Direct Healthcare Professional Communication

Dec 2023

Azithromycine: Reminder of risk of QT prolongation and method of IV preparation and administration

Dear Healthcare Professional,

The General Administration for Pharmaceutical Vigilance of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to Remind you of the following **risk of QT prolongation and method of IV preparation and administration**

Summary:

- Prolongation of cardiac repolarisation and of the QT interval, which is associated with the risk of cardiac arrhythmias and torsade de pointes, has been observed during treatment with macrolides, including azithromycin
- Particular caution must therefore be exercised when using azithromycin in patients with pre-existing proarrhythmic disorders
- The risk groups include:
  - Individuals with congenital or proven QT prolongation
  - Under treatment with other active substances which have a QT prolonging effect, such as antiarrhythmic drugs of classes IA (quinidine and procainamide) and III (dofetilide, amiodarone and sotalol), cisapride and terfenadine. antipsychotics such as pimozide, antidepressants such as citalopram and fluoroquinolones such as moxifloxacin and levofloxacin
  - Individuals with electrolyte imbalances, in particular hypokalaemia and hypomagnesaemia
  - Individuals with clinically significant bradycardia, cardiac arrhythmias, or severe cardiac insufficiency
  - Elderly patients: the elderly may possibly be sensitive to drug-associated effects on the QT interval.

- **Method of administration:**
  - Azithromycin **should be administered only as an intravenous infusion after dissolution and dilution of the powder.**
  - Azithromycin **must not be administered as an intravenous bolus injection or intramuscular injection**.
  - Azithromycin solution for infusion should be given **at a concentration 1 mg/ml over 3 hours or 2 mg/ml over 1 hour.**

  Higher concentrations should be avoided as local reactions at the infusion site occurred in all patients who received higher concentrations than 2 mg/ml.

- **Duration of administration**
  For the administration of a 500 mg dose of azithromycin, the infusion should be administered over at least 60 minutes.

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- **Preparation of the infusion solution:**
  - Reconstitution Azithromycin 500 mg powder for solution for infusion is for single use only. The initial solution of azithromycin is prepared **by adding 4.8 ml of sterile water for injections to a 500 mg vial of powder to get 5 mL of concentrate solution** (using a standard 5 ml syringe so the volume of water of 4.8 ml can be measured accurately).
  - The contents of the vial should be shaken until all of the powder is dissolved. **Each ml of the solution prepared in this way contains 100 mg azithromycin (100 mg/mL).**
  - The reconstituted medicinal product is chemically and physically stable for 24 hours, when stored at 30°C. Parenteral administration drugs should be inspected visually for particulate in suspension prior to administration.

  - Only clear solutions practically free from particles should be used. If particulate in suspension is evident in reconstituted solution, the drug solution should be discarded. The reconstituted solution must be further diluted prior to administration as instructed below.
  - Dilution For a concentration of 1.0 mg/ml, transfer 5 ml of the 100 mg/ml azithromycin solution to 500 ml of any of the diluents listed below. For a concentration of 2.0 mg/ml, transfer 5 ml of the 100 mg/ml azithromycin solution to 250 ml of any of the diluents listed below.

Diluents:
0.9% Sodium Chloride Injection
0.45% Sodium Chloride
5% Dextrose in Water for Injection
Lactated Ringer's Injection
5% Dextrose in 0.45% Sodium Chloride Injection with 20 mEq Potassium Chloride
5% Dextrose in Lactated Ringer's Injection
5% Dextrose in 0.3% Sodium Chloride Injection
5% Dextrose in 0.45% Sodium Chloride Injection

Concentration (mg/mL) of final infusion solution	**Quantity of diluent (mL)**	**Time of infusion**
1.0 mg/mL	500 mL	3 hours
2.0 mg/mL	250 mL	1 hour

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Further information on the safety Issue and the recommendations

Azithromycin is indicated for the treatment of community-acquired pneumonia requiring hospitalisation caused by azithromycin-sensitive pathogens, including Legionella pneumophila, in patients who initially need intravenous therapy. Pneumonia caused by Gram-negative pathogens, with the exception of Haemophilus and Moraxella catarrhalis, were excluded from the clinical studies. Pelvic Inflammatory Disease Consideration should be given to official guidance regarding the appropriate use of antibacterial agents.

Azithromycin is a semi-synthetic azalide derivative with a 15-membered lactone ring from the group of macrolide antibiotics. Azithromycin binds to the 23S rRNA of the 50S subunit of the bacterial ribosome. It blocks protein synthesis by inhibiting the transpeptidation/translocation step of protein synthesis and by inhibiting assembly of the 50S subunit of the ribosome. This results in a primarily bacteriostatic effect.

Reference:

MHRA:
https://mhraproducts4853.blob.core.windows.net/docs/a61c1cdefd2a9c830de326ccc553f80c93acae4c

Call for reporting

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

Name: General Administration for Pharmaceutical Vigilance

Email: pv.followup@edaegypt.gov.eg

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

Hotline: 15301

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