NHS
Shropshire
Clinical Commissioning Group

Essential Shared Care Agreement for Methotrexate (Oral and Parenteral) for dermatological indications

This local safety monitoring schedule supports clinicians providing shared care under the Local Enhanced Service for High Risk Drug Monitoring (formerly Near Patient Testing)
This shared care agreement outlines suggested ways in which the prescribing responsibilities can be shared between the specialist and GP. GPs are invited to participate. If the GP feels that undertaking the roles outlined in the shared care agreement is outside their area of expertise or have clinical concerns about the safe management of the drug in primary care, then he or she is under no obligation to do so. In such an event, clinical responsibility for the patient's health remains with the specialist. If a specialist asks the GP to prescribe, the GP should reply to this request as soon as practicable. Sharing of care assumes communication between specialist, GP and patient.

Consultant details	GP details	Patient details
Name:	Name:	Name:
Address:	Address:	NHS Number:
Email:	Email:	Date of birth:
Contact number:	Contact number:	Contact:

Signing indicates agreement with the responsibilities suggested in this document, and that the patient has been informed of the need to report any issues with their treatment to their doctor.

Specialist signature: **Date:**	**General Practitioner signature:** **Date:**

Introduction

Methotrexate is an anti-metabolite and folate antagonist.

Licensed indications: severe psoriasis unresponsive to conventional therapy
Unlicensed indications: scleroderma; Crohn's disease[i]

For **rheumatological** indications, please refer to the separate rheumatology ESCA.

Adult dosage and administration

Dermatology: usual dose range is 7.5 mg to 15 mg ONCE each week, starting with 2.5 mg to 10 mg ONCE weekly increased according to response in steps of 2.5 mg to 5 mg at intervals of at least 1 week. Max. weekly dose 30 mg.

Always prescribe oral methotrexate in multiples of 2.5 mg tablet strength.
The 10 mg tablets must NOT be used.
Patients on subcutaneous methotrexate may have supplies made through the hospital via a homecare company.

Once weekly dosing – it is good practice to specify the day of administration on the prescription. Monday should be avoided as this has been misread as 'morning'.

Dose adjusted, as recommended, 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 in the frail elderly or if there is significant renal or hepatic impairment.
Methotrexate may take up to 12 weeks to take effect, so steroids/NSAIDs may be needed initially.

Folic acid: Folic acid is always co-prescribed alongside methotrexate, to reduce the risk of gastrointestinal and haematological toxicity. A typical dose is 5mg once each week, taken two to three days after methotrexate dose. Sometimes the dose/frequency of folic acid is increased and occasionally folinic acid is used instead.

Specialist responsibilities

- Discuss with the patient options for treatment and the suitability of methotrexate, including the potential benefits and side-effects of treatment.
- Provide the patient/carer with relevant (written) information on use, side-effects and need for monitoring of infection. **Advise on need for effective contraception.**
- **Varicella Zoster –** consider immunisation of non-immune patients before starting immunosuppression (after discussion with appropriate specialist)
- Ask the GP whether they are willing to participate in shared care, and who will discuss this with the patient.
- Arrange pre-treatment baseline investigations either in secondary or primary care.
- Baseline tests:[ii]
    - **FBC**
    - **LFT**
    - **U&E** (incl. creatinine)
    - **Chest X-ray** (pulmonary function tests may be considered in select patients)
    - **Type III procollagen (PIIINP)** (dermatology only- baseline test and at hospital review)[ii]

- Titrate methotrexate to an effective dose. Review results of safety monitoring and request additional tests as required. If both GP and consultant feel it is appropriate, shared care may be initiated before the patient is stabilised on the effective dose, as long as the dose is stable until the next Specialist appointment.
- When prescribing, ensure the exact day of the week for dosing is clearly specified.
- Provide patient with handheld monitoring booklet and record baseline results
- Monitor disease response to treatment and need to continue therapy
- When transferring to primary care, provide GP with clear written advice on required dosage and frequency of both methotrexate and folic acid, written monitoring guidelines and drug information. Check for interactions with other medicines.
- Continue to review the patient at agreed specified intervals (at least annually), sending a written summary to the GP whenever the patient is reviewed, including advice on dosage adjustment and when and how to stop treatment.
- Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition, and ensure that clear backup arrangements exist for GPs to obtain advice and support.
- Provide any other advice or information for the GP if required
- Report adverse events to the MHRA via Yellow Card Scheme

Primary Care responsibilities

- Notify the specialist within 2 weeks whether they agree to enter into shared care.
- Ensure the correct formulation of methotrexate is prescribed. Parenteral methotrexate is usually prescribed by the hospital specialist only (and should be added to the "hospital only" section of the medicines list).
- **Oral and parenteral methotrexate must <u>not</u> be prescribed concomitantly.**
- Prescribe oral methotrexate (2.5 mg tablets only) to be taken ONCE each week, specifying the day as outlined above (not on Monday). Ensure an oral methotrexate dose is prescribed as XX tablets of 2.5 mg; "as required" or "as directed" dosing instructions are unsuitable.
- Ensure no drug interactions with other medicines
- Check patient is using effective contraception, if appropriate
- Arrange and record ongoing monitoring as agreed with specialist:[i]
    - **FBC, U&E and LFT**
        - Every 2 weeks until 6 weeks after last dose increase and provided it is stable, monthly thereafter. Once the patient is stabilised, in consultation with the specialist, this monitoring interval may then be increased to every 2-3 months
- **Repeat prescriptions should be removed from the surgery repeats pile and retained separately for prescribers to review prior to signing. Maximum 28 days' supply.**

- Continue prescribing for patients receiving regular appropriate blood monitoring with monitoring results within acceptable range.
- Administer influenza vaccine annually unless otherwise advised by the initiating specialist
- Check patient has had ONE DOSE of pneumococcal vaccine (revaccination is not recommend except every five years in patients who antibody levels are likely to have declined more rapidly (e.g. asplenia) – see BNF or Green Book.
- Passive immunisation using Varicella immunoglobulin (VZIG) should be considered in non-immune patients if exposed to chickenpox or shingles.
- Report any adverse drug reactions to initiating specialist and the usual bodies (e.g. MHRA)
- Any dosage change should be followed by an FBC one week later
- Ask about oral ulceration/sore throat, unexplained rash or unusual bruising at every consultation
- If patient develops symptoms/signs of systemic infection, this should be treated promptly and methotrexate withheld until the infection has cleared.
- Ensure a clinician updates the patient's record following specialist review.

Withhold methotrexate and contact specialist if:

- WCC <3.5 x 10^9 /L
- Neutrophils <2 x 10^9 /L
- AST/ALT/ALP/GGT >2 times the upper limit of normal (minor elevations are common)
- eGFR <30 ml/min/1.73m^2
- Unexplained fall in albumin (in absence of active disease)
- New or increasing dyspnoea or cough (contact on call Med Reg if pneumonitis strongly suspected)
- MCV >105 fL – withhold and check serum B12, folate and TFT and discuss with specialist team is necessary
- Oral ulceration/sore throat
- Unexplained rash or bruising
- Nausea and vomiting, diarrhoea
- Established local or systemic infection

Please note: a rapid increasing or decreasing trend in any values should prompt caution and extra vigilance. Some patients may have abnormal baseline values, specialist will advise. Results should be recorded in the patient's monitoring booklet.

Adverse effects, precautions and contra-indications[iii]

Myelosuppression & decreased resistance to infection: especially respiratory/ urinary tract or shingles/chickenpox. Temporarily withhold methotrexate if patient is systemically unwell with significant infection requiring anti-infective intervention.

Hepatotoxicity: methotrexate may be hepatotoxic, particularly at high cumulative dosages.

Nausea: commonly encountered, may resolve with dose reduction and/or 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. **If pneumonitis strongly suspected, urgently contact specialist team.**

Alcohol: patients are advised that alcohol consumption should be avoided or kept to a minimum (well below 14 units weekly for women, or 21 units for men), due to the increased potential for liver toxicity. It is recommended that no more than 4-6 units of alcohol per week are consumed by patients receiving methotrexate.

Vaccines: Avoid immunization with live vaccines during treatment, and consider live vaccines prior to commencing methotrexate (see Green Book re zoster vaccine).

Contraindications include:

- Hypersensitivity to methotrexate
- Severe renal (CKD stage 5) or hepatic impairment
- Chronic or recurrent infections especially respiratory or urinary tract
- Severe anaemia, leucopenia or thrombocytopenia
- Untreated folate deficiency
- History of alcohol abuse/cirrhosis

Pregnancy: female patients must be advised not to conceive whilst receiving methotrexate. A reliable form of contraception should be used by men and women whilst on methotrexate and for at least 6 months after discontinuing it. Discontinue methotrexate and refer immediately if a patient or partner discovers they are pregnant whilst taking methotrexate.
Breast Feeding: Women being treated with methotrexate should not breastfeed.

Common drug interactions

Do **NOT** prescribe concomitant **trimethoprim** or **co-trimoxazole** due to risk of pancytopenia

Co-prescription of drugs with potential hepatotoxic or nephrotoxic effects is not advisable. Many medicines can affect the methotrexate transport function of renal tubules, therefore it is recommended that the relevant SPC is consulted.[iii]

NSAIDs & Aspirin (<300mg): unlikely to cause any clinically significant adverse effects and treatment can be continued

Herbal remedies: avoid if possible due to unknown interaction potential

Clozapine may cause increased risk of agranulocytosis

Communication

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

This information is not inclusive of all prescribing information, potential adverse effects and drug interactions Please refer to full prescribing data in the Summary of Product Characteristics (www.medicines.org.uk) or the British National Formulary (www.bnf.org)

Adapted with permission from work by MG, NHS Telford and Wrekin CCG Medicines Management

[i] British National Formulary, Edition 68, Section 1.5.3 and 13.5.3, Methotrexate

[ii] Suggestions for Drug Monitoring in Adults in Primary Care. NHS UKMi, February 2014. Available at www.evidence.nhs.uk

[iii] Maxtrex Tablets 2.5mg – Summary of Product Characteristics. Available at www.medicines.org.uk/emc/medicine/6003