SHARED CARE AGREEMENT

Name of medicine Methotrexate oral & subcutaneous

Indication For the treatment of adults with inflammatory rheumatic, bowel and skin conditions

Version: **2.0** **Approval date: December 2022** **Review date: December 2025**

The Shared Care Agreement (SCA) is intended to facilitate the accessibility and safe prescribing of complex treatments across the secondary/primary care interface. It does not contain all of the relevant product information, which should be sought using the current British National Formulary and manufacturer's Summary of Product Characteristics. The SCA must be used in conjunction with the NHS Lothian Procedure for the Shared Care of Medicines, available here.

Roles and responsibilities

Listed below are specific responsibilities that are additional to those included in the NHS Lothian Policy and Procedures for Shared Care. Please refer to the policy for core roles and responsibilities that apply to all Shared Care Agreements.

Consultant

- Assessing the need for methotrexate therapy
- Undertaking and assessing the relevant baseline investigations
- Stating the target dose
- Arranging for the patient to receive verbal and written information on oral or subcutaneous methotrexate and to receive education on self-administration of the Metoject® pre-filled pen if required.
- Counselling patients on the risk of methotrexate in pregnancy and the need for contraception in women of child bearing potential
- Treatment will be initiated by the consultant and the supply made by secondary care for the first 8 weeks. During this time the specialist service will provide comprehensive patient support including monitoring for adverse effects, addressing any treatment-related issues and responding to patient queries.
- Making arrangements for the results of blood tests to be reviewed during the initial 6 weeks of treatment with methotrexate
- Making arrangements for the patient to be reviewed 3-4 months after initiation of treatment to assess response
- Providing advice to the GP regarding monitoring, adverse effects and dose modifications when required
- Making arrangements for the patient to be kept under long term review
- Providing initial sharps bin for the safe disposal of used methotrexate injections.
- Ensure appropriate folate supplementation prescribed on initiation of methotrexate.
- Specialist service to refer patients for vaccinations which are out with routine vaccination schedules or recall programmes via the clinician referral form (http://intranet.lothian.scot.nhs.uk/Directory/publichealth/Immunisation/Pages/VTP-(Vaccine-Transformation-Programme).aspx). Please note that Patient Specific Directions (PSD) are required for bespoke vaccination schedules where there is no PGD in place. The referral forms should be sent to the partnership that is responsible for administering vaccinations to their residents.

General Practitioner and primary care non-medical prescribers

- Prescribing methotrexate after the initial 8 week supply provided by secondary care
- On initiation of treatment, the specialist service will provide patients with pre-labelled forms for blood tests.
- Bloods are taken in primary care and reported to the specialist service during the first 6 weeks of treatment. The GP is to arrange for blood tests to be taken at appropriate intervals thereafter as detailed in "Monitoring"
- Arranging for blood tests to be taken during the initiation period, when switching from oral to s/c and at appropriate intervals thereafter as detailed in `Monitoring` on page 3.

- Monitoring for side effects as detailed in the manufacturer's Summary of Product Characteristics and "Monitoring" on page 3 after the first 8 weeks of treatment
- Advising on a suitable form of contraception where relevant
- Encourage participation in relevant national cancer screening programmes
- A suitable purple-topped (cytotoxic) sharps bin (e.g. 4 litre size) will usually be provided directly from the patient's usual community pharmacy. If the appropriate sharps bin is not available directly from the pharmacy, the patient may request that this is prescribed by the GP.
- Ongoing monitoring for pulmonary toxicity throughout treatment. Discontinue methotrexate immediately if the patient becomes breathless and seek specialist advice.
- Ensure continuation of appropriate folate supplementation.

Patient, relatives, carers

- As listed in the NHS Lothian Policy and Procedures for the Shared Care of Medicines.
- Ensuring adherence to phlebotomy requirements throughout treatment
- Relatives or carers who are pregnant should not handle or administer subcutaneous methotrexate.
- Seal sharps bin, complete label and return to community pharmacy for disposal
- Patients can access advice from the relevant specialist team as follows:
    - Rheumatology patient helpline: 0131 537 1405
    - Inflammatory Bowel Disease patient helpline: 0131 537 1272 (WGH) or 01506 523861 (SJH)
    - Dermatology - contact the relevant consultant's secretary via switchboard: 0131 536 1000

Support and Advice for the GP and primary care non-medical prescribers

Rheumatology

SPR or Rheumatology Consultant on call 13.00-17.00 on weekdays and 09.00-12.00 on Saturdays and public holidays via the switchboard (0131 537 1000). Urgent queries outwith these times will be dealt with by the on-call medical team. GPs can access advice from the rheumatology specialist service using the rheumatology on call e-mail which aims to give advice with a 24 hour response time: rheumatology.oncall@nhslothian.scot.nhs.uk. Advice will be communicated back to the GP by e-mail. E-mail requests should copy in the practice's clinical e-mail address and ask that the reply is sent to all, so that the reply is picked up even if the sender is not available.

Dermatology

Contact the relevant consultant's secretary as detailed on clinic letter. For urgent queries please contact the Dermatology registrar on call via the switchboard (0131 536 1000), available Monday to Thursday 9am-9pm (excluding bank holidays), Friday to Sunday 9am-5pm (and bank holidays).

Gastroenterology

Western General Hospital: SPR on call via switchboard 0131 537 1000 Bleep: 8279

Healthcare professionals can also contact the service for advice using the following email addresses: WGH.IBDConsultants@nhslothian.scot.nhs.uk or IBDNurses@nhslothian.scot.nhs.uk . E-mail requests should copy in the practice's clinical e-mail address and ask that the reply is sent to all, so that the reply is picked up even if the sender is not available.

Royal Infirmary of Edinburgh: SPR on call via switchboard 0131 536 1000 Bleep: 2117

St John's Hospital: SJHGastro@nhslothian.scot.nhs.uk or IBD nurse led service: 01506 523 861

Key Information on the Medicine

Please refer to the current edition of the British National Formulary (BNF), available at www.bnf.org, and Summary of Product Characteristics (SPC), available at www.medicines.org.uk for detailed product and prescribing information and specific guidance.

Background to disease and use of drug for the given indication

Rheumatology: Methotrexate is generally the first-choice disease modifying anti-rheumatic drug (DMARD) used in the management of a number of inflammatory rheumatic conditions. It may be used as monotherapy or in combination with other DMARDs and biologic drugs. Subcutaneous injection is often better tolerated and achieves higher bioavailability than oral tablets.

Gastroenterology: Methotrexate is generally prescribed for the maintenance of remission of Crohn's Disease and in combination with anti-TNF inhibitors to reduce immunogenicity. Subcutaneous injection is used in preference to oral tablets in most GI patients.

Dermatology: Methotrexate is licensed for the treatment of psoriasis but is used off label in the management of atopic eczema and many other inflammatory and autoimmune skin conditions. Helpful information on methotrexate use in dermatology can be found in the 2016 British Association of Dermatologists' guideline for the safe and effective prescribing of methotrexate for skin disease. Link: https://onlinelibrary.wiley.com/doi/full/10.1111/bjd.14816

Preparations Available

Oral: Only prescribe the 2.5mg tablet formulation. The **10mg tablets must not be prescribed** in any circumstances.

Subcutaneous: Metoject® pre-filled pen is the preferred brand of methotrexate subcutaneous injection. Patients will be initiated and counselled on use of the Metoject® device by the specialist service.

Other brands are available. Should any change in brand be required the prescriber must consider need for patient education on use of the device and the disposal of used injections, which may not be compatible with the patient's sharps bin. If an alternative brand to Metoject is initiated in secondary care, this should be indicated clearly within the TRAK note following the patient's 6 week DMARD review.

Switching formulation: Patients may be switched from oral to subcutaneous methotrexate to improve efficacy and/or tolerability as advised by the specialist service. A change in formulation should be treated like a change in dose by reverting to fortnightly monitoring for 6 weeks (undertaken in primary care).

Dosage and administration

Starting doses generally range from 5 – 15mg **once weekly** and are titrated in increments of 2.5 – 5mg to achieve the desired target dose.

It is good practice to specify on the prescription the day of the week the dose is to be taken.

The target dose is no greater than 30mg once weekly. Lower doses are likely to be used in elderly patients or those with renal impairment.

Folic acid 5mg (orally) should be prescribed the day after methotrexate. However, folic acid can be used up to 6 days a week to improve tolerability of methotrexate. It is not to be taken on the same day as methotrexate due to risk of reducing efficacy.

Monitoring

On initiation of treatment, patients are provided with pre-labelled forms for blood tests. Bloods are taken in primary care and reported to the specialist service during the first 6 weeks of treatment.

Note that abnormal trends in blood monitoring should prompt extra vigilance and may be a sign of toxicity even if absolute levels are normal.

Test	Frequency	Abnormal Result	Action if Abnormal Result
FBC	Every 2 weeks* until on a stable dose for 6 weeks. Then, monthly for 3 months.	Platelets 100-140 WCC 2.0-3.5 Neutrophils 1.0-1.6	Withhold therapy for 2 weeks and recheck. If normal recommence at lower dose i.e. reduce methotrexate dose by 5mg/week.

	Thereafter, every 3 months. Revert to initial schedule in the event of a dose increase, change from oral to subcutaneous or when a new DMARD is added. When leflunomide is used in combination with methotrexate, monitoring should be carried out monthly. *Dermatology may request weekly bloods for first month, with FBC performed before dosing in week 2.	Platelets < 100 WCC < 2.0 Neutrophils < 1.0 Lymphocytes <0.5	Withhold treatment and contact specialist service.
		MCV >105	Check B12, folate, TFTs and consider discussing with specialist service.
LFTs (including albumin)		ALT >100	Withhold therapy for 2 weeks, and recheck. If ALT <100, recommence at lower dose i.e. reduce methotrexate dose by 5mg/week.
		ALT 50-100	Continue treatment and recheck. If ALT stable, continue treatment. If ALT rising, contact specialist service. Repeat LFTs in 2- 4 weeks
		Albumin <30	If albumin <30g/L on 2 or more occasions contact specialist service.
Creatinine		Creatinine: note trend	If rising, reduce dose by 50%, and contact specialist service.
Advice on avoiding conception /contraception as appropriate if patient circumstances change			
Monitoring of respiratory system for signs of pneumonitis – see below			

Cautions, contraindications - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

- Temporarily discontinue during a serious infection.

Adverse effects - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

- **Symptoms indicating potentially severe lung injury (interstitial pneumonitis)** are dry, non-productive cough, shortness of breath and fever. If any of these symptoms occur and/or if pneumonitis is suspected clinically, methotrexate should be discontinued and the specialist service should be contacted immediately for advice.
- Temporarily withdraw if the patient reports an unexplained **sore throat, bleeding or bruising, mouth ulcers** or other signs of blood dyscrasia or evidence of infection. Perform repeat blood monitoring.

In the event of an unexplained **acute widespread rash**, withhold methotrexate and seek urgent specialist (preferably dermatological) advice. Inform specialist service

Drug interactions - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

- NSAIDs and aspirin (not including low dose aspirin 75mg) can reduce the excretion of methotrexate, possibly increasing the risk of toxicity. NSAIDs are commonly used in conjunction with methotrexate in inflammatory rheumatic diseases therefore, increased monitoring is essential in patients who are newly started on NSAIDs until they are stable on both treatments.

PPIs have also been found to reduce methotrexate excretion and increase risk of toxicity. Any patients newly started on a PPI should revert to increased monitoring until stable on both treatments.

Pregnancy & Fertility

- Methotrexate is contraindicated during pregnancy since there is evidence of a teratogenic risk. Women of childbearing potential should be fully informed of the potential hazard to the foetus should they become pregnant during methotrexate therapy.
- Women on methotrexate therapy should use adequate contraception during and for 6 months after treatment.
- Women who are on methotrexate and are planning to conceive should be referred back to the specialist service for further advice and management.
- Methotrexate should be discontinued in women of child-bearing potential at least 6 months prior to conception.
- The product license for methotrexate advises effective contraception during and for 6 months after treatment in both men and women. There is limited, low quality data to suggest that the risk of foetal

malformation is not increased significantly in men who are taking methotrexate at the time of conception. The specialist service can provide advice on a case by case basis.

Vaccinations

- Individuals with immunosuppression should be given inactivated vaccines in accordance with national recommendations.
- It is recommended that patients with autoimmune inflammatory diseases should be offered pneumococcal and influenza vaccination.
- Immunosuppressed patients who are 70 to 79 years of age should be offered the varicella-zoster vaccine, Shingrix, to help protect them against shingles. Shingrix is a non-live alternative to the live shingles vaccine, Zostavax.
- When considering suitability for live vaccines concurrent DMARD therapy should also be taken into account.
- For further information see: https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book

The presence of this SCA does not compel a primary care prescriber to prescribe if they feel that it is out with the scope of their competencies (as per GMC guidance on safe prescribing) or resources, as ultimate responsibility lies with the prescribing, not the recommending, clinician.

Approved by the General Practice Prescribing Committee December 2022