Methotrexat "Ebewe"
2.5 mg Tablets
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 and with some of the hematological indications (as prescribed by the physician according to the treatment protocol), 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.**
- **Decide together with the patient on which day of the week the patient consumes methotrexate and request the patient to make a record of that day on the patient information card.**

1. Purpose of this guide

This guide is provided to doctors, nurses and other healthcare professionals who prescribe, dispense or work with patients who use methotrexate and is intended to ensure that the medicine is used correctly.

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 in this guide. All healthcare professionals are further referred to the Prescribing information (PI) and Patient Information Leaflet (PIL) accompanying this guide for full prescribing information.

2. Prescribing Methotrexat "Ebewe" 2.5 mg Tablets

Methotrexate is available as 2.5 mg tablets

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

- Acute lymphoblastic leukaemia and Burkitt's lymphoma
- Severe cases of uncontrolled psoriasis, unresponsive to conventional therapy.
- Adults with severe, active, classical or definite rheumatoid arthritis who are unresponsive or intolerant to conventional therapy.

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

Potential causes for medication errors with this product include:

Inadvertent daily dosing instead of weekly dosing [in arthritis, psoriasis and some of the hematological indications (as prescribed by the physician according to the treatment protocol)].

3. Prescribing the correct dose

***Acute Lymphoblastic Leukaemia*:**

Paediatric population

In acute lymphoblastic leukaemia remissions are usually best induced with a combination of corticosteroids and other cytotoxic agents.

Methotrexate 15mg/m^2, given orally once weekly, in combination with other drugs, appears to be the treatment of choice for maintenance of drug-induced remissions.

***Burkitt's Lymphoma*:**

Paediatric population

Some cases of Burkitt's lymphoma, when treated in the early stages with courses of 15mg/m^2 daily orally for five days, have shown prolonged remissions. Combination chemotherapy is also commonly used in all stages of the disease.

***Psoriasis*:**

Adults

It is recommended that a test dose of 5-10mg should be administered, one week prior to therapy to detect idiosyncratic adverse reactions.

In most cases of severe uncontrolled psoriasis, unresponsive to conventional therapy, 10-25mg orally once a week and adjusted by the patient's response is recommended.

The use of methotrexate in psoriasis may permit the return to conventional topical therapy which should be encouraged.

***Rheumatoid arthritis*:**

Adults

It is recommended that a test dose of 5-10mg should be administered, one week prior to therapy to detect idiosyncratic adverse reactions.

In adults with severe, acute, classical or definite rheumatoid arthritis who are unresponsive or intolerant to conventional therapy, 7.5mg orally once weekly. The

schedule may be adjusted gradually to achieve an optimal response but should not exceed a total weekly dose of 20mg. Once response has been achieved, the schedule should be reduced to the lowest possible effective dose.

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

Direct the patient/caregiver to the Patient Information Leaflet

It is important to carefully explain to patient/caregiver

- 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 3 of Patient Information 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 (e.g. 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 and for some of the hematological indications (as prescribed by the physician according to the treatment protocol)**, it is very important to remind the patient/caregiver 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 regimen [methotrexate is never taken every day for arthritis or skin diseases or for some of the hematological indications (as prescribed by the physician according to the treatment protocol)]
- Which same day of the week the dose should be taken on each week

5. PHARMACISTS - Dispensing Methotrexat “Ebewe” 2.5 mg Tablets

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/caregiver
- Reiterate the dosing regimen with the patient/caregiver
- Check to see they have understood
- The importance of adhering to the correct dose and frequency should be discussed with the patient/caregiver
- Refer the patient/caregiver to the list of side effects in section 4 of the Patient Information Leaflet and advise that they should contact a doctor/pharmacist immediately if side effects are experienced
- Suggest that if the patient/caregiver 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, skin diseases or some of the hematological indications (as prescribed by the physician according to the treatment protocol), it is prescribed as a weekly dosing regimen
- Weekly dosing should be taken on the **same day of the week**

6. Adverse event reporting

Methotrexat “Ebewe” 2.5 mg Tablets 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 undesirable effect.

Adverse events can be reported to the Ministry of Health via
https://sideeffects.health.gov.il/

You may also report to the registration holder, Novartis Israel LTD. at:
safetydesk.israel@novartis.com

7. Where can I obtain more information?

For further information, please refer to the Prescribing Information. Additional copies of this guide can be obtained by contacting the Novartis office, Phone number 03-9201111

This document has been determined by the Ministry of Health and the content therefore has been checked and approved in May 2023.