EMA reviewing risk of dosing errors with methotrexate after cases of overdoses continued to be reported

18.06.2018 | Circular Number P08/2018

Information on Methotrexate

- Methotrexate is a cytotoxic agent that is used to treat various types of cancers (such as acute lymph). It is also used to treat various inflammatory diseases such as rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis and psoriatic arthritis
- Methotrexate can be taken orally or given by injection.

In Malta the following products are authorised through various licensing procedures

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	MAH/license holder
Methotrexate 2.5mg	Methotrexate 2.5mg film-coated tablets	Film-coated tablet	POM	AA084/05701	Remedica Limited
Methotrexate 2.5mg/ml	Methotrexate 2.5mg/ml Solution for Injection	Solution for injection	POM	AA734/00201	Hospira UK Limited
Methotrexate 25 mg/ml	Methotrexate 25mg/ml Solution for Injection	Solution for injection	POM	AA734/00202	Hospira UK Limited
Methotrexate 25 mg/ml	Methotrexate 25mg/ml solution for injection	Solution for injection	POM	MA054/06501	Accord Healthcare Limited
Methotrexate 100 mg/ml	Methotrexate 100mg per ml (5ml vial)	Concentrate for solution for infusion	POM	MA054/06502	Accord Healthcare Limited
Methotrexate 100 mg/ml	Methotrexate 100mg per ml (10ml vial)	Concentrate for solution for infusion	POM	MA054/06503	Accord Healthcare Limited
Methotrexate 100 mg/ml	Methotrexate 100mg per ml (50ml vial)	Concentrate for solution for infusion	POM	MA054/06504	Accord Healthcare Limited
Methotrexate 25mg/ml	Methotrexate Actavis	Solution for infusion or injection	POM	MA628/09201	Actavis Group PTC ehf
Methotrexate 2.5mg	Methotrexate Tablets 2.5mg	Tablet	POM	AA996/00401	Morningside Healthcare Limited
Methotrexate 100mg/ml	Methotrexate Solution for Injection 100mg/ml	Solution for injection	POM	AA734/00203	Hospira UK Limited
Methotrexate 2.5mg	Methotrexate 2.5mg Tablets	Tablet	POM	MA054/12401	Accord Healthcare Limited

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Methotrexate 10mg	Methotrexate 10mg Tablets	Tablet	POM	MA054/12402	Accord Healthcare Limited

Information from the EMA's review on risk of dosing errors with methotrexate

The Pharmacovigilance Risk Assessment Committee (PRAC) initiated the review of methotrexate at the request of Spain, under Article 31 of Directive 2001/83/EC.
The risk of dosing errors with methotrexate has been recognised for many years and several measures are already in place in some EU countries to reduce this risk, including the use of visual reminders on the medicine packs. However, a recent assessment found that serious adverse events related to overdose, including fatalities, are still occurring. The Spanish medicines regulator, AEMPS, therefore asked EMA to further investigate the reasons why dosing errors continue to occur in order to identify measures to prevent them.

- When used for inflammatory diseases methotrexate is taken once a week whereas for some types of cancer the dose is higher and the medicine is used more frequently.
- Dosing errors have led to some patients incorrectly receiving a dose every day instead of every week when methotrexate is used to treat inflammatory conditions.
- The higher doses have led to serious consequences, even fatalities in some cases.

The review of methotrexate has been initiated and is being carried out by the PRAC which will recommend whether further measures are needed to minimise risk of dosing errors. Risk of dosing errors will be issued in due course.

For more information, please see the European Medicines Agency's methotrexate press release.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on methotrexate containing products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form (available from: http://www.medicinesauthority.gov.mt/adrportal), fill and send by mail to Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or by email to postlicensing.medicinesauthority@gov.mt or to the marketing authorization holder or their local representatives.

Post-Licensing Directorate
Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this formt (address side up), stapling the ends and then posting (no stamp required)

Feedback:

We thank you for your interest and look forward to hearing your opinion.

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Pharmacovigilance Section

Post-Licensing Directorate

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