Methotrexate - Safe use of Oral Methotrexate

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Summary  This policy replaces Information Bulletin 93/31. Policy and risk management strategies to reduce the risk of error when oral methotrexate is prescribed, dispensed and administered for the treatment of inpatients or outpatients. Oral methotrexate is considered a high alert medicine due to the potential for error with its once a week dosage regimen, which is unusual compared to the daily dosing of most other medicines.

Author Branch  Clinical Excellence Commission
Branch contact  

Applies to  Area Health Services/Chief Executive Governed Statutory Health Corporation, Board Governed Statutory Health Corporations, Affiliated Health Organisations, Public Health System Support Division, Community Health Centres, Divisions of General Practice, Government Medical Officers, Private Hospitals and Day Procedure Centres, Private Nursing Homes, Public Hospitals

Audience  Administration, medical, pharmacy, nursing

Distributed to  Public Health System, Community Health Centres, Divisions of General Practice, Government Medical Officers, Health Professional Associations and Related Organisations, NSW Ambulance Service, Ministry of Health, Public Hospitals, Private Hospitals and Day Procedure Centres, Private Nursing Homes, Tertiary Education Institutes

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POLICY FOR THE SAFE USE OF ORAL METHOTREXATE

This Policy Directive replaces Information Bulletin 93/31, Administration of Methotrexate Tablets in Public Hospitals.

It contains updated information and policy to ensure the safer use of oral methotrexate based on recent guidelines and alerts issued by the Victorian Therapeutics Advisory Group, the Institute for Safe Medication Practices (USA) and the National Patient Safety Agency (UK). This policy directive has been compiled in consultation with the Safer Medicines Group of the NSW Therapeutics Advisory Group.

1. Introduction

Methotrexate is a cytotoxic medication that is available in oral and injectable forms.

Oral methotrexate is used in the treatment of autoimmune or inflammatory disorders such as rheumatoid arthritis and severe psoriasis. It is taken either as a single dose once a week or as a divided dose at 12-hourly intervals over two days, once a week.

Oral methotrexate is also used in the treatment of malignancies as part of specialised protocols, usually at a once a week dosage.

It is never given daily, seven days a week.

The once a week dosage regimen is unusual compared to other medicines and has lead to errors occurring with the use of oral methotrexate since clinicians and patients are much more familiar with daily dosing of medicines.

Methotrexate is safe and effective when prescribed and administered at the correct dose and frequency and with appropriate monitoring. However, the drug is associated with a high rate of adverse events, sometimes resulting in fatal toxicity, particularly in cases where the once a week dosage is inadvertently exceeded.

Prescribing, dispensing and administration errors, lack of regular monitoring and poor patient awareness have been identified as contributing factors to the development of methotrexate toxicity. Some examples include:

- Prescribing daily dosage in error due to various factors eg unclear instructions from a specialist, unfamiliarity with specialist protocols, ambiguous directions from a hospital medical officer to a general practitioner, computer errors – selecting ‘once daily’ instead of ‘once weekly’.

- Prescribing of other drugs concurrently, that can result in an increase in toxicity of methotrexate eg aspirin, phenytoin, trimethoprim, trimethoprim-sulfamethoxazole combination, penicillins (not an all inclusive list).
Dispensing errors due to misinterpretation of prescription instructions, pharmacist unaware of the prescribing indication, dispensing into medication compliance aids with a daily dose instead of a weekly dose, labelling “as directed”.

Misinterpretation of a medication chart order resulting in administration of daily doses. The risk of daily dosing continuing undetected is increased when a sufficient quantity of the tablets is held in stock on the ward.

Methotrexate is a folate antagonist. Folic acid (or folinic acid) is usually prescribed to reduce the risk of methotrexate toxicity - that is, myelosuppression, elevated liver enzymes, and mucosal and gastrointestinal effects. As both tablets are yellow, caution must be exercised so as not to confuse the two tablets, particularly where the dosage instructions differ.

Poor nutritional status can increase susceptibility to methotrexate toxicity due to low folate levels.

Insufficient frequency of monitoring for adverse effects, eg blood tests for liver function and full blood counts; failure to review blood tests or to act on abnormalities.

Excessive weekly doses especially in the elderly and patients with renal impairment (methotrexate is largely eliminated by the kidney).

2. Risk Management Strategy

The following precautions provide a strategy to reduce the risk of error when oral methotrexate is prescribed, dispensed or administered for the treatment of inpatients and outpatients.

They must be observed by all medical, pharmacy and nursing staff that are involved in the supply and use of methotrexate in health care facilities. Health professionals in the community should observe the same principles.

2.1 Drug and Therapeutics Committees are to:

- Ensure that a suitable policy and procedure based on this policy directive is developed for the use of methotrexate.

- Consider the development of a list of high alert medications for the information of staff and include methotrexate on such a list.

- Ensure that the policy includes the education of staff on the risks associated with the use of methotrexate, providing awareness of:
  - The once weekly dosing regimen of oral methotrexate for most conditions;
The potentially fatal toxicity of methotrexate tablets if the prescribed once weekly dosage is exceeded;

The risk of using the patient’s own supply, and that this is not to be used. A supply brought in by a patient may provide sufficient tablets for the administration of a daily dose in error;

The presentation of methotrexate tablets in two strengths, 2.5mg and 10mg;

The symptoms of methotrexate toxicity and the need for regular monitoring.

Such education must ensure that staff in all areas are alert to these precautions as patients receiving this drug may be admitted or receive outpatient treatment for co-existing conditions.

- Review reports on incidents associated with methotrexate use to identify system deficiencies, take follow-up action as necessary and provide feedback to staff.

- Ensure that the counselling of patients is included in the policy on methotrexate. Medical, pharmacy and nursing staff may all be involved in education of the patient. Refer to 2.6 Patient Counselling.

- Ensure that the policy includes the involvement of the patient in checking processes during the prescribing and administration of the drug, such as asking the patient how often they take the medication and on which day.

2.2 Hospital management are to

Ensure that the policy on methotrexate developed by the Drug Committee is implemented.

2.3 Medical Staff

- When a weekly dose is prescribed, the prescriber must clearly specify on the medication chart or prescription that methotrexate is to be given once a week, written in full and underlined, not abbreviated, for example to “ow”, and must specify the day (or days if the dose is to be divided over two days) on which the drug is to be administered. For example, Methotrexate 5mg orally once a week on Tuesday.

- Do not choose Monday as the administration day. Mon for Monday can be mistaken for mane, meaning each morning.

- The prescriber must score out the days on the medication chart when methotrexate is not to be administered.

- As methotrexate can be prescribed at a more frequent dosage for some indications in haematology and oncology with proper patient monitoring, prescribers should include the prescribing indication in all orders or
prescriptions for oral methotrexate to alert pharmacists and nurses to any potential prescribing errors where a once weekly dose was intended.

- The prescriber must verbally inform the nurse taking care of the patient and/or the nurse in charge of the ward, that the dosage schedule is **once a week**, not daily, and that this dosage must not be exceeded. A note made in the patient’s clinical notes by the prescriber about this dosage instruction is an additional strategy.

- Medical staff must remain alert to patients presenting with symptoms that may be signs of methotrexate toxicity or intolerance. Such signs may present as, for example, breathlessness, dry persistent cough, nausea and vomiting, diarrhoea, sore throat, mouth ulcers and bruising.

- As renal impairment can result in accumulation of methotrexate, the patient’s renal status should be determined prior to and during methotrexate therapy. Where necessary, dosage should be reduced or discontinued.

- Elderly patients that have diminished hepatic and renal functions and decreased folate states may require lower doses and should be closely monitored.

- The prescriber should counsel the patient about the drug (refer to 2.6 Patient Counselling).

### 2.4 Pharmacy Staff

- As oral methotrexate is available in two strengths, that is, 2.5mg and 10mg, Pharmacy Departments should consider whether both strengths or only the lower 2.5mg strength should be stocked. If both strengths are stocked, the Pharmacy should take special precautions to prevent dispensing errors, such as warning signs on shelves and separation of stock.

- Methotrexate tablets must **not** be available in wards as imprest stock or in the After Hours Supply.

The patient’s own supply must not be used when Pharmacy is open. (Refer below in regard to after hours times).

- Methotrexate must be dispensed for individual patients, from a medication chart order or prescription. The label should state the dose and day of the week it is due and include a cytotoxic warning.

- Prior to supply being made, the pharmacist must confirm that the dosage schedule is appropriate and clearly written, and that the days on which the drug is not to be administered are scored out. If the latter has not been done, the pharmacist should score out the days on the chart.
Pharmacy should supply only the exact amount required for the weekly dose (that is, one week’s supply only, to be given over one or two days) at each dispensing, preferably on the day it is due.

Pharmacy Departments should consider the development of a fact sheet on oral methotrexate, for the information of medical and nursing staff, which can be used to accompany supplies of methotrexate tablets to wards. The fact sheet should address aspects such as dosage, administration, precautions (including drug interactions), monitoring, and symptoms of toxicity.

Pharmacists should provide counselling to patients on methotrexate, where possible (refer to 2.6 Patient Counselling).

Strategies should be in place for after hours times when the Pharmacy is closed in order to limit easy access to stock when a pharmacist has not reviewed the medication order. Suggested strategies might include:

- The on-call pharmacist should be called to attend the hospital to dispense a supply for the patient, or, if this is not possible, to confirm whether the dosage prescribed is appropriate and whether the patient’s own supply can be used in this emergency circumstance.
- Where no on-call pharmacist is available and the Pharmacy is accessed after hours, the stock on Pharmacy shelves should be flagged with a warning regarding the once a week dosage regimen.
- Where appropriate, administration of methotrexate could be deferred until a pharmacist has reviewed the medication order.

Consideration should be given to risk management strategies that can be put in place in facilities such as small rural hospitals where there are limited or no pharmacy services on site.

Strategies might include faxing the medication chart to the nearest Base Hospital Pharmacy for dispensing the medication (during opening hours); alert stickers applied to any methotrexate stock that is supplied to the smaller hospital and restrictions on location of storage; nursing staff alert to any order for methotrexate that is not written by the medical officer as “once a week”.

2.5 Nursing Staff

As is the case on every occasion that a medication is administered to a patient, the administering nurse must refer directly to the medical officer’s instructions for methotrexate on the medication chart.

Where a nurse finds a medication order to be unclear or has reason to query the dosage prescribed, he/she must contact the prescriber or a pharmacist for clarification prior to administration.
Nursing staff should be equipped to provide counselling on methotrexate to patients.

2.6 Patient Counselling

All patients receiving methotrexate should be counselled and be provided with a copy of the Consumer Medicine Information leaflet for methotrexate. Patients should also be provided individual written information on their dosage regimen that specifies the patient’s dose and names the day of the week for taking the tablet(s).

Counselling should include:

- Emphasis on the once a week dosage by naming the day of the week (when a weekly dose is prescribed). It should be stressed that additional doses of the medication must not be taken “as needed” for symptom control.

- Information on the importance of regular monitoring tests, on the symptoms of toxicity and on the need for early intervention if such symptoms appear.

- Emphasis on the similar appearance of methotrexate and folic acid tablets (if the patient is also on this supplement) and the difference in the dosage of the two medicines.

3. Other Considerations

In addition to the above specific precautions for the use of oral methotrexate, staff should remain aware, when handling this drug, of the occupational health and safety procedures that apply to the handling of any cytotoxic drug and related waste.