هيئة الدواء المصرية

IN THIS ISSUE

Prepared by:
Reem Hossam
Aliaa Mo'anes
Dina Gawish

Designed by:
Reem Tarek

Chief editor

Aalaa Afdal
Head of Egyptian Pharmacovigilance Center

Under supervision of

Dr. Sherin Abdel Gawad
Head of the C.A for Pharmaceutical Care

The Egyptian Pharmaceutical Vigilance center
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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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Direct Healthcare Professional Communication (DHPC): Amiodarone Hydrochloride 50 mg/ml Concentrate for Solution for Injection/Infusion - Potential for crystallisation

EPVC in agreement with market authorization holders (MAH) of products containing amiodarone hydrochloride 50 mg/ml concentrate would like to inform you of the following:

Summary:
Reports have been received of visible crystals of amiodarone hydrochloride within the solution of a small number of ampoules of marketed product.
Healthcare professionals are advised to:

- Visually inspect ampoules of amiodarone for clarity, particulate matter, discolouration and the integrity of the container
- Only use the solution if it is clear and the container is undamaged and intact

Background on the safety concerns

Amiodarone hydrochloride is an antiarrhythmic used for the management of life-threatening ventricular arrhythmias (tachycardia or fibrillation) and supraventricular arrhythmias (fibrillation or flutter) and Wolff-Parkinson-White Syndrome.

The potential for amiodarone solutions to crystallize and the associated potential for amiodarone induced phlebitis are known and have been previously discussed in the scientific literature.

Amiodarone in aqueous solution is associated with crystallization due to poor solubility. To overcome this, the molecule is typically solubilized as part of a micellar system using an excipient, such as polysorbate 80, which acts as a surfactant. Any breakdown of this micellar system can lead to crystallisation of amiodarone in solution, which has been observed both at high concentrations of amiodarone (e.g. in ampoules of concentrate) and at low concentrations (e.g. in infusion bags during administration).

While the potential for amiodarone solutions to crystallize is known, following receipt of a small number of reports of crystallization in ampoules from separate batches of product, and the subsequent investigations undertaken, the Marketing Authorisation Holders would like to highlight this potential for crystallization to healthcare professionals.

Adverse reactions

As noted in the prescribing information for the products, infusion phlebitis is listed as one of the most common adverse drug effects reported with intravenous amiodarone hydrochloride.

There has been no identified increase in the reporting of adverse reactions that would be considered related to the crystallisation of amiodarone during infusion (e.g. phlebitis, thrombophlebitis). While this doesn't exclude the possibility of adverse health consequences, it further supports the overall probability that the occurrence of such reactions is low.

Direct Healthcare Professional Communication (DHPC): Amiodarone Hydrochloride 50 mg/ml Concentrate for Solution for Injection/Infusion - Potential for crystallization Continued

Recommendations for use :

To inform healthcare professionals of the potential for crystallization, the Marketing Authorization Holders, in agreement with the EPVC, have issued this Direct Healthcare Professional Communication to provide additional information for healthcare professionals.

Healthcare professionals should continue to follow the advice below:

Before use, the sterile concentrate should be visually inspected for clarity, particulate matter, discoloration and the integrity of the container. The solution should only be used if it is clear and the container is undamaged and intact.

Although the use of in-line filters is not considered to be standard practice for all infusions of medicinal products, healthcare professionals may wish to consider the use of in-line filters for infusions of solutions that are known to crystalize, including solutions of amiodarone

References:

MHRA (Click here)

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Case Report from Alexandria: A Case of Drug Dependence and Overdose Resulted in Atrophic rhinitis, Nasal Septal Mucosa Necrosis, Chronic Nasal Congestion, Nasal Dryness and Palpitations Following Xylometazoline Nasal Drops Prolonged Administration

The regional center in Alexandria received an ICSR concerning a 46 years old male dentist who suffered from common cold and nasal congestion. He was prescribed Xylometazoline nasal drops (1 mg/ml, GlaxoSmithKline) three times daily in 1998 and have been using it since that date. As a result of the continued use of Xylometazoline nasal drops, in 2021 the patient experienced atrophic rhinitis, nasal septal necrosis, chronic nasal congestion, severe sinus headache, nasal sinus dryness, insomnia, palpitations, poor concentration and cognitive disorders (weren't diagnosed by a physician).

The reporter mentioned that the he took Xylometazoline for 24 years and he couldn't stop its administration except for a few days, where he took antihistaminic oral drugs and Corticosteroids nasal inhaler but without any improvement then Xylometazoline was retaken again.

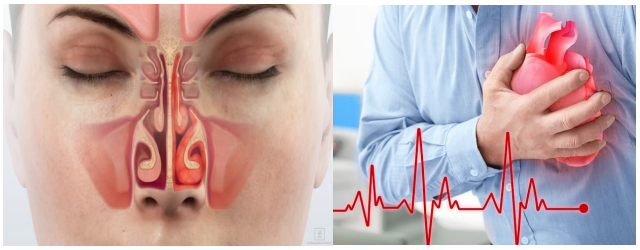
The reporter described Xylometazoline administration as a type of addiction (drug dependence), where he could not breath normally without its administration and every time, he needed to increase its dose till reached 2 drops every 2 or 3 hours daily (overdose).

The reporter added that all otorhinolaryngologists, advised him to stop its administration for at least 15 days but he couldn't.

Both atrophic rhinitis, nasal necrosis were serious medically important adverse drug reactions (ADRs).

Background:

Xylometazoline is an imidazoline derivative with sympathomimetic and nasal decongestant activity.



Xylometazoline works by binding to alpha (α)-adrenergic receptors to activate the adrenal system causing systemic vasoconstriction, thereby easing nasal congestion.

Xylometazoline is available in over-the-counter (OTC) nasal sprays or drops to temporarily relieve nasal congestion due to cold, hay fever or other respiratory allergies.

Labeled information:

Xylometazoline nasal drops adverse effects include headache, irregular and increased heart rate, nasal dryness and discomfort, occasional intranasal burning, stinging, and sneezing [1]

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Case Report from Alexandria: A Case of Drug Dependence and Overdose Resulted in Atrophic rhinitis, Nasal Septal Mucosa Necrosis, Chronic Nasal Congestion, Nasal Dryness and Palpitations Following Xylometazoline Nasal Drops Prolonged Administration Continued

Serious Reactions[2]:

- Large doses may produce tachycardia, palpitations, light-headedness, nausea, and vomiting.
- Overdosage may produce hallucinations, CNS depression, seizures, drowsiness and trouble in sleeping and weakness.
- Prolonged use may result in rebound congestion.

The rebound phenomenon[3]: it's official name is rhinitis medicamentosa as a result of overusing decongestant nasal sprays. These sprays contain chemicals that shrink congested blood vessels. That's how they open up the clogged passages.

Because they're applied directly to the nose, they give a quick relief. After a few days, though; the blood vessels don't respond to the medication anymore. The problem just gets worse. This cycle can continue for months, years, and even decades, That's why every bottle comes with a warning: "Do not use for more than 3 to 5 days".

As a result, you may need to use more and more of the medication to control congestion. The congestion also may worsen if the medication stopped. Some people may mistake this rebound effect for addiction, but it isn't.

True addiction is a compulsive physiological need for and use of a habit-forming substance known to be physically, psychologically or socially harmful. Over-the-counter nasal sprays don't cause the physiological cravings that mark an addiction[5].

Patients who misuse nose drops usually have some underlying nasal disease such as vasomotor rhinitis, nasal polyposis, etc. Perhaps these patients have a more pronounced rebound swelling than healthy subjects. The swelling might also last longer, since it has been reported that sustained use of decongestants aggravates vasomotor rhinitis. Therefore, it must be recommended that the use of drugs of this kind is limited in time. It is not known why the rebound swelling occurs. The swelling could either be due to a vascular dilatation or an intravascular edema.

It is also observed that despite long-term use of vasoconstrictors stuffiness is immediately relieved by an additional dose of the decongestant. The reason why patients increase the application of nasal decongestants after prolonged use of these drugs is thus not because the decongestion effect is reduced, but probably because the duration of action is decreased[6].

Nasal septal perforation is a serious underlying systemic or local disease secondary to rhinitis medicamentosa that linked nasal perforations to the prolonged use of topical vasoconstrictors. The persistent deprivation of oxygen to the nasal septum during long-term vasoconstrictor use is believed to induce osteocartilaginous necrosis in a manner similar to the way cocaine does, but possibly with a less rapid onset[7].

Case Report from Alexandria: A Case of Drug Dependence and Overdose Resulted in Atrophic rhinitis, Nasal Septal Mucosa Necrosis, Chronic Nasal Congestion, Nasal Dryness and Palpitations Following Xylometazoline Nasal Drops Prolonged Administration Continued

Warnings and Recommendations:

1. Healthcare professional should advise the patient to use Xylometazoline nasal drops once every 12 hours for a maximum of 7 consecutive days to avoid rebound effect and drug-induced rhinitis.
2. The patients should not share their spray dispenser with anyone, to prevent the spread of infection.
3. No addiction for any decongestant nasal spray, it is only rebound effect that can be treated by immediately stopping its administration that expected to be miserable for a few days while the body recovers, so Make sure you throw out every nasal spray decongestant you have, or you won't be able to stop using it
4. There are several other treatment options for nasal congestion that won't trigger a dependence, such as; nasal saline that can flush out stuffy airways or if the problem is allergies, topical nasal steroids reduce allergic inflammation over a couple days.
5. Children under six years, women who are pregnant or nursing, and people who have had an allergic reaction to oxymetazoline shouldn't use it.
6. This medication should be used with caution in individuals who have kidney or liver disease.
7. It is recommended that individuals with diabetes, thyroid disease, heart problems, and a history of stroke or high blood pressure discuss the use of Xylometazoline with their healthcare provider
8. Decongestants do not solve the problem that prompts their use, except in the case of a transient cold.
9. Decongestants should not be used for chronic conditions like seasonal or persistent allergies.

References:

1. *EMC (Click here)*
2. *Science direct (Click here)*
3. *Pubmed (Click here)*
4. *WebMD (Click here)*
5. *Mayo Clinic (Click here)*
6. *Pubmed (Click here)*
7. *Sage Journals (Click here)*

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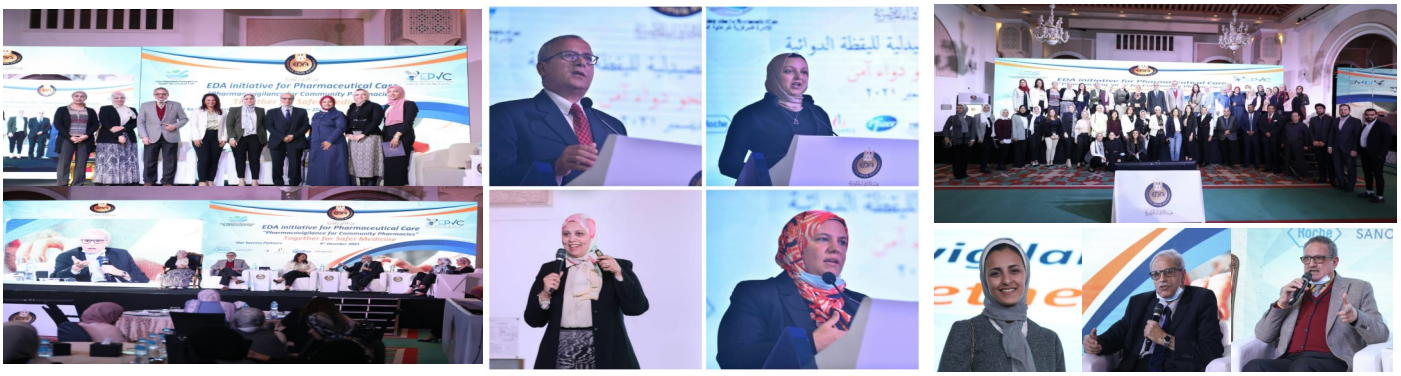
The Egyptian Drug Authority (EDA) Launches the "Together Towards Safe Medicine" Initiative

The Egyptian Drug Authority has announced the launch of an initiative entitled "Together Towards Safe Medicine" contributing to the development of pharmaceutical care in community pharmacies in Egypt by applying Pharmacovigilance activities and ensuring access to safe pharmaceutical products for patients.

The initiative also aims to enhance community pharmacies service to receive reports of adverse events from medicines and raise the technical performance level of pharmacists to ensure safe medicine and medical devices reaching the Egyptian patient. Also, launching the "EPVC Community Club", which will include pharmacies applying the activities of pharmaceutical vigilance in their community pharmacies.

The opening ceremony included speeches by Dr. Ayman Al Khatib, Vice President of the EDA, Dr. Rasha Ziada, EDA Chairman's Assistant for Technical Development and Capability Building Affairs, Dr. Sherin Abdel Gawad, Head of the Central Administration of Pharmaceutical Care.

The speeches presented the role of the Authority in strengthening pharmaceutical care in Egypt in accordance with the implementation of Egypt's Vision 2030, providing safe and effective medicines to the Egyptian patient, the importance of the role of Pharmaceutical Vigilance in ensuring the safety of medicines in the Egyptian market, and strengthening the role of Community pharmacies in Egypt to ensure the application of the highest levels of pharmaceutical care to achieve the vision of "Egypt 2030" by applying International Safety Activities for the sake of patient safety.



Acknowledgment of Alexandria University Hospitals Co-operation Efforts with EPVC

EPVC would like to express it's gratitude to Alexandria University Hospitals for their excellent cooperation, effort and support in pharmacovigilance field. Also it is worth recalling that the following topic in the last newsletter "A Case of Drug Abuse Resulted in Acute Renal Injury, Cardiomegaly, Muscle Weakness, Ulcers, Sepsis and Finally Death Following Paraffin Oil, Anabolic Steroids and Synthol Local Administration" was reported by The Clinical pharmacy team in critical care department in Alexandria main University Hospital.

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

Address: 21 Abd El Aziz AlSoud Street. El-Manial, Cairo, Egypt, PO Box: 11451
Hotline: 15301
Fax: +202 – 23610497
Email: pv@edaegypt.gov.eg,
pv.followup@edaegypt.gov.eg
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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