Direct Healthcare Professional Communication

January 2022

Amiodarone Hydrochloride 50 mg/ml concentrate for solution for Injection/Infusion - Potential for crystallisation:

Dear Healthcare Professional,

The Egyptian Pharmaceutical Vigilance Center of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority 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 supra-ventricular 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 crystallization 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).

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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.

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

https://assets.publishing.service.gov.uk/media/613f46acd3bf7f05b7bcb602/Amiodarone_DHPC_24_Aug_2021.pdf

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

Name: Egyptian Pharmaceutical Vigilance Center

Address: 21 Abd El Aziz Al Soud Street, El-Manial, Cairo, Egypt, And PO Box: 11451 Telephone: +202- 25354100, Extension: 1470 Fax: +202 – 23610497

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Email: pv.followup@edaegypt.gov.eg

Online reporting: https://primaryreporting.who-umc.org/EG

QR Code:

Hotline: 15301

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