HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

METHOTREXATE – NEW MEASURES TO AVOID DOSING ERRORS

Methotrexate* is authorised across the European Union for the treatment of both inflammatory diseases and cancers and is available in both oral and injectable formulations. When used in the treatment of inflammatory diseases, such as rheumatoid arthritis and psoriasis, methotrexate should be taken once a week. However, when used in the treatment of some cancers methotrexate may be taken more frequently. Errors in the prescribing or dispensing of methotrexate, as well as misunderstandings regarding the dosing schedule, have led to patients inadvertently taking the medicine daily instead of weekly for inflammatory diseases, with serious consequences, including fatality.

The risk of medication error with methotrexate is well known and several measures are already in place to reduce the risk of such errors. However, despite these measures, a recently completed safety review at EU level indicated that medication errors continue to be reported at all stages of the medication process. Information regarding the risk of medication errors with methotrexate has previously been highlighted in the HPRA's Drug Safety Newsletter on a number of occasions, most recently in the 89th Edition.

The EU review undertaken by the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) examined the available evidence and, following consultation with patients and healthcare professionals, recommended additional measures to reduce the risk of medication errors with methotrexate. The measures include introduction of educational materials for oral methotrexate products for both patients and healthcare professionals, including a patient alert card, a recommendation to restrict prescribing of methotrexate-containing medicines, and making warnings on the packaging of such medicines more prominent. In addition, methotrexate tablets will be provided in blister packs instead of bottles in order to help patients follow the once-weekly dosing. Please note that an implementation period for the introduction of blister packs for methotrexate tablets has been agreed with the companies responsible for the marketing of the products concerned. Thus, blister packs will not be immediately available for all methotrexate tablets.

Advice to Healthcare Professionals

- Only physicians with expertise in the use of methotrexate-containing medicines should prescribe them.
- Provide patients/carers with clear and complete dosing instructions on the once-weekly dosing regimen.
- Check carefully at every new prescription/dispensing that the patient/carer understands that the medicine must only be used once a week.
- Decide, together with the patient/carer, on which day of the week the patient is to use methotrexate.
- Inform the patient/carer of signs of overdose and instruct them to promptly seek medical advice in case of suspected overdose.

Key Message

Medication errors with serious consequences, including fatalities, have been reported when methotrexate intended for once-weekly use in inflammatory diseases was taken daily.

Healthcare professionals prescribing/dispensing methotrexate for inflammatory diseases should provide patients/carers with clear and complete dosing instructions and ensure that the patient/carer understands that the medicine is only to be taken once weekly.

The packaging and product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)) for methotrexate-containing products will be updated to make warnings regarding dosing errors more prominent and to reflect that the medicine is only to be prescribed by a doctor with expertise in the use of methotrexate.

Educational materials, including a patient alert card, will be developed by the companies responsible for the marketing of oral methotrexate products and will subsequently be provided to patients and healthcare professionals following approval by the HPRA.

Methotrexate tablets for weekly use will be provided in blister packs instead of bottles or tubes, when available.

A Direct Healthcare Professional Communication (DHPC) was circulated by the MAH, following approval by the HPRA, in November 2019.

All reports of suspected adverse reactions should be reported to the HPRA via the available methods (www.hpra.ie).

**Methotrexate-containing products include Jylamvo, Methofill, Methotrexate, Metoject and Nordimet. Further details are available on www.hpra.ie and www.ema.europa.eu.*