Health and Social Care Board

Interface Pharmacist Network Specialist Medicines

Methotrexate oral (adult)

Dermatology / Gastroenterology / Immunology / Neurology / Ophthalmology / Respiratory / Rheumatology shared care guideline.

Specialist details	Patient identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

Introduction

This shared care guideline refers to the use of methotrexate in the treatment of NON-CANCER CONDITIONS ONLY.

Licensed indications: rheumatoid arthritis, psoriasis.
Unlicensed indications: psoriatic arthritis, severe eczema, chronic urticaria, connective tissue disease (cutaneous and systemic lupus, scleroderma), myositis, vasculitis, blistering conditions, dermatomyositis, sarcoidosis, lymphomatoid papulosis, refractory Crohn's disease, severe refractory asthma, inflammatory eye disease, inflammatory neuropathies.

Adult dosage and administration

The dose is variable with the usual range being between 5mg and 25mg **once a week**. Treatment is generally started at a dose of 10 - 15mg and increased gradually as determined by the specialist. A weekly dose of 25mg should in general not be exceeded. Doses outside these ranges may be considered with prior agreement of initiating specialist and GP.
Once weekly dosing – specify day of administration (not Monday).
Dose reduction should be considered in frail elderly patients or if there is significant renal or hepatic impairment.
Available as: always prescribe methotrexate in multiples of the 2.5mg tablet strength.
The 10mg tablets must not be used because of previous serious incidents where doses have been confused (NPSA advice).
Where possible, tablets should be prescribed. In exceptional circumstances, a **10mg/5ml** oral solution is available – this is the standard strength that must be used
Folic acid: usual dose of 5mg once each week, taken one to two days after the methotrexate. This may reduce the risk of gastrointestinal and haematological toxicity. In some instances, dose of folic acid may vary – specialist will advise.

Hospital specialist responsibilities

- Assess patient's suitability for treatment with methotrexate.
- Agree shared care with patient's GP.
- Advise GP on dose of methotrexate and folic acid to be prescribed.
- Provide the patient/carer with relevant (written) information on use, side effects and need for monitoring of medication. Advise on need for adequate contraception.
- If the liquid formulation is used, provide training on safe handling, storage, spillage and waste disposal (provide a cytotoxic spill kit and cytotoxic sharps box if necessary).
- Provide pre-treatment information as per NPSA methotrexate monitoring record booklet (can be ordered from pharmacystationeryorders@hscni.net).
- Undertake baseline tests as indicated in monitoring table.
- Review results of safety monitoring and request additional tests as required.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required.

Monitoring table		Hospital specialist	GP			Hospital specialist
			During Treatment			
Test	**Indication**	Pre-treatment baseline	Until on stable dose for 6 weeks	Next 3 months	Thereafter *	Annual review
FBC LFTs U&Es, eGFR	Baseline assessment, dose adjustment	✓	Every 2 weeks	Every month	Every 3 months*	As part of annual review or as clinically indicated
ESR/CRP (Rheumatology and Gastroenterology only)	Disease activity scoring	✓	Every 3 months			
Height & weight PIIINP (Dermatology only)	Baseline assessment	✓	Not routinely required			If clinically indicated
Blood pressure Chest x-ray PFTs, TB screening if indicated	Baseline assessment, respiratory and TB screening	If clinically indicated				
Ask about oral ulceration, sore throat, unexplained rash or unusual bruising/bleeding		✓	At every consultation			✓

If a further DMARD is added as combination therapy, or the dose is increased, the initial starting schedule should be reinstated. There may be clinical circumstances where the frequency of monitoring may vary and this should be specified by the initiating specialist.

* If used in combination with leflunomide, monthly monitoring should continue. Patients who have been stable for 12 months can be considered for reduced frequency monitoring on an individual patient basis.

GP responsibilities

- Prescribe methotrexate (2.5mg tablets only) once each week (specify day not Monday). “As required” or “as directed” are **unsuitable** dosage instructions for oral methotrexate.
- Prescribe folic acid as specified by the hospital specialist.
- Arrange and record ongoing monitoring as advised by specialist (see monitoring table), ensuring practice systems are in place to recall patients for monitoring blood tests.
- Prevent ongoing prescription if patient is not compliant with monitoring. Liaise with specialist if appropriate.
- Report any adverse drug reactions to initiating specialist and the usual bodies (e.g. MHRA/CHM).
- Ensure no drug interactions with other medicines.
- Check patient is using adequate contraception.
- Administer **inactivated** influenza vaccine annually unless otherwise advised by the initiating specialist.
- Check patient has had ONE DOSE of pneumococcal vaccine (revaccination is not recommended except every five years in patients whose antibody levels are likely to have declined more rapidly e.g. asplenia), see BNF or Green Book.
- Passive immunization using varicella immunoglobulin (VZIG) should be considered in non-immune patients if exposed to chickenpox or shingles. Contact Regional Virus Laboratory, Royal Group of Hospitals, duty virologist 07889 086 946 for advice if exposure is suspected. For other queries eg. those concerning exposure, infection or any recommendations relating to healthy susceptible household contacts, consult the Green Book and/or take additional advice from Regional Virus Laboratory, Royal Group of Hospitals.
- Ask about oral ulceration/sore throat, unexplained rash or unusual bruising/bleeding at every consultation.

Withhold methotrexate and contact specialist if:

- WCC < 3.5 x 10^9/L
- Neutrophils < 1.6 x 10^9/L
- Unexplained eosinophilia > 0.5 x 10^9/L
- Platelets < 140 x 10^9/L
- MCV > 105fL, (check B12 & folate & TFT)
- AST/ALT > 3 times the upper limit of normal (for results between 2 - 3 x ULN, continue methotrexate, repeat bloods and seek specialist advice). Minor elevations of AST/ALT are common
- If renal impairment develops
- Unexplained fall in serum albumin
- Oral ulceration / sore throat
- Unexplained rash / abnormal bruising
- New or increasing dyspnoea or dry cough.

Normal reference range may vary slightly between labs.
Results should be recorded in the patient's NPSA methotrexate monitoring record booklet.
Please note an unusual fall or rise or a consistent downward or upward trend in any value should prompt review of the patient and extra vigilance. Some patients may have abnormal baseline values, specialist will advise.

Adverse effects, precautions and contraindications

Infection. Immunosuppressants can increase susceptibility to infection. It is advisable not to commence or continue treatment with methotrexate when patients have a confirmed or established local or systemic infection. It is advisable to recommence once the infection has been treated. Precise period of discontinuation depends on the nature and severity of infection and the activity of the underlying disease.
Blood disorders: leucopenia, thrombocytopenia, anaemia. GPs should be alert to any unexplained bruising/bleeding.
Hepatotoxicity: methotrexate may be hepatotoxic, particularly at high cumulative dosages.
Cancer risk. Patients receiving long-term immunosuppressive drugs are at increased risk of developing a malignancy. The most frequently occurring types are lymphoma and skin malignancy. The avoidance of excessive exposure to the sun, and the use of high factor sunscreen and protective clothing are advised. Adherence to population screening programmes is particularly important in this population.
Nausea, dizziness and headache may be encountered, and may resolve with dose reduction and in the case of nausea, addition of anti-emetic medication.
Alopecia, stomatitis, diarrhoea: contact the initiating specialist if severe or persistent.
Respiratory function. Infrequently, methotrexate can cause interstitial pneumonitis, pulmonary oedema and fibrosis. Patients complaining of unexplained dyspnoea or unexplained non-productive cough should be referred immediately to the initiating specialist.
Alcohol: patients should be advised that alcohol consumption should be avoided or kept well within recommended safe national guidelines, due to the increased potential for liver toxicity.
Contraindications include:

- Immunodeficiency syndrome
- Severe renal or hepatic impairment
- Active, chronic or recurrent infections especially respiratory or urinary tract
- History of alcohol abuse/cirrhosis
- Untreated folate deficiency
- Ulcers of the oral cavity and known active gastrointestinal ulcer disease
- Severe anaemia, leucopenia or thrombocytopenia.

Pregnancy / contraception. Methotrexate at any dose should be avoided in pregnancy. A reliable form of contraception should be used by men and women whilst on methotrexate and for at least 3 months after discontinuing it. In women treated with methotrexate within 3 months prior to conception, folic acid supplementation (5mg/day) should be continued prior to and throughout pregnancy. In the case of accidental pregnancy on methotrexate, the drug should be stopped immediately, folic acid supplementation (5 mg/day) continued and refer to initiating specialist.
Breast feeding. Women being treated with methotrexate should not breastfeed.
Live vaccines. Consult the Green Book and take additional advice from initiating specialist if required.

Common drug interactions

Trimethoprim or **co-trimoxazole** increase the risk of pancytopenia. Do not co-prescribe except on specialist advice.
Co-prescription of **drugs with potential hepatotoxic effects** is not advisable eg retinoids.
Ciclosporin: increased risk for nephrotoxicity - can be prescribed concomitantly on specialist advice.
NSAIDs & aspirin (<300mg) may reduce excretion of methotrexate. Clinically significant interactions between NSAIDs and methotrexate are rare but clinicians should be vigilant. Additional monitoring may be required.
Clozapine: increased risk of agranulocytosis.
Leflunomide: increased risk of toxicity.
Herbal remedies: avoid if possible due to unknown interaction potential.

Communication

For any queries relating to this patient's treatment with oral methotrexate, please contact the specialist named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC or the BNF

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