Health and Social Care Board

Interface Pharmacist Network Specialist Medicines

Methotrexate oral (paediatric & adolescent)

Dermatology / Gastroenterology / Ophthalmology / Rheumatology shared care guideline.

This guideline is relevant to the care of children and adolescents up to the age of 18 or until they transition to adult services.

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.**

Unlicensed indications: juvenile idiopathic arthritis (JIA), juvenile dermatomyositis, vasculitis, SLE, localised scleroderma, systemic sclerosis, sarcoidosis, Crohn's disease, severe uncontrolled psoriasis unresponsive to or intolerant to conventional therapy, eczema, scleroderma, inflammatory eye disease.

Paediatric & adolescent dosage and administration

Indications	**Dosing schedule** (BNFc September 2016)
JIA, juvenile dermatomyositis, vasculitis, inflammatory eye disease, SLE, localised scleroderma, systemic sclerosis and sarcoidosis	Child 1 month - 18 years: 10 - 15mg/m^2 once weekly initially, increased if necessary to max 25mg/m^2 once weekly
Maintenance of remission of severe Crohn's disease	Child 7 - 17 years: 15mg/m^2 (max 25mg) once weekly. Dose reduced according to response to lowest effective dose
Severe uncontrolled psoriasis unresponsive to or intolerant to conventional therapy	Child 2 - 17 years initially 200micrograms/kg (max 10mg) once weekly increased according to response to 400micrograms/kg (max 25mg) once weekly. Stop treatment if inadequate response after 3 months at the optimum dose
Body surface area tables can be found in BNFc	

The dose is adjusted by specialist according to response. Doses outside these ranges may be considered with prior agreement of initiating specialist and GP. Lower doses should be used if there is significant renal or hepatic impairment.

Once weekly dosing – specify day of administration (not Monday).

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 and 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 risk of gastrointestinal and haematological toxicity. In some instances dose of folic acid may vary - specialist will advise.

Hospital specialist responsibilities

- Agree shared care with patient's GP and document in patient's notes.
- 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 appropriate.
- 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.
- Check vaccination history as live vaccines cannot be given while on immunosuppressant treatment.
- Zoster immune status: if non-immune, consider immunisation prior to starting treatment.
- 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.

<table>
<tr><th colspan="2">Monitoring table</th><th>Hospital specialist</th><th colspan="2">GP</th><th>Hospital specialist</th></tr>
<tr><th rowspan="2">Test</th><th rowspan="2">Indication</th><th rowspan="2">Pre-treatment baseline</th><th colspan="2">During treatment</th><th rowspan="2">Annual review</th></tr>
<tr><th>Month 1 - 3</th><th>After month 3</th></tr>
<tr><td>FBC
LFTs</td><td>Baseline assessment, dose adjustment</td><td rowspan="3">✓</td><td rowspan="2">Every 2 – 4 weeks (as advised by specialist)</td><td rowspan="2">Every month</td><td rowspan="3">As part of annual review or as clinically indicated</td></tr>
<tr><td>ESR/CRP
(Rheumatology and Gastroenterology only)</td><td>Disease activity scoring</td></tr>
<tr><td>Serum creatinine</td><td>Dose adjustment</td><td colspan="2">Every six months</td></tr>
<tr><td>Height & weight
PIIINP
(Dermatology only)</td><td>Baseline assessment</td><td>✓</td><td colspan="2" rowspan="2">Not routinely required</td><td rowspan="2">If clinically indicated</td></tr>
<tr><td>Blood pressure
Chest x-ray
PFTs, TB screening if indicated</td><td>Baseline assessment, respiratory and TB screening</td><td>If clinically indicated</td></tr>
<tr><td colspan="2">Ask about oral ulceration, sore throat, unexplained rash or unusual bruising/bleeding</td><td>✓</td><td colspan="2">At every consultation</td><td>✓</td></tr>
<tr><td colspan="6">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</td></tr>
</table>

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 if appropriate.
- Administer **inactivated** influenza vaccine annually unless otherwise advised by the initiating specialist. Note the live formulation (eg. Fluenz Tetra®) must not be used.
- Check patient has received pneumococcal vaccine according to BNF or Green Book schedule.
- Provide varicella zoster vaccination if requested by specialist prior to treatment. 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 and anaemia. GPs should be alert to any unexplained bruising or 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. Where applicable, patients are advised that alcohol consumption should be avoided or kept to a minimum, 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
- Severe anaemia, leucopenia or thrombocytopenia
- Ulcers of the oral cavity and known active gastrointestinal ulcer disease.

Pregnancy / contraception. Where applicable for sexually active young patients, 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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