Methotrexate 2.5 mg Tablets / Methotrexate 10 mg Tablets

Prescribing and Dispensing Guide for Healthcare Professionals

July 2020

Cipla

Prescribing and Dispensing Guide for Healthcare Professionals
Methotrexate 2.5 mg Tablets / Methotrexate 10 mg Tablets

The following educational material has been prepared to increase the awareness of healthcare professionals (HCPs) and patients on the risk of medication errors with methotrexate for oral use following inadvertent administration of a once daily dose instead of the once-a-week indicated dose. Severe, life-threatening and fatal cases of overdose have been reported for methotrexate oral dosage forms in those cases. These overdose cases are mainly reported in patients taking methotrexate for non-oncological indications (i.e. rheumatoid arthritis, psoriasis and Crohn's disease).

Methotrexate 2.5 mg Tablets/ Methotrexate 10 mg Tablets for oral use are indicated for:

- Active rheumatoid arthritis in adult patients.
- Severe recalcitrant disabling psoriasis, which is not adequately responsive to other forms of therapy such as phototherapy, PUVA, and retinoids, and severe psoriatic arthritis in adult patients.

In autoimmune disease indications, methotrexate must be taken **once a week**.

It is important to note that for some oncological indications, oral methotrexate is approved for once-a-week dosing as well.

This educational material for HCPs should be read in conjunction with the Summary of Product Characteristics (SmPC) for methotrexate as well as local protocols for prescribing and dispensing methotrexate in the indications relevant for this communication. The information regarding this risk of overdose due to inadvertent administration of once-daily dose instead of the once-a-week dose is included in the Special warnings and precautions for use and Overdose sections of the SmPC.

Patients with autoimmune diseases must be told that methotrexate must only be taken once a week.

Because of the possibility of severe or even fatal toxic reactions, patients should be extensively informed by the treating doctor of the risks involved (including early signs and symptoms of toxicity) and the recommended safety measures. Patients should be informed that they must notify the doctor immediately if any symptoms of an overdose occur and that the symptoms of the overdose need to be monitored (including regular laboratory tests) (See SPC section 4.4 for details). Symptoms commonly reported with overdose are hematological and gastrointestinal reactions. For example, leukopenia, thrombocytopenia, anemia, pancytopenia, bone marrow suppression, mucositis, stomatitis, oral ulceration, nausea, vomiting, gastrointestinal ulceration, gastrointestinal bleeding.

Patients should be advised to write the treatment day on their Patient Reminder Card, and to carry it with them.

Methotrexate is a cytotoxic agent, daily administration of a weekly dose can lead to overdose and to serious adverse outcomes, including death. Elderly patients are especially susceptible to serious toxicities. Despite risk minimisation measures are already in place, errors continue to be reported.

To minimize these medication error, Cipla. has included a visual reminder on the outer and immediate packaging for methotrexate tablets to emphasize once-a-week dosing.

This medication error may occur at any point in therapy.

When writing prescriptions for autoimmune diseases treatment, prescribers should:

- Include instructions for **once-a-week** dosing, including the day of the week to take medication (the day of intake should be decided with the patient).
- Do not use abbreviations.
- Specify the indication, strength and dose (in mg) within the prescription.
- Verify dosing and administration instructions for methotrexate tablets by at least two HCPs.
- Prescribers should carefully review prescribing and dosing instructions with patients/relatives/carers and indicate the specific day of the week to take medication with every new/repeat prescription.
    - Highlight the importance of taking methotrexate as prescribed (emphasize the danger with taking daily or extra doses)
    - Ask patients to repeat back the instructions for taking oral methotrexate to validate understanding
    - At each consultation the physician should judge if the patient's situation (e.g. mental status, living conditions, comorbidities, co-medications) is compatible with the method of self-administration
    - Ensure patients are aware of the "Patient reminder card". Transfer of care is a vulnerable stage in the medication process and the patient reminder card is especially helpful at this stage.
- On dispensing the pharmacist should counsel the patient about the importance of once-weekly dosing.
    - Write the day of the week for intake in the space provided on the outer packaging

- Highlight the importance of taking methotrexate as prescribed (emphasize the danger with taking daily or extra doses).
- Ask patients to repeat back the instructions for taking oral methotrexate to validate understanding and remind the patient to write it on the patient reminder card.
- Remind patients to review the patient reminder card that will be included in/with the packaging when they receive their medication from the pharmacy and contact their physician promptly if the signs and symptoms of overdose and any potential/actual medication errors occur.

Therapeutic management of overdose (SPC section 4.9): In cases of overdose, symptoms that have been commonly reported are haematological and gastrointestinal reactions. The toxicity of methotrexate affects mainly the haematopoietic organs. Calcium folinate neutralises effectively the immediate haematopoietic toxic effects of methotrexate. Parenteral calcium folinate therapy should be started within one hour of the intake of a methotrexate overdose. The dose of calcium folinate should be at least as high as the dose of methotrexate received by the patient. Massive overdose requires hydration and alkalinisation of the urine to prevent precipitation of methotrexate and/or its metabolites in the renal tubules. Haemodialysis or peritoneal dialysis has not been found to affect the elimination of methotrexate. Instead, effective clearance of methotrexate has been achieved by intermittent haemodialysis using a so-called “high-flux” dialyser. Observation of serum methotrexate concentrations is relevant in determining the right dose of calcium folinate and the duration of the therapy.

Adverse Reaction reporting

Methotrexate 2.5mg and 10mg Tablets, even at the correct dose can cause Adverse Drug Reactions and it is important to report any suspected adverse drug reaction that are serious or result in harm (even if the causal relationship is in doubt. If it is in doubt, then please state this in the report).

Healthcare professionals are encouraged to report suspected adverse reactions online via the Yellow Card website -https://yellowcard.mhra.gov.uk/, by searching for MHRA Yellow Card in the Google Play or Apple App Store or to Cipla at drugsafety@cipla.com.

If you have any questions or require additional information, please contact Cipla at 08000472144.