SHARED CARE AGREEMENT

Name of medicine Methotrexate - Oral and Subcutaneous

Indication For the treatment of paediatric inflammatory rheumatic and bowel conditions

Version: 2.0 **Approval date: September 2022** **Review date: September 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.

Secondary Care Consultant/ Speciality Doctor/ Specialist Nurse/ Hospital Pharmacy

- Assessing the patient's need for methotrexate therapy.
- Undertaking and interpreting baseline investigations (FBC, U&E, creatinine, LFTs and confirmation of VZV status).
- Specify the starting dose of methotrexate and communicating changes in dose to the primary care provider.
- Initiating treatment with oral or subcutaneous methotrexate and providing initial supply for 12 weeks (3 months).
- Supplying the patient/parent/carer with verbal and written information on methotrexate.
- Ensure patient/family has adequate instruction on the administration of oral or subcutaneous methotrexate to safely administer at home or that suitable alternative arrangements are in place for community administration (Community Children's Nurse (CCN)).
- Teaching guidelines for administration of subcutaneous methotrexate should be completed and evidence of competency uploaded to TRAK.
- Providing male and female patients from 12 years of age with advice on fertility, pregnancy, and the need for contraception.
- Prescribe folic acid for the initial 3 months. Folic acid should be given the day after the methotrexate dose.
- The specialist team are to provide initiation blood monitoring and interpretation as detailed in "Key Information on the Medicine", monitoring of adverse effects of the medicine and comprehensive patient support for queries and treatment related issues for the first 12 weeks.
- Arrangement for review of methotrexate treatment should be scheduled by the secondary care team after 3 – 4 months of treatment.
- Secondary care are to provide ongoing advice to the GP regarding monitoring, adverse effects and dose modifications when required.
- Ensure that, when necessary, patients receive a cytotoxic (purple lid) sharps bin for safe disposal of cytotoxic waste and arrangements are made for returning bins for disposal.
- Ensure that patients with negative antibody status are offered oral aciclovir treatment if significant varicella contact occurs.
- 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.
- Secondary care will arrange for continuing, long term review.

General Practitioners and primary care non-medical prescribers

- Prescribing methotrexate in consultation with the specialist service after the first 12 weeks (3 months).
- Prescribing folic acid if required on advice from specialist service.
- Arrange for blood tests to be taken at appropriate intervals thereafter as detailed in "Key Information on the Medicine" monitoring.

- Ongoing vigilance for chickenpox contacts in children known to be varicella negative. Seek advice from the specialist service in the event of contact with chickenpox.
- Monitor for adverse effects of methotrexate treatment as detailed in the BNFc, medicines summary of product characteristics and information in the monitoring section of this document.
- Advise on a suitable form of contraception where relevant.

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.
    - Dispose of cytotoxic waste safely using the sharps bin provided.
    - Be aware of child's varicella zoster status and action required in the event of possible contact with chickenpox.
    - Parents/family who are pregnant should not handle or administer methotrexate.

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

Gastroenterology

Royal Hospital for Children and Young People, Edinburgh: GI Registrar. On call between 09:00 and 17:00 Monday to Friday via switchboard 0131 536 1000 Bleep: 9434

Rheumatology

Royal Hospital for Children and Young People, Edinburgh: Clinical Nurse Specialists between 09:00 and 17:00 Monday to Friday via switchboard 0131 537 1000 Bleep: 9114

Healthcare professionals can also contact the service for advice using the following email addresses: PaediatricRheumNurses@nhslothian.scot.nhs.uk

Key Information on the Medicine

Refer to current edition of the British National Formulary (BNFc), 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 paediatric inflammatory rheumatic conditions. It may be used as monotherapy or in combination with other DMARDs and biologic drugs.

Gastroenterology: Methotrexate is generally prescribed for the maintenance of remission of Crohn's Disease and in combination with anti-TNF inhibitors to reduce immunogenicity.

Preparations Available

Oral – Only prescribe 2.5mg tablets. The 10mg tablets MUST NOT be prescribed in any circumstance. A 2mg/1ml oral liquid is available from specialist suppliers.

Subcutaneous – Please prescribe Metoject® pre-filled pens, this is the chosen brand that patients will be trained on for home administration. PFP strengths available: 7.5mg, 10mg, 12.5mg, 15mg, 17.5mg, 20mg, 22.5mg & 25mg.

Switching formulation: Patients may be switched from oral to subcutaneous methotrexate to improve efficacy and/or tolerability as advised by the specialist service.

Dosage and administration

Starting dose 10-15mg/m^2 ONCE WEEKLY orally or subcutaneously. The dose may then be increased (usual maximum 20mg/m^2 ONCE WEEKLY) or decreased depending on efficacy. **The maximum single dose is 25mg ONCE WEEKLY**.

The maintenance dose is 10-15mg/m^2 ONCE WEEKLY orally or subcutaneously.

Prescriptions should specify the day of the week the dose is to be taken.

Folic acid 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.

<table>
<tr><th>Test</th><th>Frequency</th><th>Abnormal Result</th><th>Action if Abnormal Result</th></tr>
<tr><td>FBC</td><td rowspan="3">Every 2 weeks until on a stable dose for 6 weeks.*

Then, monthly for 2 months.

Thereafter, every 3 months if stable on a standard dose of methotrexate.

*Rheumatology will occasionally decrease the initial blood monitoring to monthly for the first 3 months.

If results are abnormal contact specialist team for advice.</td><td>Neutrophils <1 x 10^9/L
Platelets <100 x 10^9/L
WCC < 3.5 x 10^9/L</td><td>Withhold dose until discussed with clinical nurse specialist or consultant</td></tr>
<tr><td>LFT</td><td>ALT > Three times the upper normal limit</td><td>Withhold dose until discussed with clinical nurse specialist or consultant</td></tr>
<tr><td>U&E and Creatinine</td><td>Creatinine elevated above normal range for age</td><td>Caution and extra vigilance. Discuss with clinical nurse specialist or consultant</td></tr>
<tr><td colspan="4">Advice on avoiding conception/contraception as appropriate if patient circumstances change</td></tr>
<tr><td colspan="4">Monitoring of respiratory system for signs of pneumonitis – see below</td></tr>
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Antiemetic treatment is also common practice with patients taking methotrexate. Ondansetron should be prescribed as required before and after the methotrexate dose as per BNFc.

Monitoring

GPs may refer patients for phlebotomy directly through the RHCYP OPC appointment line on 0131 312 1547 or 0131 312 1548.

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

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

- Temporarily discontinue methotrexate treatment during 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. Interstitial pneumonitis is rare in children and young people.
- 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 advice. Inform specialist service.

Drug interactions

- NSAIDs and aspirin (not 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 and Fertility

- Methotrexate is contraindicated during pregnancy since there is evidence of a teratogenic risk. All patients should be fully informed of the potential hazard to the foetus during methotrexate therapy.
- Reliable contraception should be considered for use by both males and females being treated with methotrexate and for six months after treatment is discontinued.

Vaccinations

- Individuals who on immunosuppressant therapy should be given inactivated vaccines in accordance with national recommendations.
- It is recommended that patients with autoimmune inflammatory diseases on immunosuppressant therapy should be offered pneumococcal, COVID19 and influenza vaccination.
- 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 GP 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