



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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New measures to avoid potentially fatal dosing errors with methotrexate for inflammatory diseases

EMA has recommended new measures to prevent serious and potentially fatal errors with the dosing of methotrexate for treating inflammatory diseases such as rheumatoid arthritis, psoriasis and Crohn's disease. The recommendations result from a review of reports that patients are using methotrexate incorrectly despite previous measures to prevent errors.

For inflammatory conditions, methotrexate must be used just once a week. Using methotrexate more frequently than intended can result in serious side effects. The review found that the error in dosing frequency can occur at any step from prescribing the medicine to the patient taking it.

The new measures to prevent errors include restricting who can prescribe these medicines, making warnings on the packaging more prominent and providing educational materials for patients and healthcare professionals. In addition, to help patients follow the once-weekly dosing, methotrexate tablets will be provided in blister packs and not in bottles (or tubes). The measures were agreed after consultation with patients and healthcare professionals.

Information for patients

- If you are taking methotrexate for rheumatoid arthritis, psoriasis or Crohn's disease, you must take it just once a week.
- Take your methotrexate medicine on the same day every week.
- Follow the instructions on the packaging of your methotrexate medicine.
- You will receive a patient card with your methotrexate tablets (or oral liquid). Read it carefully because it tells you how to take your medicine.
- Show your patient card to any new healthcare professional who treats you so that they know that you take your methotrexate medicine once a week.
- See your doctor at once if you get a sore throat, fever, mouth ulcers, diarrhoea, vomiting, skin rashes, bleeding or unusual weakness. These can be signs of taking too much methotrexate.
- Always attend your scheduled clinic visits and blood test appointments. They are important for making sure that your methotrexate medicine is working and that it is not causing any concern.
- If you are not sure about how to take your methotrexate medicine or you have any questions about it, talk to your doctor or pharmacist.

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Information for healthcare professionals

Healthcare professionals should follow these recommendations:

- Methotrexate for inflammatory conditions is intended for use just **once a week**. Serious side effects including fatalities have occurred when methotrexate is taken more often.
- Only physicians with expertise in using methotrexate medicines should prescribe them.
- Healthcare professionals who prescribe or dispense methotrexate for inflammatory conditions should:
 - read the educational materials for oral methotrexate medicines;
 - ensure that they are familiar with the latest changes to the summaries of product characteristics for methotrexate medicines used for inflammatory conditions;
 - give clear instructions to the patient (or carer) about once-weekly dosing;
 - check carefully that the patient (or carer) understands that the medicine must be used once a week, and do this each time a new prescription is issued or the medicine is dispensed;
 - decide together with the patient (or carer) on which day of the week the patient uses methotrexate;
 - counsel the patient (or carer) about signs of methotrexate overdose and give instructions to promptly seek medical advice in case of suspected overdose.

More about the medicine

Methotrexate is authorised in the EU for two different groups of indications, each with a different administration schedule:

- treatment of cancer for which the dosing frequency depends on the regimen and can involve daily administration of methotrexate;
- treatment of inflammatory diseases including rheumatoid arthritis, psoriasis and Crohn's disease, which require once-weekly use of a low dose of methotrexate.

Methotrexate can be taken orally or given by injection.

Most methotrexate-containing medicines have been authorised via national procedures. They are marketed in all EU countries under several brand names including: Ledertrexate, Maxtrex, Metex and Metoject. Jylamvo (for use by mouth) and Nordimet (for injection) are the only centrally authorised medicines containing methotrexate.

More about the procedure

The review of methotrexate medicines was initiated on 22 March 2018 at the request of the Spanish Agency for Medicines and Health Products, under [Article 31 of Directive 2001/83/EC](#).

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which made a set of

recommendations. The PRAC recommendations were sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States in due course.