intravenous drugs used in diagnostic imaging procedures to enhance the quality of magnetic resonance imaging (MRI) or magnetic resonance angiography (MRA).

***Cardiac arrest*:** [3] Cardiac arrest occurs when the heart suddenly and unexpectedly stops pumping. If this happens, blood stops flowing to the brain and other vital organs.

Drug interaction: [4] A drug interaction is a reaction between two (or more) drugs or between a drug and a food, beverage, or supplement. Taking a drug while having certain medical conditions can also cause a drug interaction

Reported adverse effects for Gadoteric Acid : [5, 6]

Hypersensitivity reactions:

Uncommon: hypersensitivity, anaphylactic reaction, anaphylactoid reaction

In hypersensitivity reactions, the reactions most frequently observed are skin reactions, which can be localized, extended, or generalized.

These reactions occur most often immediately (during the injection or within one hour after the start of injection) or sometimes delayed (one hour to several days after injection), presenting as skin reactions in this case.

Immediate reactions include one or more effects, which appear simultaneously or sequentially, which are most often cutaneous, respiratory, gastrointestinal, articular, and/or cardiovascular reactions. Each sign may be a warning sign of a starting shock and leads very rarely to death.

Cardiac disorders:

Very rare: cardiac arrest, bradycardia, tachycardia, arrhythmia, palpitations

Vascular disorders:

Very rare: hypotension, hypertension, vasodilatation, pallor

Respiratory, thoracic, and mediastinal disorders:

Very rare: respiratory arrest, pulmonary edema, bronchospasm, laryngospasm, pharyngeal edema, dyspnea, nasal congestion, sneezing, cough, dry throat

Drug interactions:

Coadministration of ketamine with other central nervous systems (CNS) depressants e.g. (Midazolam), including alcohol, may result in profound sedation, respiratory depression, coma, and death.

Case Report from Alexandria: Gadoteric Acid - Two Cases of Cardiac Arrest Following Administration Continued

Recommendations for Healthcare Professionals :

1. Hypersensitivity: Anaphylactoid/anaphylactic reactions with cardiovascular, respiratory, or cutaneous manifestations, ranging from mild to severe, including death, have uncommonly occurred. Monitor patients closely for the need for the emergency cardiorespiratory support.
2. The risk for Nephrogenic Systemic Fibrosis (NSF) appears highest among patients with: Chronic, severe kidney disease (GFR < 30 mL/min/1.73m2), or Acute kidney injury.
3. Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (for example, age > 60 years, hypertension, or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing (5.1). elimination of GBCAs. Higher than recommended dosing or repeat dosing appear to increase the risk.
4. Do not use Gadoteric acid by the intrathecal route. Take care to maintain strictly intravenous injection: extravasation may result in local intolerance reactions, requiring the usual local care.
5. The usual precaution measures for MRI examination should be taken, such as exclusion of patients with pacemakers, ferromagnetic vascular clips, infusion pumps, nerve stimulators, cochlear implants, or suspected intracorporal metallic foreign bodies, particularly in the eye.
6. As the renal clearance of gadoteric acid may be impaired in the elderly, it is particularly important to screen patients aged 65 years and older for renal dysfunction.
7. In patients with severe cardiovascular disease, gadoteric acid should only be administrated after careful risk-benefit assessment because only limited data are available so far.
8. Nausea and vomiting are known possible undesirable effects when using MRI contrast agents. The patient should therefore refrain from eating for 2 hours prior to the investigation.

References:

1. *FDA (Click here)*
2. *FDA (Click here)*
3. *NIH (Click here)*
4. *FDA (Click here)*
5. *EMA (Click here)*
6. *EMC (Click here)*

Vaccines Pharmacovigilance Training in East Medical District - Alexandria

As part of the Egyptian Pharmaceutical Vigilance Center's (EPVC) vision and mission to promote pharmacovigilance and the culture of reporting side effects among healthcare professionals to encourage the safe and effective use of vaccines available on the Egyptian market, 24 pharmacists from the East Medical District participated in a training on Vaccine Pharmacovigilance.

The training includes a presentation on the fundamentals of Vaccine Pharmacovigilance, its importance, how to report adverse events following immunization, and other safety data relevant to the various types of vaccinations.

Egyptian Pharmaceutical Vigilance Center EPVC Recognition for El-Agamy Medical District

Egyptian Pharmaceutical Vigilance Center expresses sincere gratitude to El-Agamy Medical District for its efforts in promoting pharmacovigilance and spreading the culture of reporting side effects among healthcare professionals to encourage the safe and effective use of various pharmaceutical products.

Together for Safe Medicine Initiative Progress

Through the support of Egyptian Drug Authority (EDA), EPVC offered free invitations to participating pharmacists from the first three waves of the "Together for Safe Medicine" initiative to attend the workshop on "combating antimicrobial resistance." Twenty pharmacists attended the workshop, and four of them submitted a report on the proper use of antibiotics, dosing, administration, and rational use of them, as well as how to apply pharmacovigilance.

The participating pharmacist of the initiative made activities linked between international events such as Med safety week, and World Antibiotic Awareness Week and their role in applying, practicing and spreading the science of Pharmacovigilance. The Egyptian pharmacovigilance center is Extremely thankful to all participating pharmacists in 3rd wave of the Initiative for their important role in increasing the ADRs reporting rate as they had sent 644 adverse drug reaction reports to the Pharmacovigilance national database starting from 20 September 2022 till now. Here are some photos for 3rd wave pharmacists' activities .

Egyptian Pharmaceutical Vigilance Center (EPVC) Decentralization Trainings for Raising Reporting Awareness

EDA - EPVC expresses its heartfelt appreciation and gratitude to the Specialized Medical Centers (SMCegy) for their participation in the Decentralization program. We especially thank the most cooperative hospitals: Qena Cancer Center, Nasser Institute, and Damanhur Cancer Center. We appreciate and are grateful to the Specialized Medical Centers' pharmaceutical administration for their effort and wish them continued success.

EPVC Tips On Pharmacovigilance

Importance of Reporting Suspected Side Effects

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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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