Guide for Healthcare Professionals

Methotrexate

2.5 mg, Tablet
Methotrexate

to minimize the risk of overdose from patients incorrectly taking methotrexate daily instead of once weekly for autoimmune diseases

SANDOZ A Novartis Division

Guide for Healthcare Professionals
Information to minimize the risk of medication error

NOTE: Special warnings and precautions for use

- Methotrexate should only be prescribed by physicians with expertise in the use of methotrexate and a full understanding of the risks of methotrexate therapy. Patients with **rheumatological or dermatological diseases** must be informed unequivocally that treatment is to be taken just **once a week and not daily.**
- Incorrect use of methotrexate can result in severe and even fatal adverse reactions.
- Medical staff and patients must be clearly instructed.

1. Purpose of this guide

This guide is provided to inform about the potential for fetal overdose due to medication errors, including daily instead of once weekly use.

The main objective of this guide is to help mitigate against the potential risk of medication errors.

Please be aware of the special warnings and precautions for use detailed on the cover of this guide. All healthcare professionals are further referred to the Summary of Product Characteristics (SmPC) and Patient Leaflet (PL) accompanying this guide for full prescribing information.

2. Prescribing methotrexate 2.5 mg tablet

Methotrexate is available as 2.5 mg tablet

Methotrexate is **taken once a week (on the same day each week)** to treat:

- Rheumatoid arthritis [RA]
- Juvenile idiopathic arthritis [JIA]
- Psoriasis

The prescribing physician is responsible for determining which patients are suitable for home or self- administration of methotrexate. Each patient/carer should be assessed to determine whether they are able to measure the dose correctly. Only after such an assessment should patients/carers start to administer methotrexate at home.

Potential causes for medication errors with this product include:
Inadvertent daily dosing (in arthritis and psoriasis indications) instead of weekly dosing

3. Prescribing the correct dose

Psoriasis

The recommended initial dose is a single dose of 7.5 mg once weekly., Depending on the individual activity of the disease and tolerability by the patient, the dose may be increased gradually by 2.5 mg per week.

Rheumatoid arthritis
Initial dose of 7.5 mg (10mg) weekly given as a single dose, with escalation of 5 mg every month up to the maximum tolerated level not exceeding 25 (30) mg/week; parenteral administration should be considered in the case of inadequate clinical response or intolerance.

Dose in children and adolescents with polyarthritic forms of juvenile idiopathic arthritis. The recommended dose is 10-15 mg/m^2 body surface area (BSA)/week. In therapy-refractory cases the weekly dose may be increased up to 20mg/m^2 body surface area/week. However, an increased monitoring frequency is indicated if the dose is increased.

4. What to discuss with patients for home use or self-administration

Direct the patient/carer to the Package Leaflet
It is important to carefully explain to patient/carer

- When and how they should take their dose
- The types of side effects/symptoms that might indicate the early signs of overdose toxicity such as bleeding, unusual feeling of weakness, ulcers in the mouth, feeling sick, vomiting, black or bloody stools, coughing up blood or vomiting blood and reduced urinary output (see section 4 of Package Leaflet) and advise them to contact a doctor/pharmacist immediately if they experience those side effects
- That they should tell their doctor immediately or contact the nearest hospital casualty department if they have any signs or symptoms of overdose (eg. bleeding etc) or if they know or suspect that they (or someone else) have taken too much methotrexate and that they should write down what they took and when

For **arthritis and psoriasis patients**, it is very important to remind the patient/carer and to be sure that they have understood:

- The need to **maintain the prescribed dosing regimen of methotrexate**
- That greater doses may be associated with an increased risk of side effects, the potential for severe side effects and even death
- That it is a **weekly regime** (methotrexate is never taken every day for arthritis or skin diseases)
- Which same **day of the week** the dose should be taken on each week
- That the tablets should be taken 1 hour before or 1.5-2 hours after a meal.

5. PHARMACISTS - Dispensing methotrexate 2.5 mg tablet)

Recommendations for dispensing:

- Always double check the prescription describes an appropriate dose
- Ensure the day of the week (in full , no abbreviations) the dose should be taken is included on the label, if appropriate
- Open the container and show the actual medication to the patient/carer
- Reiterate the dosing regime with the patient/carer
- Check to see they have understood
- The importance of adhering to the correct dose and frequency should be discussed with the patient/carer
- Refer the patient/carer to the list of side effects in section 4 of the Package Leaflet and advise that they should contact a doctor/pharmacist immediately if side effects are experienced
- Suggest that if the patient/carer does accidently make an error that they write down what they took and when and to contact a doctor immediately (“as a precaution”)

Points to consider:

- Methotrexate is never taken every day for arthritis or skin diseases, it is prescribed as a weekly dosing regime
- Weekly dosing should be taken on the **same day of the week**

6. Follow-up visits and medication errors

Patients should be monitored for signs and symptoms of overdose (these predominantly affect the haematopoietic and gastrointestinal systems), such as bleeding, unusual feeling of weakness, ulcers in the mouth, feeling sick, vomiting, black or bloody stools, coughing up blood or vomiting blood and reduced urinary output.

7. Therapeutic management of overdose

Calcium folinate is the specific antidote for neutralizing the adverse toxic effects of methotrexate. In the event of overdose, a dose of calcium folinate equal to or higher than the offending dose of methotrexate should be administered intravenously or intramuscularly within 1 hour, and dosing continued until serum levels of methotrexate are below 10^{-7} mol/L.

In the event of a massive overdose, hydration and alkalinisation of the urine may be required to prevent precipitation of methotrexate and/or its metabolites in the renal tubules. Neither haemodialysis nor peritoneal dialysis has been shown to improve the elimination of methotrexate. Effective clearance of methotrexate is reported to be achieved with acute intermittent haemodialysis using a high-flux dialyser.

8. Adverse event reporting

Methotrexate 2.5 mg tablet even at the correct dose can cause adverse reactions and it is important to report any and all adverse events (even if the causal relationship is in doubt - if it is in doubt, then please state this in the report).

The report of a suspicion on an undesirable effect after marketing authorization is of high importance. It makes a continuous monitoring of the benefit-risk-ratio of a drug possible. HCPs are requested to report every suspected case of an undesirbale effect to: The Saudi Food and Drug Authority National Pharmacovigilance Center and to Sandoz Company.

9. Where can I obtain more information?

Additional copies of this guide can be obtained by contacting the Patient Safety Department of Sandoz Company.

Please refer to SPC or PIL for further information.

This document has been approved by Saudi Food and Drug Authority (SFDA).

SANDOZ A Novartis Division

You can report any problem or adverse events or request additional copies of the materials through:
Patient Safety Department Novartis Pharma AG - Saudi Arabia -.
Toll Free Number: 8001240078
Phone: +966112658100
Fax: +966112658107
Email: adverse.events@novartis.com
Or by online: http://report.novartis.com/
Saudi Food and Drug Authority National Pharmacovigilance Center
Unified Contact Center: 19999
Fax: +966112057662
Email: npc.drug@sfda.gov.sa
Or by online: https://ade.sfda.gov.sa

يمكنك الابلاغ عن أي أعراض جانبية أو شكاوى أو لطلب نسخ اضافية من خلال:
شركة نوفارتس - السعودية - قسم سلامة المرضى:
الرقم المجاني: 8001240078
الهاتف: ٠٠٩٦٦١١٢٦٥٨١٠٠
الفاكس: ٠٠٩٦٦١١٢٦٥٨١٠٧
الايميل: adverse.events@novartis.com
أو عن طريق الإنترنت: http://report.novartis.com/

الهيئة العامة للغذاء والدواء المركز الوطني للتيقظ الدوائي:
مركز الاتصال الموحد: 19999
الفاكس: ٠٠٩٦٦١١٢٠٥٧٦٦٢
الايميل: npc.drug@sfda.gov.sa
أو عن طريق الإنترنت: https://ade.sfda.gov.sa/

EU RMP V 6.0 Feb 2021