EGYPTIAN DRUG AUTHORITY

هيئة الدواء المصرية

IN THIS ISSUE

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EPVC

The Egyptian Pharmaceutical Vigilance center

مركـــز اليـــقظة الصـــيدلية المـــصري

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 Unictam 1500 mg Vial Counterfeit

The Egyptian Drug Authority (EDA) through the Central Administration of Operations announced an alert regarding the presence of counterfeited Unictam 1500 mg vials antibiotic packs in the market. EDA started to quarantine the known counterfeited packs with batch number 211891 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

High-dose methotrexate (MTX-HD): Reminder of General Measures to Prevent the Nephrotoxicity Risk

High-dose methotrexate (doses ≥ 500 mg/m²) indicated for the treatment of hematological malignancies and osteosarcomas presents a risk of nephrotoxicity (acute renal failure). This risk is accentuated in the event of an overdose, by delayed elimination. Therefore; EPVC is reminding healthcare professionals of the general principles of prevention.

Before initiation of treatment with MTX-HD and before each dose

* **Evaluation of the patient's kidney function**

  Before each administration of MTX-HD, it is essential to check the patient's renal function (in addition to the minimum verification of CBC, platelet count, liver function, albuminemia).

  If the patient has impaired renal function before initiation of treatment and of old age, methotrexate should be used with caution and an adjustment of the dose of methotrexate should be considered.

  Refer to the SPCs of the MTX use at high doses.

* **Consideration of concomitant nephrotoxic treatments or treatments interfering with the elimination of MTX-HD**

  All of the drug interactions of methotrexate should generally be taken into account before initiating treatment.

  Refer to the SPCs of MTX used at high doses and to the Thesaurus for drug interactions.

  The main drugs likely to interfere with renal function and increase the toxicity of methotrexate are detailed below according to the level of constraint of their association with MTX:

  ⇒ **Contraindication** : acetylsalicylic acid (at analgesic, antipyretic or anti-inflammatory doses), trimethoprim (alone or combined with sulfamethoxazole), probenecid.

  ⇒ **Combination not recommended** : nonsteroidal anti-inflammatory drugs, proton pump inhibitors, ciprofloxacin, penicillins, phenytoin, fosphenytoin, tedizolid.

  ⇒ **Precaution for use** : acetylsalicylic acid (at **antiplatelet** doses), cyclosporine, antibacterial sulfonamides, other nephrotoxic drugs such as iodinated contrast products, aminoglycosides, organoplatins, antivirals (foscarnet, "ciclovirs"), pentamidine, tacrolimus, ponatinib, etc.

  Some drugs should be stopped early enough based on their half-life to avoid interference with the elimination of MTX-HD.

  Concomitant use of drugs with inherent renal toxicity increases the risk of nephrotoxicity. If such an association is necessary, monitoring of renal function and methotrexataemia should be reinforced.

* **Hydration**

  Hydration is generally provided by 5% glucose and/or 0.9% NaCl solutions, in addition to the patient's oral hydration.

* **Urine alkalinization and urinary pH control**

  Alkalinization is usually provided by solutions of sodium bicarbonate. It is recommended that the urinary pH be above 7 before initiating treatment.

During and/or after administration of MTX-HD

* **Monitoring of urinary pH and diuresis – secondary alkalinization**

High-dose methotrexate (MTX-HD): Reminder of General Measures to Prevent the Nephrotoxicity Risk Continued

It is recommended to maintain a urinary pH above 7 and to monitor diuresis during and after the administration of MTX-HD. Secondary alkalinization consisting of the administration of alkalinizing products can be considered when urinary pH control is not satisfactory.

* **Monitoring of renal function and methotrexataemia**

  It is strongly recommended to monitor at regular intervals and until complete elimination of methotrexate:

  ⇒ Kidney function

  ⇒ Methotrexataemia

* **Sequential administration of folinic acid (calcium folinate/calcium levofolinate)**

  This administration is recommended after treatment with MTX-HD. The dosing regimen of folinic acid supplementation is highly dependent on the dosage, the patient's renal function, and methotrexataemia.

  Refer to the SPCs of the MTX and the SPCs of the folinic acid indicated for the prevention and correction of toxic accidents caused by methotrexate.

In case of delayed elimination of MTX-HD (prolonged elimination half-life) associated with impaired renal function

* **Administration of folinic acid (calcium folinate/ calcium levofolinate)**

  The management of an overdose of methotrexate consists of the systematic administration of folinic acid. This administration must be carried out as soon as possible. The dosage will be adjusted according to the residual plasma levels of methotrexate and this should determine the optimal duration of treatment.

  Refer to the SPCs of the MTX and the SPCs of the folinic acid indicated for the prevention and correction of toxic accidents caused by methotrexate.

* **Monitoring of renal function, methotrexataemia, diuresis and urinary pH - intensification of alkaline hyperhydration**

  Maintaining sufficient alkaline diuresis should always be ensured and renal function monitored. Urinary pH should be checked in order to keep it above 7. Alkaline hyperhydration may be necessary in order to limit the precipitation of methotrexate and/or its metabolites in the renal tubules, in an acid medium, and until total elimination of methotrexate. A nephrologist should be consulted in case of delayed elimination of MTX-HD or deterioration of renal function.

* **Extrarenal purification**

  Extrarenal purification methods can be considered although they do not represent an optimal management solution given the pharmacokinetic characteristics of methotrexate.

  Standard hemodialysis and peritoneal dialysis have not shown efficacy in the elimination of methotrexate. High-flux hemodialysis, hemoperfusion, and acute intermittent hemodialysis using a high-flux dialyzer have shown efficacy on methotrexate clearance.

* **Use of glucarpidase in case of severe poisoning**

  In certain situations of severe intoxication with MTX-HD, the use of glucarpidase or carboxypeptidase G2 may be considered in addition to symptomatic treatment. Glucarpidase is indicated to reduce the toxic plasma concentration of methotrexate in adults and children (from 28 days) with delayed methotrexate elimination or risk of methotrexate toxicity.

References:

ANSM (Click here)

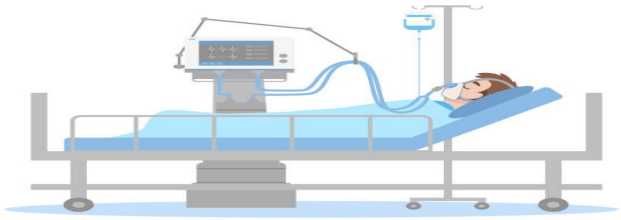
Case Report from Sohag: Paclitaxel - Convulsions & Coma

The regional center in Sohag received a case related to convulsions and coma with the use of Paclitaxel.

A female patient 24 years old 97 kg received Paclitaxel 100 mg for breast cancer with dose of 350 mg as IV infusion. She suffered from convulsions and coma while she was on infusion, so the infusion had been stopped.

The patient received Solucortif, Avil, Dexamethasone & Adrenaline as treatment for the reaction.

The patient was on carboplatin 450 mg & 150 mg and granisetron IV as concomitant drugs for the treatment of breast cancer.



Background:

Convulsions: It is a sudden attack of brain activity that causes loss of control of your actions. You may have jerking of your face, arms, or legs. There are many different kinds of seizures. Seizures may last seconds or minutes and can happen to people of any age.

Coma : Is a prolonged state of unconsciousness. During a coma, a person is unresponsive to their environment. The person is alive and looks like they are sleeping. However, unlike in a deep sleep, the person cannot be awakened by any stimulation, including pain.

Paclitaxel : Chemotherapy that interferes with the growth of cancer cells and slows their growth and spread in the body used in the treatment of some cancers, especially those of the breast and ovary.

Labeled information:

According to Paclitaxel Summary of product Characteristics (SmPC) it was stated under sections:

* Adverse Event Experiences by Body System:

  Neurologic: Other than peripheral neuropathy, serious neurologic events following paclitaxel administration have been rare (<1%) and have included grand mal seizures, syncope, ataxia, and neuroencephalopathy & Convulsions has been reported.
* Undesirable effects:

  Nervous system disorders: Uncommon: Syncope, tremor, sensory loss
* Side Effects:

  For Healthcare Professionals: Cardiovascular: Uncommon (0.1% to 1%): Syncope, Very rare (less than 0.01%): Shock & Nervous system: Very rare (less than 0.01%): Grand mal seizures, convulsions, encephalopathy
* Abstract:

  Following chemotherapy (paclitaxel and cisplatin) in patient of carcinoma cervix it was stated: Central nervous system (CNS) neurotoxicity of cisplatin is rare, but seizures, hemiparesis, cortical blindness, aphasia, and coma attributed to cisplatin therapy have been reported .

Case Report from Cairo: Paclitaxel - Convulsions & Coma Continued

Recommendations for Healthcare Professionals

1. Usual Adult Dose for Breast Cancer was 175 mg/m2 IV over 3 hours every 3 weeks.
2. All patients should be pre-medicated with corticosteroids, antihistamines and H2-receptor antagonists prior to receiving this drug to prevent severe hypersensitivity reactions.
3. Paclitaxel must be given as a slow infusion over 3 to 24 hours.
4. Paclitaxel is usually given once every 2 to 3 weeks..
5. Administer taxane derivatives before platinum derivatives (cisplatin, carboplatin) in sequential infusions to limit myelosuppression and to enhance efficacy.
6. Seizures occur in <1% of patients treated with systemic chemotherapy. Implicated agents include methotrexate, cisplatin, L-asparaginase, 5-fluorouracil, busulfan, ifosfamide, cyclosporine, and paclitaxel.
7. CNS toxicity was observed immediately at the end or shortly after the end of the administration, often when the total dose was >200 mg/m^2.

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. *Lexico (Click here)*
4. *Medical dictionary (Click here)*
5. *FDA (Click here)*
6. *EMA (Click here)*
7. *Drugs.com (Click here)*
8. *Drugs.com (Click here)*
9. *Drugs.com (Click here)*
10. *Drugs.com (Click here)*
11. *Pubmed (Click here)*
12. *Medscape (Click here)*
13. *NCBI (Click here)*

The Egyptian Pharmaceutical Vigilance center
مركز اليقظة الصيدلية المصري

Participation of the Egyptian Drug Authority in the "Step On The Way" Conference Fourteenth Edition

The Egyptian Drug Authority, represented by the Pharmaceutical Vigilance Sohag regional center, participated in the "Step On The Way" conference in its fourteenth edition, which was organized by the Pharmaceutical Education committee at the Faculty of Pharmacy- Assiut University affiliated to the Egyptian Pharmaceutical Students Federation (EPSF).

In the context of the keenness of EPVC to educate students about the importance of reporting the adverse effects of drugs, EPVC Sohag accepted the invitation of EPSF, and the center participated in a workshop entitled (Guide to pharmacovigilance) to introduce the importance of the role of pharmaceutical vigilance and how to report the adverse effects of drugs, in the presence of 300 students from various medical specialties at Assiut University "pharmacy, medicine, nursing, physical therapy". The workshop resulted in students interaction and prepared them to report adverse drug effects.

The conference, in turn, aims to train pharmacy college students in Egyptian universities and Prepare them to be qualified for the labor market in various functional fields represented in the field of community pharmacy, industrial pharmacy, advertising and pharmacovigilance. The conference was not limited to providing scientific lectures only, but also discussed the development of general skills among students.

The conference was launched in the presence of :

* Prof. Dr. Maha Kamel Ghanem, Vice President of Assiut University for Community Service and Environmental Development
* Prof. Dr. Ahmed Mohamed Abdel Mawla, Dean of the Faculty of Pharmacy, Assiut University
* Dr. Nermin El-Iraqi is the pioneer of the Scientific Society for Students of the Faculty of Pharmacy, Assiut University
* Dr. Mai Diaa El-Din Mohamed, President of the Scientific Association for Students of the Faculty of Pharmacy, Assiut University

It is worth mentioning that the EPSF was established in 1928 and is a full member of the International Pharmaceutical Students Federation (IPSF). It includes 38 universities at the level of the Republic & aims to enable faculty of Pharmacy to produce highly qualified and experienced pharmacists in various fields of pharmacy.

Egyptian Drug Authority Participation in Shefaa Al-Orman Hospital Conference "Upper Egypt No Cancer"

The Egyptian Drug Authority (EDA) is glad to announce its participation in the second annual scientific conference of Shefaa Al-Orman Hospital in Luxor, which was held under the slogan "Upper Egypt No Cancer" from 23rd to 25th March, with a lecture on the role of pharmaceutical vigilance at the EDA. This comes from the belief of the EDA in the importance of participation in various medical events in order to spread the concept of pharmaceutical vigilance and its important role in maintaining the safety and security of the Egyptian patient in general and cancer patients in particular, who are served by hospitals in Upper Egypt.

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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https://sites.google.com/view/epvc-reporting/healthcare-professional-public-adverse-drug-event-reporting/reporting-other-adverse-drug-event-cases

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