Methotrexate/Pfizer 2.5mg Tablets (Methotrexate Sodium)

The following educational material has been prepared to inform healthcare professionals (HCPs) and patients about the risk of incorrect use of oral methotrexate following the accidental administration of the daily dose intended for weekly use. In these cases, serious, life-threatening, and fatal overdose cases have been reported with oral forms of methotrexate. These overdose cases are primarily reported in patients receiving methotrexate for non-oncological indications (e.g., for rheumatoid arthritis and psoriasis).

Oral methotrexate is indicated for:

- A range of oncological diseases as an anticancer chemotherapy
- Psoriasis
- Rheumatoid arthritis, including Juvenile Rheumatoid Arthritis (JRA) with polyarticular involvement

It is important to note that in some countries within the European Economic Area (EEA), oral methotrexate has been approved for weekly administration and for various oncological indications.

The educational material for healthcare professionals should be used in conjunction with the Summary of Product Characteristics (SmPC) for methotrexate. Information regarding the overdose risk due to accidental daily administration of the dose intended for weekly use is included in the "Special warnings and precautions for use" and "Overdose" sections of the SmPC (please refer to the attached SmPC).

Methotrexate is a cytotoxic agent. Daily administration of the weekly dose can lead to overdose and severe adverse outcomes, including death. Elderly patients are particularly vulnerable to severe toxicities. Despite the risk minimization measures already in place, errors continue to be reported.

To minimize these medication errors, Pfizer, Inc. has included a visual reminder on the outer and immediate packaging of methotrexate tablets to emphasize the weekly administration of the dose.

This medication error can occur at any stage of the treatment. Doctors and nurses should:

- Specify the indication, strength, and dosage on the prescription for patients and pharmacists.
- Confirm the dosage and administration instructions for methotrexate tablets with at least two healthcare professionals.
- Provide clear instructions regarding oral methotrexate prescriptions:
    - To include the strength and dose in mg.
    - To provide instructions on the weekly dosing regimen, including the specific day of the week when the medication should be taken.
    - Not to use abbreviations.
- For each new or repeat prescription, doctors should carefully review the methotrexate prescribing and dosing instructions with the patients/family members/caregivers and specify a particular day of the week for taking the medication.
    - Emphasize the importance of taking methotrexate as prescribed (highlighting the risk of taking the daily dose or additional doses).
    - Ask patients to repeat the instructions for taking oral methotrexate to ensure they are understood.
    - In every counselling discussion, the doctor should assess whether the patient's condition (e.g., mental state, living conditions, comorbidities, concomitant medications) is compatible with self-administration of the medication.
    - Ensure that patients are informed about the "Patient Warning Card." Referral for care to another healthcare provider is a sensitive stage in the medication process, and the patient warning card can be particularly helpful in this case.

- Doctors, pharmacists, and nurses should advise the patient regarding the accidental daily administration of the dose instead of the weekly dose.
    - To emphasize the importance of taking methotrexate as prescribed (highlighting the risk of taking the daily dose or additional doses).
    - To ask patients to repeat the instructions for taking oral methotrexate to ensure they are understood and remind the patient to write it on the patient warning card.
    - To remind patients to check the patient warning card, which will be included in the packaging when they receive their medication from the pharmacy, and to contact their doctor immediately if any signs or symptoms of overdose appear.
    - To ensure that an appropriate rescue procedure is available (Reference: SmPC). Folinic acid is indicated for minimizing toxicity and addressing the effects of accidentally administered methotrexate overdose.

Invitation to report suspected/possible adverse drug reactions and early signs/symptoms of toxicity and potential/actual medication errors.

ADR Reporting

Suspected Adverse Drug Reactions or medication errors should be reported to the Malta Medicines Authority via the ADR reporting form, available online at http://www.medicinesauthority.gov.mt/adrportal.

The ADR reporting form can be sent by post to Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or via email to postlicensing.medicinesauthority@gov.mt.

Alternatively, adverse drug reactions can also be reported to Central Procurement & Supplies Unit, (Head Office),UB002, Industrial Estate, San Gwann - SGN3000 or via email: info.cpsu@gov.mt.