

SHARED CARE FRAMEWORK

The Pan Mersey Area Prescribing Committee recommends the prescribing of METHOTREXATE for patients within adult services.

SHARED CARE

1. Background

Methotrexate is a folic acid antagonist and is classified as an antimetabolite cytotoxic agent.

Methotrexate is used in the treatment of rheumatoid arthritis, psoriasis, Crohn's disease, and other indications as outlined below.

Dose adjustments and monitoring requirements for disease-modifying drugs (DMDs) (licensed and unlicensed indications) included in this Framework are in line with national guidance published by the British Society for Rheumatology 2017¹.

2. Licensed Indications

- Rheumatoid arthritis
- Psoriasis

3. Locally agreed off-label use

- Inflammatory bowel disease
- Steroid sparing agent
- Other dermatology conditions
- Myasthenia gravis, inflammatory myopathies and neuropathies, vasculitis, and other immune-mediated central and peripheral nervous system diseases
- Interstitial lung disease or cardiac involvement with sarcoidosis
- Inflammatory arthropathies
- Juvenile idiopathic arthritis (JIA)
- Atypical neuroinflammatory disease
- Off-label doses above the licensed dose for various indications

4. Initiation and ongoing dose regime

Transfer of monitoring and prescribing to primary care is normally after three months. The duration of treatment will be determined by the specialist based on clinical response and tolerability.

Dosing information

The dose is variable (higher doses may be off-label) depending on the clinical indication and will be decided by the specialist initiating treatment. Time to response is variable. In psoriasis, a significant effect may not be seen before a

Supporting information

month or more. For other indications, a response may not be expected before two to three months and in some cases may not occur until six months of treatment.

Lower doses may be considered in renal or hepatic impairment or in the elderly: chronic kidney disease (CKD)3, reduce dose by 50%; contraindicated in CKD 4+5.

The usual starting dose is 10-15mg once a week and increased by 2.5-5mg per week as directed by a specialist.

The maximum licensed oral dose in rheumatoid arthritis is 20mg.

Variable dose: the usual range is 2.5mg-30mg ONCE a WEEK on the same day each week.

All dose or formulation adjustments are the responsibility of the initiating specialist unless otherwise discussed and agreed with the primary care clinician.

Dose increases should be monitored using FBC, creatinine/eGFR, ALT and/or AST and albumin every two weeks for six weeks after a dose increase, then revert back to the previous schedule.

Termination of treatment will be the responsibility of the specialist.

5. Baseline investigations, initial monitoring and dose titration to be undertaken by specialist

Baseline

- Height, weight, BP, FBC, creatinine/eGFR, ALT and /or AST, albumin.
- Vaccinations against pneumococcus and influenza are recommended.
- Shingles vaccine (Zostavax) is recommended as per the JCVI for eligible patients; however, it is contraindicated in doses greater than 0.4mg/kg/week
- Specialist to highlight in the first clinic letter notifying the GP of the decision to initiate DMDs that the GP will need to give the shingles vaccine if the patient is aged 70 years or older and for those 69 years and younger but are deemed clinically eligible for Zostavax by the specialist team. The pneumococcal vaccine should also be administered, if not already given. The GP should also be advised to add the patient to the influenza vaccine list.
- DMDs should be started two to four weeks AFTER administration of the shingles vaccine (Zostavax) as stated in the Green Book, therefore the specialist team should arrange this with the GP, in a timely manner so as not to delay commencement of DMDs.
- For hepatology indications, a fibroscan should be carried out before initiation
- Patients should be assessed for comorbidities that may influence DMD choice, including evaluation of respiratory disease and screening for occult viral infection
- Treatment should not be started for 4 weeks after live vaccines (eg oral typhoid, MMR, BCG, yellow fever)

Initiation

- FBC, creatinine/eGFR, ALT and /or AST and albumin every two weeks until on stable dose for six weeks.
- Once on a stable dose, monthly FBC, creatinine/eGFR, ALT and /or AST and albumin for three months.

Thereafter, FBC, creatinine/eGFR, ALT and/or AST and albumin at least every 12 weeks.

Baseline chest X-ray according to indication. Spirometry in smokers, patients with known respiratory disease or older than 65 years.

6. Ongoing monitoring requirements to be undertaken by primary care

Monitoring	Frequency
FBC, Creatinine/eGFR, ALT and/or AST, Albumin CRP and ESR (rheumatology patients only)	After the initial monitoring period (see section 5), every 12 weeks, or more frequently in patients at higher risk of toxicity as advised by the specialist team. NB: Some

Supporting information

	of the initial monitoring (likely to be 1-2 months of monthly monitoring) may take place in primary care. The exact frequency of the monitoring is to be communicated by the specialist in all cases. When methotrexate is prescribed with leflunomide, monthly monitoring is recommended for the first 12 months.
P3NP (psoriasis patients only) This test can be requested via the EMIS or Vision system and the normal range is 1.7-4.2 micrograms/L. Three P3NP levels >4.2mcg/L but <8.0mcg/L or two P3NP levels >8.0mcg/L over a 12-month period should be reported to the specialist.	Annually or every 12 weeks after a raised value (>4.2mcg/L) NB: There is a 4-week turnaround for this test.

7. Pharmaceutical aspects

Route of administration

Oral or subcutaneous injection

Formulation

Oral – **only the 2.5mg strength tablet is to be prescribed**, irrespective of dose, to avoid overdose with the 10mg tablet.

Solution for injection, various strengths, pre-filled syringe - methotrexate injection must be prescribed using the brand name and also the generic name (if this facility is available on the prescribing system).

Administration details

The day of the week should be specified and consistent.

The provision of cytotoxic waste disposal needs to be arranged according to locally commissioned service.

Other important information

Patients should also receive folic acid 5mg tablets daily, one to six times a week during treatment with methotrexate (but not on the same day as methotrexate) as advised by the specialist. Folic acid is to be prescribed by the specialist until the GP takes over the prescribing of methotrexate.

8. Contraindications

Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction.

- Hypersensitivity
- Significantly impaired hepatic function
- Significantly impaired renal function (CKD 4 + 5)
- Pre-existing blood dyscrasia
- Severe acute or chronic infections and immunodeficiency syndrome
- Methotrexate should not be used concomitantly with drugs with antifolate properties eg trimethoprim
- **Pregnancy and breastfeeding**
- Hypersensitivity to methotrexate or any of its excipients.
- SPC cautions administration of live vaccines; however, JCVI and BSR recommend that oral DMD therapy at standard doses is not a contraindication in most patients, clinician discretion is advised.

9. Significant drug interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics. [SPC](#)

Supporting information

Seek advice from the initiating specialist if there are any concerns about interactions.

Concomitant administration of folate antagonists such as trimethoprim, co-trimoxazole, and nitrous oxide should be avoided.

10. Adverse effects and management

Adverse effect	Management
Abnormal bruising or severe sore throat	Stop the drug until FBC results are available, contact the Specialist Practitioner (SP)
New or increasing dyspnoea or dry cough	Stop the drug and contact SP urgently.
Fall in WCC $<3.5 \times 10^9/l$ Fall in neutrophils $<1.6 \times 10^9/l$ Fall in platelets $<140 \times 10^9/l$	Stop the drug and contact SP.
Increased MCV $>105f/l$	Check folate, B12 and TSH, treat if abnormal, contact SP for advice and management if normal.
Unexplained reduction in albumin $<30g/l$ (added from BSR) Abnormal LFTs – AST or ALT $> 100U/l$ Rash Mouth ulcers	Stop the drug and contact SP.
Taste loss	Reassure, continue the drug.
Nausea, vomiting, diarrhoea	Discuss with SP. N.B. nausea relating to methotrexate should be managed initially by prescribing anti-emetics.
Increase in serum creatinine $>30\%$ over a period of 12 months or less OR decline in eGFR $> 25\%$	Contact SP if new or unexplained renal impairment

11. Advice to patients and carers

The specialist will counsel the patient about the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual drugs.

12. Pregnancy and breast feeding

- **Contraindicated in pregnancy and breast feeding.** The manufacturer advises effective contraception² during and for at least six months after treatment in both men and women. Patients planning to become pregnant should be seen by a specialist.
- In the case of inadvertent exposure to low-dose methotrexate in pregnancy, the drug should be stopped immediately, folate supplementation (5mg/day) continued, and a careful evaluation of foetal risk carried out by local experts³. If a patient becomes pregnant while on treatment, they should be referred back to the hospital immediately for review.
- Methotrexate is present in breast milk in low concentrations, breast feeding should be stopped before treatment.

It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.

13. Specialist contact information

See appendix 2

Supporting information

14. Additional information

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.

15. References

1. BSR (2017) [BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs](#)
2. MHAR (2010) [Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed?](#)
3. BSR (2016) [BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids](#)
4. [The Green Book - Immunisation against infectious diseases](#)

To be read in conjunction with the following documents.

1. Policy for Shared Care (Appendix 1).
2. Shared care agreement (Appendix 2).

When two or more DMDs are initiated, one shared care agreement form should be completed that includes all relevant drugs.

Appendix 1

Policy for Shared Care

Shared care is only appropriate if it provides an optimum solution for the patient, and it meets the criteria outlined in the shared care section of the [Pan Mersey Definitions and Criteria for Categorisation of Medicines](#).

Before prescribing responsibilities are transferred to primary care:

- > Prescribing responsibility will only be transferred when the consultant and the patient's GP agree that the patient's condition is stable.
- > All information required by the shared care framework for the individual medicine has been provided to the patient's GP.
- > Patients will only be referred to the GP once the GP has agreed to the Shared Care Agreement and returned signed copies.

Inherent in any shared care agreement is the understanding that participation is at the discretion of the GP, subject to the availability of sufficient information to support clinical confidence.

Specialist Responsibilities in Shared Care

- > To initiate the medicine, prescribe, monitor for toxicity and efficacy as described by the shared care framework until the patient is stabilised.
- > To ensure the patient or their carer:
 - > Is counselled with regard to the risks and benefits of the medicine.
 - > Provide any necessary written information to the patient with regard to the individual medicine including patient information leaflets on individual drugs.
 - > Obtain and document informed consent from the patient when any medicines are prescribed for an off-label indication for any condition
- > To be familiar with the shared care framework.
- > To provide all information to the patient's GP as required by the shared care framework when prescribing responsibility is initially transferred and at any subsequent times as necessary for safe and effective treatment of the patient.
- > To assess the patient regularly as necessary for the duration of therapy.
- > To review the patient promptly if required by the GP concerned.
- > To meet any additional requirements as required by the individual medicine shared care framework.
- > To communicate the failure of a patient to attend a routine hospital review and advise the GP of appropriate action to be taken.
- > Addition of a second DMD: Following the addition of a new drug to an existing regime covered by a Shared Care Agreement, the Specialist must initiate, prescribe, and monitor the new drug in accordance with the relevant shared care agreement including subsequent review and inform the GP of this. A new Shared Care Agreement must then be initiated for the new drug.

Supporting information

Primary Care Responsibilities in Shared Care

- > To reply to a written request for Shared Care within 21 days ensuring both copies of the Shared Care Agreement are signed if appropriate.

If agreeing to shared care, the GP is asked:

- > To provide prescribe or manage and monitor the medicine as advised by the Specialist and in line with the individual Shared Care Framework.
- > To review the patient as required by the Shared Care Framework
 - To make appropriate and contemporaneous records of prescribing and/or monitoring and to note the existence of the Shared Care Agreement on the patient's clinical record. A Snomed code of "268529002 Shared Care- Specialist/GP" can be used.
- > To be familiar with the individual Shared Care Framework.
- > To report any adverse effects of treatment to the specialist team.
- > To inform the Specialist of any relevant change in the patient's circumstances.
- > To seek Specialist advice as appropriate.
- > To meet any additional requirements as required by the individual Shared Care Framework.
- > To respond to Specialist communication relating to any change or addition to the patient's treatment covered by the Shared Care Agreement.

Where the GP wishes to withdraw prescribing, for example when the patient fails to attend for monitoring, they need to give the specialist team a minimum of 14 days' notice of their need to resume responsibility for prescribing. The specialist is required to acknowledge this request within the 14-day time period.

Appendix 2

Shared Care Agreement

Disease modifying drugs (DMDs)

Request by Specialist Clinician for the patient's GP to enter into a shared care agreement

Part 1

To be signed by Consultant /Prescribing member of Specialist Team (circle or underline as appropriate)

Date

Name of patient

Address

.....

Patient NHS No

Patient hospital unit No

Diagnosed condition

Dear Dr

I request that you prescribe (include doses)

(1)

(2)

(3)

(4)

for the above patient in accordance with the enclosed shared care framework.

Last Prescription Issued: / /

Next Supply Due: / /

Date of last blood test: / /

Date of next blood test: / /

Frequency of blood test:

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care Framework and Policy.

I confirm that if this is a Shared Care Agreement for a drug indication which is unlicensed or off label, informed consent has been received.

Details of Specialist Clinicians

Name

Date

Consultant / Prescribing member of Specialist Team (circle or underline as appropriate)

Signature

In all cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a prescriber who is not the specialist, it is the supervising consultant who takes medico-legal responsibility for the agreement.

Please add patient addressograph here

Supporting information

Consultant:

Contact details:

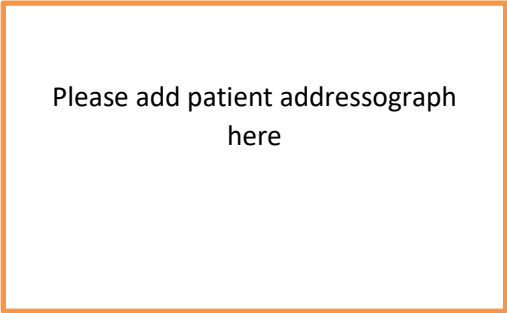
.....

Telephone number: Ext:

Address for return of documentation

.....

.....



Part 2

To be completed by Primary Care Clinician

I agree to prescribe for the above patient in accordance with the enclosed shared care framework.

GP signature Date

GP name Please print

GP: please sign and return a copy within 21 calendar days to the address above

OR

If you do not agree to prescribe, please delete the section above and provide any supporting information as appropriate below: