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

April 2023

Volume 14 **Issue 4**

Consumer Update

Clopidogrel has been shown to increase rosuvastatin exposure in patients

EDA performs label update to include the following:

Clopidogrel has been shown to increase rosuvastatin exposure in patients by 2-fold (AUC) and 1.3-fold (Cmax) after administration of a 300 mg clopidogrel dose, and by 1.4-fold (AUC) without effect on Cmax after repeated administration of a 75 mg clopidogrel dose.

Background:

Clinical Comment:

The dose of rosuvastatin should not exceed 20 mg daily when used concomitantly with clopidogrel

Clopidogrel use:

Clopidogrel is a prodrug of a platelet inhibitor used to reduce the risk of myocardial infarction and stroke. Clopidogrel is indicated to reduce the risk of myocardial infarction for patients with non-ST elevated acute coronary syndrome (ACS), patients with ST-elevated myocardial infarction, and in recent MI, stroke, or established peripheral arterial disease. It has been shown to be superior to aspirin in reducing cardiovascular outcomes in patients with cardiovascular disease and provides additional benefit to patients with acute coronary syndromes already taking aspirin staying aware as a patient.

Consult your doctor for advice when in doubt.

References:

TGA: *(Click here)*

HAPPY EASTER

EPVC Investigation reports

FINGOLIMOD INDUCED BRADYCARDIA

Between the Egyptian Pharmaceutical Vigilance Center (EPVC) received 12 individual case safety reports of multiple sclerosis patients experienced bradycardia after receiving Fingolimod 0.5 mg.

Background:

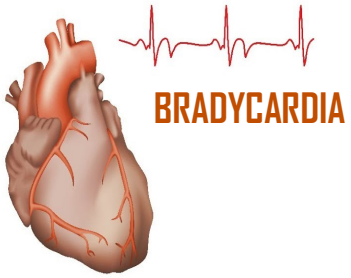
The risk of bradycardia with Fingolimod is already described in the product information: The FDA reported that bradycardia occurs in 0.6% of patients receiving Fingolimod 0.5 mg. According to the European Medicines Agency summary of product characteristics (SPCs), bradycardia is COMMON side effect for Fingolimod. While Lexicomp concluded that 3% of MS patients experienced bradycardia with Fingolimod.

Recommendations for Healthcare Professionals related to Fingolimod-induced bradycardia:

- Initiation must occur in a setting with resources and personnel capable of appropriately managing symptomatic bradycardia. Following the first dose, heart rate may decrease as soon as 1-hour post dose, with the maximal decrease usually occurring ~6 hours post dose with recovery (but not to baseline levels) 8 to 10 hours post dose.
- A second heart rate decrease occurs within 24 hours after the first dose and may be more pronounced than the first 6-hour rate decrease.
- Most patients are asymptomatic; however, hypotension, dizziness, fatigue, palpitations, and/or chest pain may occur; symptoms usually resolve within 24 hours.
- With the second dose, heart rate may also decrease, but to a lesser magnitude than observed with the first dose. Heart rate typically returns to baseline after 1 month of chronic therapy.

First dose cardiac monitoring:

- ECG (baseline; repeat after initial dose observation period); heart rate, BP, and signs and symptoms of bradycardia (hourly for 6 hours following first dose).
- If 6-hour post dose heart rate is <45 bpm in adults, <55 bpm in patients ≥12 years of age, or <60 bpm in patients 10 to 11 years of age, 6-hour post dose heart rate is lowest post baseline measurement, or new-onset second-degree or higher AV block occurs on repeat ECG, continued observation is required until resolved, even if asymptomatic.
- If postdose symptomatic bradycardia occurs and no pharmacologic treatment is necessary, provide continuous ECG monitoring until symptoms are resolved.
- If postdose symptomatic bradycardia occurs and pharmacologic intervention is necessary, provide overnight continuous ECG monitoring in a medical facility and repeat the 6-hour observation period for the second dose.



- Patients also require overnight continuous ECG monitoring in a medical facility if they have a prolonged QTc interval at baseline or 6 hours post dose (>450 msec: adult and pediatric males; >470 msec: adult females; >460 msec: pediatric females); additional risks for QT prolongation (eg, hypokalemia, hypomagnesemia, congenital long-QT syndrome); concurrent therapy with QT prolonging agents with a known risk of torsades de pointes or medications that slow heart rate or AV conduction; preexisting ischemic heart disease, history of myocardial infarction, heart failure, history of cardiac arrest, cerebrovascular disease, uncontrolled hypertension, history of symptomatic bradycardia, history of recurrent syncope, severe untreated sleep apnea, AV block, or sinoatrial heart block.

Recommendation for re-initiating FINGOLIMOD therapy after treatment interruption:

The same first dose monitoring as for treatment initiation is recommended when treatment is interrupted for:
One day or more during the first 2 weeks of treatment.
More than 7 days during weeks 3 and 4 of treatment.
More than 2 weeks after at least 1 month of treatment

References:

EMA : Click Here
FDA: Click Here
Info of Fingolimod: Click Here

Revised by: Ola Fahmy

Pipazetate hydrochloride Accidental Overdose causes Dizziness, Unconsciousness, Seizure, Hypoxia, Dizziness, QT interval prolonged, Supraventricular tachycardia

The regional center in Cairo received a case for a 3 years old female child suffered from cough. Her mother gave her 5 ml of Pipazetate hydrochloride (40 mg/ml) oral drops once (unintended overdose). The stating dose for the drops for her age as prescribed in the medication package insert is:
Children 2-6 years old: 8 drops Up to 3 times daily.
About half an hour after taking the dose, the child showed symptoms of severe heart palpitations, dizziness, and then the child lost consciousness. She was immediately transferred to the emergency unit at private clinics, and while being transferred, she suffered from convulsions. She was diagnosed by the emergency physician as suffering from convulsions, supraventricular tachycardia and drug poisoning.
Immediately, the child was transferred to the care, and a set of comprehensive analyzes as well as electrocardiogram were performed, which revealed the presence of heart rhythm disorders (cardiac arrhythmia), prolonged QT syndrome, and hypoxia.
Corrective interventions were performed in the form of anticonvulsant, intravenous fluids, Lidocaine intravenous solution and oxygen.
By asking the patient relatives the following was detected:
Her younger brother took 4 drops from the same bottle orally two days ago, and he did not have any similar reaction. The child took the same medicine about a year ago and did not suffer from any similar symptoms.
The child recovered after one day and became fully conscious except minor ECG changes. After the last follow up with the case the following was detected:
The child is fully recovered and the ECG became normal after 3 days from the reaction.
No concomitant drugs were administered and no other medical history was stated.
General laboratory tests were performed at the time of admission and regularly during the hospitalization and all were within normal range.
ECG performed showed prolonged QT wave on time of admission and lasted for three days.

Background:

Pipazetate hydrochloride is a non-narcotic oral antitussive agent. It acts centrally on the medullary cough center and is used for the treatment of cough.

Labeled information:

According to Pipazetate hydrochloride (Pipazetate hydrochloride) medication package insert [2] it was stated under Warnings and Precautions section; PIPAZETATE HYDROCHLORIDE may cause drowsiness, therefore patients in charge of vehicles or machinery should be cautioned.
Dosage and Administration: Children 2-6 years old»»» 8 drops Up to 3 times daily.

Recommendations for Healthcare Professionals:

1. Although the toxicity of this drug is rarely reported [3, 4], it was recommended to use the measuring scale present within the package to measure the correct dose and avoid the use of tablespoon or teaspoon to measure the dose.
2. The dosage of the drops must be based on age, weight, medical condition, and response to treatment.
3. The patient should be advised to follow the specific dosing instructions on the package, which corresponds to his age or body weight.

References:

Pipazetate info : (Click here)
Pipazetate SmPC(Click here)
Pipazetate Toxicity (Click here)
Embase: (Click here)

Two case reports from Alexandria: two cases of intentional Dexamethasone misuse resulting in Type 2 diabetes mellitus/ Polycystic ovary/Moon face/ Buffalo hump

The regional center in Alexandria received the first ICSR concerning a 23-year-old female patient who weighed 53 kg and wants to increase her weight, administered orally Dexamethasone 0.5 mg tablets three times daily starting for 6 months (Intentional drug misuse). The reporter mentioned that after 6 months of Dexamethasone administration, the patient experienced Cushing syndrome symptoms including moon face, buffalo hump, obesity (her weight become 81 kg), and stretch marks. The patient complained of period irregularity, and she went to a gynecology clinic, where she was diagnosed with a polycystic ovary. The gynecologist prescribed Estradiol valerate and Norgestrel as a treatment for polycystic ovary but all ADRs were not recovered till now.

The patient took concomitantly Cyproheptadine HCL 4 mg twice daily for weight gain, did not suffer from any diseases in her medical history. The reporter added that many girls misused Corticosteroids for weight gain with or without a physician's prescription, resulting in a lot of serious ADRs.

No more relevant information was available.

The second ICSR concerned a 29-year-old female patient who weighed 62 kg and wants to increase her weight was administered orally Dexamethasone 0.5 mg three times daily starting for 9 months (intentional drug misuse) without prescription, where the patient's weight increased and reached 85 kg. The reporter mentioned that during Dexamethasone administration, the patient experienced some symptoms of Cushing syndrome including moon face, buffalo hump, and stretch marks. After stopping Dexamethasone by two months, the patient experienced a decrease in her weight to 75 kg, excessive thirst, dry mouth, and an increase in urination frequency. The reporter advised the patient to perform random blood glucose and glycated hemoglobin tests which measured 325 mg/dL and 7.8 %, respectively. The patient went to a physician, who diagnosed the patient's case as Type 2 diabetes mellitus and prescribed Insulin 30 IU in the morning and 10 IU in the evening for three months. The patient took concomitantly Cyproheptadine HCL 4 mg twice daily for weight gain. The patient did not suffer from any diseases in her medical history.

No more relevant information was available.

Background:

Dexamethasone: a corticosteroid, is similar to a natural hormone produced by your adrenal glands. It often is used to replace this chemical when your body does not make enough of it. It relieves inflammation (swelling, heat, redness, and pain) and is used to treat certain forms of arthritis; skin, blood, kidney, eye, thyroid, and intestinal disorders (e.g., colitis); severe allergies;

Two case reports from Alexandria: two cases of intentional Dexamethasone misuse resulting in Type 2 diabetes mellitus/ Polycystic ovary/Moon face/ Buffalo hump (Continued)

and asthma. Dexamethasone is also used to treat certain types of cancer.

Type 2 diabetes: is a common condition that causes the blood sugar (glucose) level to become too high. It can cause symptoms like excessive thirst, needing to urinate a lot, and tiredness. It can also increase the risk of getting serious problems with the eyes, heart, and nerves.

Moon face: occurs when extra fat builds up on the sides of the face. It is often related to obesity but can be from Cushing's syndrome. That's why people sometimes refer to it as a Cushingoid appearance. Cushing's syndrome occurs when the body is exposed to high levels of cortisol for long periods.

Reported adverse effects of Dexamethasone:

Endocrine disorders:

Common: Cushing's syndrome.

Uncommon: Hypothyroidism.

Not known: Adrenal atrophy, steroid withdrawal syndrome, adrenal insufficiency, hirsutism, menstrual irregularity.

Metabolism and nutrition disorders:

Very common: Hyperglycemia

Common: Hypokalemia, diabetes mellitus, anorexia, increased or decreased appetite, hypoalbuminemia, fluid retention, hyperuricemia

Uncommon: Dehydration, hypocalcemia, hypomagnesemia

Not known: Glucose tolerance impaired, sodium retention, metabolic alkalosis.

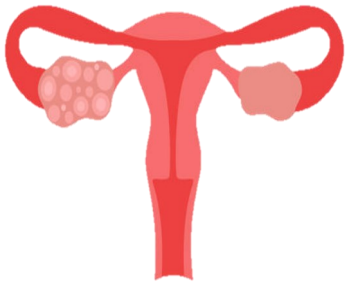
Investigations:

Common: Weight decreased, weight increased.

General:

The most commonly occurring side effects have included alteration in glucose tolerance, behavioral and mood changes, increased appetite, and weight gain; the incidence generally correlates with dosage, the timing of administration, and duration of treatment.

Genitourinary:



Frequency not reported: Menstrual irregularities, amenorrhea, increased or decreased motility and number of spermatozoa, increased urine calcium.

Contraindications of Dexamethasone:

Hypersensitivity to dexamethasone or any component of the formulation and systemic fungal infections.

Documentation of allergenic cross-reactivity for corticosteroids is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty

Two case reports from Alexandria: two cases of intentional Dexamethasone misuse resulting in Type 2 diabetes mellitus/ Polycystic ovary/Moon face/ Buffalo hump (Continued)

Several case studies were published concerning corticosteroid misuse in Arab communities, so health officials and healthcare practitioners need to promote people's awareness about the serious risks of misusing oral corticosteroids through education programs and advertisements in public health settings, media, and social media. As a result, the EPVC's duty is to publish such cases that have been detected in Egypt and highlight the serious risks associated with oral corticosteroid misuse, along with our recommendations and warnings for healthcare professionals and patients.

Special Warning and Recommendation:

- Using too much Dexamethasone or using it for a long time may increase the risk of having adrenal gland problems.
- Dexamethasone and Cyproheptadine combination is considered as an off-label use for weight management
- Dexamethasone regulates glucose metabolism and can lead to higher blood glucose levels when used to treat inflammation, and long-term usage may bring about type 2 diabetes mellitus.
- Long-term use of corticosteroids can affect periods and make them irregular, prolonged, and sometimes heavier.
- Dexamethasone may suppress the immune system, making it easier to get an infection or worsen an illness that is already present or has just occurred.
- Dexamethasone-treated patients should not be around other persons living in their household who receive live virus vaccines because there is a chance, they could pass the virus on to them.
- All vaccines may not work as well while Dexamethasone is being administered. A "live" vaccine should not be received while taking Dexamethasone, also its administration should be delayed several months after dexamethasone treatment has stopped.
- Dexamethasone should not be used in people with systemic fungal infections or with viral infections. Also, it may increase the risk of infection and its anti-inflammatory action can mask signs of infection.
- Dexamethasone should not be stopped suddenly after long-term use to allow the adrenal glands to return to their normal patterns of secretion. Too rapid a withdrawal of dexamethasone could have unpleasant withdrawal symptoms.
- Using Dexamethasone may increase the risk of cancer, including Kaposi's sarcoma.
- Using Dexamethasone for a long time might cause thinning of the bones (osteoporosis) or slow growth in children.
- Dexamethasone should be taken exactly as directed, and the dose should not increase or decrease unless directed by the doctor. Dosage requirements for dexamethasone are variable and must be individualized based on the disease and patient response.
- Dexamethasone is a prescription only medication. So, Physician and pharmacist consultation is required before using Dexamethasone to avoid its serious adverse effects.

References:

Dexamethasone (Click here)
What is type 2 diabetes? (Click here)
Moon Facies (Click here)
Neofordex SmPC (Click here)
Dexamethasone side effects (Click here)
Dexamethasone (systemic) ADRs: (Click here)
Dexamethasone misuse (Click here)
Oral corticosteroids abuse (Click here)
Evaluating Factors Related to the Abuse of Oral Corticosteroids (Click here)

Together for Safe Medicine Initiative Progress

The Egyptian pharmacovigilance center is Extremely thankful to all participating pharmacists in the first 3 waves of the Initiative "Together for Safe Medicine "for their important role in increasing the adverse drug reaction reports (ADRs) reporting rate as they had sent 1481 Individual Case Safety Reports (ICSRs)with continuous improvement in reports quality to the national Pharmacovigilance database, all participating pharmacies who passed the initiative phases successfully had received a badge to be displayed in their pharmacies indicating their valuable participation in raising Pharmacovigilance awareness all over Egypt.

Additionally, EPVC plans to announce the beginning of registration for the fourth wave in May 2023. We will be grateful to share the registration link with all community and governmental outpatient pharmacies to further spread the practice of pharmacovigilance throughout Egypt's governates.

The Egyptian Pharmaceutical Vigilance center
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Egyptian Pharmaceutical Vigilance Center (EPVC) Vigiflow expansion Trainings for Raising Reporting Awareness

The Egyptian Pharmaceutical Vigilance Center (EPVC) is delighted to continue Vigiflow expansion training in collaboration with Egyptian Healthcare Authority.

As an extension of the pharmacovigilance effort, the training seeks to teach pharmacists working in coordinating institutions how to report using the national database reporting system. Also, it aims to improve the reporting system and provide the organization with access to a strong database that improves data collection through Structured data entry, reducing the need for data cleaning while speeding up the data analysis process.

Working concurrently with the training sessions, EPVC continues to receive Individual Case Safety Reports (ICSRs) through the national database, revise them, provide feedback to the coordinating organizations, and inquire about the need for additional training as part of the effort to raise the quality of the cases entered through the database.

EPVC Pharmacovigilance Awareness Training

In the context of the vision and mission of the Egyptian Pharmaceutical Vigilance Center (EPVC) in spreading the awareness of the pharmacovigilance and the culture of reporting side effects among the Healthcare professionals to promote the safe and effective use of the different pharmaceutical products and to promote the pharmaceutical care, the center conducted an awareness training on pharmacovigilance organized by Alexandria University hospitals management , attendees were 43 of the pharmacists, nurses from different healthcare units of Elhadara University hospital (Nariman University Hospital). The training included Introduction on the basics of Pharmacovigilance, its importance, how to report adverse events and different requirements needed for implement a good Pharmacovigilance system in the hospital.

EPVC Tips On Pharmacovigilance

Medication-Overuse Headaches

Medication-overuse headaches (MOH), also known as analgesic rebound headaches, drug-induced headaches, or medication-misuse headaches, are a common neurologic disorder that results in enormous disability and suffering and plays a significant role in the transformation from episodic to chronic headache disorders. These headaches typically develop in patients with established primary headache disorders like migraine or tension-type headaches who overuse medication in an attempt to alleviate the symptoms of their primary headache. An unfortunate cycle of medication overuse results in increased headache frequency, whereby the medication indicated for the treatment of the primary headache becomes the cause of headaches

Visit EDA website to find all any medicine- related news, updates and alerts *Click here*

You will find all EPVC Newsletters and DHPCs here

You will also find all alerts regarding counterfeited and falsified products released by Central Administration of Operations *here*

The Egyptian Pharmaceutical Vigilance center
مركز اليقظة الصيدلية المصري

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

Message of Appreciation

On the 75 anniversary of WHO Foundation, EPVC would like to send a message of thanks and gratitude to WHO and all its members for their continuous help and support throughout all the previous years. Looking forward to more fruitful collaboration

75 HEALTH FOR ALL

One report counts

عيد تحرير سيناء

A call for reporting

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)

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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