

High-Risk Medicine Standard: Methotrexate (oral)

PRINTABLE STANDARD

Last updated: 26 February 2024. **Printed copies are uncontrolled and should not be relied upon as up to date.**

Methotrexate (oral) is used in the treatment of autoimmune or inflammatory disorders such as rheumatoid arthritis and severe psoriasis. Methotrexate (oral) is also used in the treatment of malignancies as part of specialised protocols.

Methotrexate (oral) is usually taken as a **single dose once a week** (on the same day each week). The once-a-week dosage regimen is unusual compared to other medicines and has led to errors with the use of methotrexate (oral).

Catastrophic adverse events associated with methotrexate (oral) toxicity can occur following administration of methotrexate (oral) at an inappropriate frequency (for example, daily) when weekly administration was indicated or intended.

This standard outlines the minimum actions required to mitigate risks associated with methotrexate (oral) use. This standard does not contain clinical guidance on methotrexate (oral) use. This standard is to be read in conjunction with: Clinical Excellence Commission [High-Risk Medicine Standard: Anticancer medicines](#).

Minimum requirements for clinical protocols

The Drug and Therapeutics Committee must approve any clinical protocols relating to methotrexate (oral) and ensure inclusion of the following, at a minimum:

- recommended patient monitoring standards
- requirement for the dose to be confirmed with the patient prior to prescribing and checked with the patient prior to each administration
- requirements for patient and/or carer education (see *Patient information/education* section).

Governance requirements

Adherence to the requirements specified in this standard is to be monitored by governance committees (for example, Drug and Therapeutics Committee) and service managers (including, but not limited to, Directors of Pharmacy and Nurse Unit Managers). An implementation checklist is available and can be used by facilities and individual units to determine compliance with these requirements.

High-Risk Medicine Standard: Methotrexate (oral)

PRINTABLE STANDARD

Prescribing

- The clinician taking a medication history on admission is to confirm with the patient: the dose, indication and day methotrexate (oral) is administered, including the last day a dose was taken. This is to be documented in the patient's health care record (such as in a Medication Management Plan).
- A senior medical officer is to confirm the continuation of methotrexate (oral) during the admission prior to prescribing.
- The medicine name, 'methotrexate' is to be written in full for all documentation. Abbreviations such as MTX are not to be used.
- The intended dose is to be prescribed in milligrams. Doses are to be rounded to the nearest full tablet size. Where doses cannot be rounded to the nearest full tablet (for example, paediatric patients), the dose is to be discussed with the original prescriber or a pharmacist.
- When a weekly dose is prescribed, the prescriber is to clearly specify on the medication order or prescription that:
 - methotrexate (oral) is to be given once a week, written in full and not abbreviated
 - the day on which methotrexate is to be administered. For example, Methotrexate 5 mg orally once a week on TUESDAY.
- Patients admitted on methotrexate (oral), are to continue to have their methotrexate prescribed on the day that they normally take their dose unless there is rationale for changing. The rationale is to be documented in the patient's health care record and the patient informed. On discharge, the patient and/or carer is to be informed when their next dose of methotrexate is due and the next dose is to be clearly documented in the discharge summary.
- Where electronic Medication Management systems (eMM) are in use, mechanisms are to be in place to prevent inadvertent daily administration of methotrexate (oral).
- Where National Inpatient Medication Charts (NIMC) are in use, the prescriber is to cross out the days on the medication chart when methotrexate (oral) is not to be administered.
- Patients at risk of adverse effects associated with methotrexate (oral) are to be assessed and prescribed with folic acid where appropriate. Folic acid and methotrexate (oral) are not to be taken on the same day.
- The prescriber is to include the indication for treatment in all orders or prescriptions for methotrexate (oral). There are limited indications/circumstances where a more frequent dosage interval may be used. Inclusion of the indication is to alert pharmacists and nurses/midwives to any potential prescribing errors where once a week dosing was intended.

High-Risk Medicine Standard: Methotrexate (oral)

PRINTABLE STANDARD

Medication review

- All patients receiving methotrexate (oral) are to have a medication review by a pharmacist prior to supply and administration at the earliest possible time. Potential drug interactions are to also be considered during this review.
- For patients admitted at times when a pharmacist is unavailable, strategies are to be in place to ensure pharmacist review of methotrexate (oral) orders occurs. For example, deferring administration of methotrexate until a pharmacist has reviewed the medication order.
- For hospitals where there are limited or no pharmacy services on site, strategies are to be put in place to ensure pharmacist review. These might include remote review of the medication order by a pharmacist from the nearest NSW Health Pharmacy Department.

Storage and supply

- As methotrexate tablets are available in two strengths (2.5 mg and 10 mg), Pharmacy Departments are to take special precautions to minimise dispensing errors. Such precautions may include alerts on shelves, barcode scanning and/or physical separation of stock.
- Methotrexate tablets are not to be available in wards as imprest stock or as 'After Hours' supply. The medicine is to be individually dispensed per patient, and remaining supply to be removed at the end of the patient care episode.
- In hospitals where after-hours medications are obtained through access to the Pharmacy Department directly, methotrexate tablets are to be stored in a location in the Pharmacy Department that prevents after-hours access. For example, in a locked room or locked storage unit. After-hours supply is only to be provisioned by the on-call pharmacist (if available).
- For hospitals where there is limited or no pharmacy services on site, use of courier services from the nearest NSW Health Pharmacy Department may be required to deliver methotrexate (oral) on the day of intended administration.
- Methotrexate (oral) is to be dispensed for individual patients from a medication order or prescription. The dispensing label is to state the prescribed dose and day of the week it is due and include a cytotoxic warning.
- Pharmacy Departments are to supply only the amount required for the weekly dose, preferably on the day it is due.
- To reduce the risk of accidental daily dosing, the patient's own supply is not to be used. Patient's own medication is to be returned to the patient/carer to be taken home or kept in locked storage to prevent duplication of dosing through self-administration.

High-Risk Medicine Standard: Methotrexate (oral)

PRINTABLE STANDARD

Administration

- Clinicians administering methotrexate (oral) are to have an understanding of methotrexate (oral), its uses, normal dosing schedule and adverse effects to safely administer methotrexate to inpatients.
- Special handling precautions are required for methotrexate (oral) doses. Personal Protective Equipment is to be worn during any activity which has potential to cause exposure to the medicine and related waste products. Refer to the Safe Work NSW [Cytotoxic Drugs and Related Waste – Risk Management](#) and eviQ webpage [Safe handling and waste management of hazardous drugs](#) for more information.
- Administering clinicians are to confirm with the patient and/or carers the day of the week on which the patient's dose is due, the normal dose and when it was last taken prior to administering a dose of methotrexate (oral).
- Methotrexate (oral) is not to be administered from an order that does not meet the criteria described in the *Prescribing* section.
- Where a medication order is unclear, or the administering clinician has reason to query the dose or frequency, they are to contact the prescriber or a pharmacist for clarification prior to administration.
- Where the medication is charted and administration required after hours, the administering clinician is to discuss with the prescriber if the dose can be delayed until the pharmacist is available to review the order. If this is not possible, the on-call pharmacist is to be contacted.
- If a patient is unable to swallow their methotrexate (oral), an alternative route of administration is to be discussed with the prescriber and pharmacist.
- Methotrexate (oral) must NEVER be cut, crushed, dispersed or dissolved by the administering clinician. Seek advice from the pharmacist where part doses are required (for example, paediatric patients).
- An independent second person check is to be employed when administering methotrexate (oral). The second person check processes are outlined in the NSW Health Policy Directive *Medication Handling* ([PD2022_032](#)) including circumstances where a second person check is not mandated (for example, when a medicine is administered by an authorised prescriber).

Patient monitoring

- Clinical staff are to recognise signs of methotrexate toxicity or intolerance. Examples include nausea, vomiting, diarrhea, headache, fatigue and mouth sores.

High-Risk Medicine Standard: Methotrexate (oral)

PRINTABLE STANDARD

- Patients on methotrexate (oral) are to have baseline monitoring of full blood count, renal and liver function undertaken. At a minimum, baseline monitoring is to be repeated every 3 months for the duration of methotrexate (oral) treatment. Greater frequency of monitoring may be required in patients at risk of toxicity or myelosuppression.

Patient information/education

- Patients and/or carers who are discharged home on methotrexate are to receive confirmation of their current methotrexate regimen at the time of discharge. If patients have been initiated on methotrexate during admission, the patient and/or their carer are to be provided with relevant education and written information (for example, a Consumer Medicines Information leaflet) regarding methotrexate. This includes:
 - emphasis on the once a week dosage by naming the day of the week (when a weekly dose is prescribed). It is to be reinforced that additional doses of the medicine must not be taken 'as needed' for symptom control
 - actions to be taken if a dose is missed
 - information on the importance of regular monitoring tests, symptoms of toxicity and the need for early intervention if such symptoms appear
 - emphasis on the similar appearance of methotrexate (oral) and folic acid tablets (if the patient is also on this supplement) and the difference in dosage of the two medicines. For example, some tablets may be the same size, shape or colour
 - in the inpatient setting, emphasis on confirming with the administering clinician the day of the week their dose is due, their normal dose and when it was last taken prior to taking a dose of methotrexate (oral)
 - details about appropriate personal protective equipment when handling methotrexate (oral)
 - specifications regarding approved containers for disposal of cytotoxic contaminated waste
 - safe administration of methotrexate (oral)
 - how to deal with accidental ingestion
 - how to dispose of unwanted or expired supply.
- Patients and/or carers who are newly initiated on methotrexate are to also be provided individualised written information on their dosage regimen (for example, a medication list) that specifies the patient's dose and day of the week for taking the medicine.
- Professional Health Care Interpreters are to be utilised for patients and/or carers who are not fluent in English or who have hearing or visual impairments.

High-Risk Medicine Standard: Methotrexate (oral)

PRINTABLE STANDARD

Staff education

- Clinicians (where relevant to their scope of practice) are to receive education on the safe use of methotrexate when working in clinical areas where methotrexate is used. This includes the work health and safety procedures that apply to the handling of cytotoxic medications and managing cytotoxic contaminated body waste related to methotrexate. Refer to the Safe Work NSW [Cytotoxic Drugs and Related Waste – Risk Management](#) and eviQ webpage [Safe handling and waste management of hazardous drugs](#) for more information.

References

- Australian Medicines Handbook. Methotrexate (antineoplastic). [Internet]. Available from: <https://amhonline.amh.net.au.acs.hcn.com.au/chapters/immunomodulators-antineoplastics/cytotoxic-antineoplastics/antimetabolites/methotrexate-antineoplastic>. Updated July 2023. Accessed November 27, 2023.
- Therapeutic Goods Administration. Australian Product Information – Methoblastin (methotrexate). [Internet]. Available from: <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-05563-3&d=20231127172310101>. Updated October 2023. Accessed November 27, 2023.