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Health and Social Care

Department of Health
An Roinn Sláinte
Männystrie O Poustie
www.health-ni.gov.uk

Interface Pharmacist Network
Specialist Medicines

Methotrexate oral (paediatric & adolescent)

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.**

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

Paediatric & adolescent dosage and administration

Indications	Dosing schedule
JIA, juvenile dermatomyositis, vasculitis, uveitis, SLE, localised scleroderma, 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 psoriasis unresponsive 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). See MHRA advice on preventing inadvertent daily dosing.
Available as: 2.5mg tablets. Always prescribe 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, a10mg/5ml oral solution is available via Rosemont this is the standard strength that **must** be used.
Carers should wear single-use gloves to handle methotrexate tablets. Anyone handling the tablets should wash their hands immediately afterwards.Pregnant people, including patients and carers, should avoid handling methotrexate.
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

- Assess if the patient is suitable for treatment with methotrexate.
- Agree shared care with patient's GP.
- Varicella Zoster immune status: if non-immune, consider immunisation prior to starting treatment.
- 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 and advice on preventing inadvertent daily dosing ensuring that the patient/carer understands the dosing schedule and is able to follow it. See MHRA advice on preventing inadvertent daily dosing.
- Photosensitivity reactions are known side effects of methotrexate treatment and can be severe. Advise patients to take precautions to protect their skin in the sun. See MHRA advice on photosensitivity precautions.
- 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).
- Undertake baseline tests as indicated in monitoring table.
- Check vaccination history as live vaccines cannot be given while on immunosuppressant 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">At review</th></tr>
<tr><th>Until on stable dose for 6 weeks</th><th>Thereafter</th></tr>
<tr><td>FBC
LFTs
U&Es, eGFR</td><td>Baseline assessment, dose adjustment</td><td>✓</td><td>Every 2 – 4 weeks (as advised by specialist)</td><td>Every 3 months</td><td rowspan="2">As part of review or as clinically indicated</td></tr>
<tr><td>ESR/CRP
(Rheumatology and Gastroenterology only)</td><td>Disease activity scoring</td><td>✓</td><td colspan="2">Every 3 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 /JAK 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. See MHRA advice on preventing inadvertent daily dosing.
- 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.
- Follow-up any non-compliance with the monitoring schedule. The risks of cessation of therapy versus risks of toxicity should be considered. Contact the specialist if treatment is stopped or further advice required.
- 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 COVID 19 vaccination as appropriate as per local arrangements and Green Book.
- Post exposure prophylaxis (antivirals or VZIG if antivirals are contraindicated) should be considered in non-immune at risk patients if exposed to chickenpox or shingles. Contact the consultant virologists, Regional Virus Laboratory, Royal Group of Hospitals on 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 < 120 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 (not always appropriate to stop but may need dose adjustment)
- Unexplained fall in serum albumin
- Oral ulceration / sore throat
- Unexplained rash / abnormal bruising
- New or increasing dyspnoea or dry cough
- Persistent diarrhoea (can be a sign of toxicity).

Normal reference range may vary slightly between labs.
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 and photosensitivity have been reported. Photosensitivity reactions are known side effects of methotrexate treatment and can be severe. Patients should be advised to take precautions to protect their skin in the sun.
See MHRA advice on photosensitivity precautions.
Stomatitis: contact the initiating specialist.
Diarrhoea: contact the initiating specialist if severe or persistent.
Respiratory function. Infrequently, methotrexate can cause interstitial pneumonitis, pulmonary oedema . 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
- Ulcers of the oral cavity and known active gastrointestinal ulcer disease.
- Severe anaemia, leucopenia or thrombocytopenia

Pregnancy / contraception. Where applicable for sexually active young patients, Methotrexate at any dose should be avoided in pregnancy. Patients planning to become pregnant should be referred to the initiating specialist at the earliest opportunity. A reliable form of contraception should be used by women whilst on methotrexate and for 3 months after discontinuing it (one month if specialist advice).
In unintended pregnancy on methotrexate, the drug should be stopped immediately, folic acid supplementation (5 mg/day) continued and refer to initiating specialist.
In women treated with low-dose (≤ 25 mg/week) methotrexate within one month prior to conception, folic acid supplementation (5 mg/day) should be continued up to 12 weeks of pregnancy.
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** 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 at www.medicines.org.uk or the BNF

Date Prepared: June 2023 (Updated July 2025) **Date of review**: June 2028