

Reminder - Oral methotrexate and risk of unintentional overdose due to medication errors

The Health Products Regulatory Authority (HPRA) would like to remind healthcare professionals of the need for vigilance when prescribing, dispensing and/or counselling patients in relation to methotrexate.

Oral methotrexate* is indicated in the treatment of active rheumatoid arthritis, adult psoriasis and in a number of oncological indications, with differing dosage regimens for the respective indications (Summary of Product Characteristics (SmPCs) available on www.hpra.ie).

For rheumatology and dermatology indications, methotrexate should be administered as a **once weekly dose only**. Patients and/or carers should be informed of the risks associated with an overdose and of the importance of adhering to once weekly dosing. For these indications, it is also suggested that the day of intake should be specified on the prescription and dispensing label.

Medication errors resulting in inadvertent overdose due to daily intake of a weekly dose have been reported in Ireland and elsewhere. These reports have included cases of serious adverse reactions, some of which resulted in a fatal outcome, particularly due to the haematological toxicity of methotrexate, but also as a result of pulmonary toxicity. Reports of medication errors have occurred in a range of areas, including prescribing and administration errors (mainly for hospitalised patients), to errors in self-administration (by patients at home, either inadvertently, or by misunderstanding the medication schedule). The HPRA would like to remind healthcare professionals of the need for vigilance when prescribing, dispensing, administering and counselling patients and/or carers in relation to methotrexate, particularly following initiation of treatment, a change in the dose, or in circumstances where therapy is re-started.

The HPRA previously highlighted the risk of inadvertent overdose due to medication errors associated with methotrexate and the recommendations to reduce this risk (HPRA Drug Safety Newsletter Edition 47) following an EU review of this issue completed in 2012. The product information (SmPC and Package Leaflet (PL)) was updated at that time to emphasise the need for adherence to once weekly dosing and to strengthen existing warnings regarding the risk of overdose. The Pharmaceutical Society of Ireland (PSI) also updated and re-issued its guidance to support safe dispensing of methotrexate around that time. A reminder of these recommendations was highlighted in the HPRA Drug Safety Newsletter edition 71 published in December 2015 and in the MIMS Compendium circulated in January 2016.

Advice to Healthcare Professionals

- Cases of overdose, sometimes fatal, due to erroneous daily instead of weekly intake of methotrexate have been reported.
- Methotrexate, for dermatology and rheumatology indications, should be taken as a single once weekly dose.
- Healthcare professionals should ensure that the patient and/or their carer understand the prescribed therapy, including the dose and frequency, with any treatment changes highlighted. Great care should be taken to give and repeat clear instructions on dosage.
- Patients and/or carers should be encouraged to read the Package Leaflet (PL) provided with their methotrexate and to discuss any concerns with a relevant healthcare professional.
- Patients and/or carers should be informed of the potential risks of serious adverse reactions in the case of overdose and of the signs and symptoms of toxicity.
- Any adverse reactions suspected to be related to a medication error with methotrexate should be notified to the HPRA in the usual way.

Key message

- Methotrexate for oral use for rheumatology and dermatology indications should be taken once a week only.
- Patients and/or carers should be informed of the risk of overdose due to erroneous daily intake of the weekly dose and should be advised to contact a healthcare professional promptly, if they consider an error in dosing has occurred.

**Further details on methotrexate products are available on www.hpra.ie*

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