Guidance for Pharmacists on Safe Supply of Oral Methotrexate

Pharmaceutical Society of Ireland

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Contents

1. Introduction

The purpose of this guidance is to highlight the need for extra vigilance when dispensing methotrexate to patients. Incorrect dispensing, prescribing and use of methotrexate can result in significant patient morbidity and mortality, due to severe adverse effects, which can occur abruptly. Such cases have been reported in Ireland and elsewhere and are of concern to all individuals involved in the supply of methotrexate.

These cases have primarily related to overdosage with oral methotrexate, where errors occurred in the prescribing, dispensing or use of the drug, most commonly where the drug was taken daily rather than weekly. Other cases of patient harm have resulted from confusion between the different strengths of oral methotrexate tablets; cases of deliberate overdosage have also been reported.

Errors in dosing may, in some cases, have been compounded by a lack of monitoring for recognised side effects and symptoms of toxicity (see Table 1. Possible Sign of Methotrexate Toxicity - Warranting Immediate Reporting and Referral).

2. Methotrexate

Methotrexate is a potent immunosuppressant used in the treatment of active rheumatoid arthritis in adults, severe recalcitrant psoriasis and some oncological indications. Oral methotrexate for rheumatological and dermatological indications is administered on a **once-weekly** basis. Pharmacists play a critical role in ensuring the safe use of methotrexate, through their participation in the educating, counselling and monitoring of patients.

3. Guidance

3.1 Patient Review

- For each and every dispensing of methotrexate, the pharmacist must personally carry out a complete **review** of the patient's previous dispensed medication history (consider a specific alert on PMR to highlight patients taking methotrexate).
- This review must include an assessment of the time period since last dispensing, a thorough interactions check and a review of the use of non-prescription or herbal medicines. Relevant information should be noted on the PMR.
- It is essential to assess the patient for the occurrence of any side effects which warrant referral, particularly sore throat or other signs of infection, since the last supply of methotrexate (see Table 1. Possible Signs of Methotrexate Toxicity- Warranting Immediate Reporting and Referral).
- It is essential to regularly ascertain the patient's awareness of the necessity for regular **blood monitoring**.
- Particular care must be taken when there is any **change of medication**, either to methotrexate or other medicines, to ensure that the patient, or patient's representative, clearly understands the adjustments.

Table 1. Possible Signs of Methotrexate Toxicity – Warranting Immediate Reporting and Referral

Features of Blood Disorders	Sore Throat/Other Infections*
	Fever/Chills*
	Mouth Ulceration
	Easy Bruising or Bleeding
Liver Toxicity	Diarrhoea
	Vomiting
	Unexplained Rash
Respiratory Effects	Breathlessness
	Dry Persistent Cough

*Signs of Neutropenia, high risk of patient mortality/morbidity

3.2 Dispensing

- The **dose** should lie in the usual dose range 7.5mg - 25mg orally once weekly: any deviation from this, or the absence of an actual dosage instruction on the prescription, should be directly confirmed/ queried with the prescriber.

- If the dosage on a prescription states a once daily dose, the pharmacist must always query with the prescriber whether this is correct.

- When a prescription is issued the pharmacist should always confirm the indication for prescribing, particularly when a prescription is issued by a non-hospital based prescriber.

- The pharmacist should be familiar with the Summary of Product Characteristics (SmPC) for the methotrexate product(s) being supplied, and refer to same when necessary. These are accessible at www.hpra.ie or www.medicines.ie.

- Gloves should always be used in the handling of methotrexate tablets outside of their packaging.

- **The labelling** must be:
  - Clear and legible, using type face which is of an appropriate size to ensure that the directions are clear. “As Directed” is never a suitable term to use to instruct a patient as to how the medicine is to be taken.
  - The medicine should be labelled appropriately to cater to the individual needs of the patient.
  - It is recommended that the dose be stated on the label in number of tablets, total dose, weekly interval and day of the week on which it is to be taken i.e. Take six x 2.5mg tablets (15mg in total) **once a week on a Friday**.

- The pharmacist should be aware that prescribers are also being encouraged to specify the day of intake on the prescription. This was highlighted in the 47th edition of the IMB (now known as the Health Products Regulating Authority) Drug Safety Newsletter, April 2012, outlining the outcome of the EU review of the issue, and to ensure that pharmacy labelling is consistent with the prescription.
- Extra caution should be taken to clarify the precise dosing instructions, where a consultant/hospital prescription has been transcribed, for example on to a GMS prescription form.
- Only in exceptional circumstances should more than a month's supply of methotrexate be dispensed, at one time.
- It is recommended that in the dispensing of a month's supply of methotrexate, where appropriate for the individual patient, the medicine be divided into individual, clearly labelled, **weekly allocations**, to aid compliance and reduce confusion.
- As manual dexterity may be a problem for some patients, an individual consultation/ assessment relating to this is necessary, to ensure that they can easily open the packaging and therefore that the tablets will not be transferred to an alternative, possibly inadequately labelled, container.
- It is recommended that the strength and quantity of the medication are always **double-checked** before delivery to the patient.
- It is important to furnish the patient with the product's patient information leaflet/ package leaflet, at each dispensing, this may require the package leaflet being copied in the case of broken bulk dispensing, in accordance with current PSI guidance.
- If folic acid is also dispensed at the same time, it should be ensured that the patient can differentiate between the methotrexate and folic acid, is completely clear on the dosage regimen of this medication and appropriate clear labelling is used.
- Patients who have previously been using 10 mg strength tablets need to be carefully and sensitively advised about switching to the use of 2.5mg tablets only.
    - Challenges for some patients in changing from 10mg to 2.5mg strength tablet are acknowledged.
    - Prescribers should be informed of the pharmacy's policy with regard to using only 2.5mg strength tablets.
    - All changes should be discussed in advance with the prescriber.
    - In cases where the patient objects or is apprehensive regarding the change, liaison with the prescriber is especially important in assuring patient safety and adherence, and preventing any discrepancies in pharmacist and prescriber advice.
    - It is important to take into account that patients/carers may be more aware of the number of tablets they take, rather than the strength of tablets.

3.3 Patient Counselling and Monitoring

- The **pharmacist should personally supply** the appropriately labelled medicine to the patient/carer, and should **verbally confirm** the dosage requirements with the patient, reinforcing the labelled instructions in a clear manner. This understanding must be confirmed demonstrably by the patient/ carer.
- An offer must be made to counsel the patient every time the patient receives methotrexate, specifically discussing the importance of adhering to the correct dose and frequency, and patient awareness of side-effects/symptoms which require immediate reporting to their doctor or pharmacist (see Table 1. Possible Signs of Methotrexate Toxicity - Warranting Immediate Reporting and Referral).

- The patient/carer should be made aware of and offered the facility of the pharmacy's patient consultation area for any counselling or discussion.
- A patient information notice, to remind the patient of these key safety issues, may be helpful to provide (see Appendix 1).
- The pharmacist should highlight the importance of **safe storage** to the patient in order to reduce the risk of inadvertent poisoning.
- Emphasize with the patient the importance of **notification to other health care professionals** that they are taking methotrexate.
- Any patient presenting at a pharmacy who is known to be taking methotrexate, or indicates that they are taking the drug, should be seen by the pharmacist, irrespective of the nature of the advice being sought.
- Any adverse drug reactions suspected to be related to methotrexate should be notified to the Health Products Regulatory Authority in the usual way, including those resulting in harm to patients associated with medication errors.

4. Policies and Procedures

Within each pharmacy the superintendent and supervising pharmacists must ensure the medication safety issues for methotrexate are considered and addressed by appropriate clinical governance measures. It is therefore important that clear documented policies and procedures are in place which address relevant patient safety and risk management issues, to ensure consistent practice in the management of methotrexate.

All pharmacists and other staff must be aware of the need for extra vigilance around the supply and use of methotrexate, in particular the importance of weekly dosing and of awareness of symptoms of overdosage or toxicity.

The methotrexate policy and procedure(s) should be reviewed and updated regularly in accordance with best professional practice, annually at a minimum and as new information or guidance emerges.

Version Number	Date Issued
1	June 2012
2	January 2015

5. Self-assessment Checklist

This self-assessment checklist is a practical tool intended to aid compliance with this guidance and to assist superintendent and supervising pharmacists in drawing up the relevant policies and SOPs. The checklist captures many important elements of the guidance; it is not exhaustive and should only be used to assess pharmacy practice in combination with this guidance and all other relevant guidance and requirements.

Ask Yourself	Yes	No	N/A	Required Action
Are all members of staff aware that all medicine/ healthcare queries from methotrexate patients, or their carers, must be referred to the pharmacist?				
Does the pharmacist carry out a complete review of the patient's medication history each time they dispense methotrexate and note any relevant information in the patient's PMR?				
Are all pharmacists aware of the usual dose range for methotrexate?				
Is methotrexate stored in the dispensary in a manner which will trigger additional safety considerations?				
Are gloves always used by staff members handling methotrexate tablets?				
Are only the 2.5mg strength tablets dispensed? Are patients encouraged and supported in taking one strength only, irrespective of dose?				
Is the dose stated on the label in number of tablets, total dose, and weekly interval? Is the day of the week on which it is to be taken stated?				
Is the strength and quantity of medication always double-checked before being supplied to the patient?				
Does the pharmacist offer to dispense methotrexate in clearly labelled, weekly allocations, where appropriate?				
Does the pharmacist counsel the patient/carer each time methotrexate is dispensed to confirm their understanding on how and when to take their medicine?				
Is a SmPC for methotrexate always provided at each dispensing?				
Is the pharmacist aware of the signs of methotrexate toxicity and do they assess the patient for the occurrence of these side effects at each consultation?				

Ask Yourself	Yes	No	N/A	Required Action
Does the pharmacist counsel the patients/carers on the signs and symptoms of methotrexate toxicity and the importance of urgently seeking medical assistance if they suspect they have these symptoms?				
Does the pharmacist ensure that they provide appropriate counselling when a patient is initiated on methotrexate, when a new methotrexate patient/ their carer presents to the pharmacy and when there is a change of dosage or a change in prescriber?				
Is additional consideration given to counselling and monitoring the needs of patients on methotrexate in residential care settings e.g. nursing homes?				
Does the pharmacist liaise with the prescriber to prevent any discrepancies in pharmacist and prescriber advice?				
Is there an alert set up on the PMR to highlight patients taking methotrexate?				
Are any adverse drug reactions suspected to be related to methotrexate notified to the HPRA?				
Are there written policies and procedures in place for all aspects of the supply of methotrexate?				
Is the superintendent pharmacist and supervising pharmacist satisfied that all pharmacists practising in the pharmacy, and relevant staff members, are trained on, and following, the policies and procedures?				

Appendix 1 : Patient Information Template

Using Your Methotrexate Safely

- Your methotrexate medicine should only be taken ONCE WEEKLY, on the same day each week.
- As you are taking methotrexate, there is a risk that this medicine can sometimes cause serious adverse effects that need immediate attention from your doctor.
- The following is a list of SOME of the signs/symptoms that you should tell your doctor or pharmacist about IMMEDIATELY.

Warning Signs and Symptoms
Sore Throat/Other Infections
Fever/Chills
Mouth Ulceration
Easy Bruising or Bleeding
Diarrhoea
Vomiting
Unexplained Rash
Breathlessness
Dry Persistent Cough

If you have any questions about methotrexate or any other medicine you are taking, please ask your pharmacist. They will be happy to help you.