

Prescribing Framework for Methotrexate for Immunosuppression in ADULTS

Patient's Name:..... NHS Number:

Patient's Address:.....(Use addressograph sticker)

GP's Name:.....

Communication

We agree to treat this patient within this Prescribing Framework

Specialist Prescriber's Name..... Prof Reg. No.

Specialist Prescriber's Signature..... Date:.....

Where prescriber is not a consultant:

Consultant's Name: GMC No

Consultant's Signature Date:.....

GP's Signature:..... Date:.....

GP's Name (if different from listed above).....

The front page of this form should be completed by the specialist and the form sent to the patient's general practitioner.

The patient's GP should sign and **send back to specialist**, to confirm agreement to enter into shared care arrangement. If the General Practitioner is **unwilling** to accept prescribing responsibility for the above patient the specialist should be informed within two weeks of receipt of this framework and specialist's letter.

Full copy of framework can also be found at: <http://www.hey.nhs.uk/amber.htm>

1. Background

Methotrexate is a folic acid antagonist and is classified as an antimetabolite cytotoxic agent. It may be used for the treatment of a wide variety of immune mediated disorders.

Methotrexate is usually used orally, however a proportion of patients are unable to tolerate a potentially effective therapy due to gastrointestinal intolerance. This group of patients often benefit from subcutaneous methotrexate given on a weekly basis.

These guidelines aim to provide a framework for the prescribing of methotrexate by GPs for patients requiring immunosuppression and to set out the associated responsibilities of GPs and hospital specialists who enter into the shared care arrangements.

*For use in treatment of cancer – methotrexate remains **Red***

This framework applies to oral methotrexate

This document should be read in conjunction with the guidance “Responsibility for prescribing between Primary & Secondary/Tertiary Care” <https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf>

2. Indication

Immune mediated disorders including moderate to severe rheumatoid arthritis, psoriasis and Crohn’s disease.

Specific information will be provided by the specialist on the indication for immunosuppression in individual patients.

3. Dose

ADULT

The usual starting dose is 7.5mg to 15mg **once a week** as a single dose. The dose may be adjusted on the basis on an individual status to a usual maximum of 25mg per week subject to regular full blood counts.

NB: Test dose of 5mg and lower maintenance doses common in dermatology.

Folic acid should also be prescribed at a dose recommended by specialist. Folic acid should not be taken within 24 hours of methotrexate. The use of folic acid helps reduce the incidence and severity of adverse effects.

Methotrexate tablets must only be supplied in 2.5mg strengths to avoid confusion.

Subcutaneous dose:

Subcutaneous administration is recommended in patients who have not tolerated oral dose or in those whom have had sub-optimal response to oral methotrexate, as advised by the specialist. Dose would typically remain the same as previous oral dose.

4. Duration of treatment

Advice will be given to the GP on duration of treatment and dose changes for each individual patient.

5. Cautions / contraindications

Methotrexate should be discontinued and patient referred to the consultant if they develop dyspnoea or cough.

Methotrexate is contraindicated in severe renal or hepatic impairment, severe anaemia, leucopenia, thrombocytopenia or any immunodeficiency syndromes, previous hepatitis B infection and active infection.

Methotrexate should be used with caution in patients with pre-existing pulmonary fibrosis, diabetes and morbid obesity.

Methotrexate is teratogenic. It should not be administered to women who are pregnant or breast feeding. Effective contraception, in both male and female patients, should be established before commencing methotrexate and continued during treatment and continued for at least 3 months after treatment is completed.

6. Adverse effects

Principal side effects are gastrointestinal in nature (nausea, vomiting, diarrhoea, stomatitis and GI ulceration). Other side effects include hair loss and cirrhosis of the liver. Rare effects include leucopenia, thrombocytopenia and acute or chronic interstitial pneumonitis.

7. Interactions

Increased risk of toxicity when methotrexate is given with other drugs which are haematotoxic, hepatotoxic, nephrotoxic or folate antagonists. Other interactions include aspirin / NSAIDs and tetracyclines.

For a full list of interactions always check with BNF or Data Sheet (www.bnf.org or <https://www.medicines.org.uk/emc/product/511/smpc>)

Methotrexate may be prescribed in combinations with NSAIDs under specialist advice.

Patients receiving methotrexate should be advised against immunization with live vaccines. (Influenza and Pneumococcal vaccines may be given in this group of patients).

8. Monitoring

Disease monitoring: Clinical response to therapy

Drug monitoring:

Patients should have a baseline chest X-ray performed. Full blood count (including platelets), differential white cell count, LFT's and U&E's should be checked every 1-2 weeks until therapy stabilised, and provided it is stable monthly thereafter. Frequency of monitoring may be reduced further following discussion with the specialist team, providing the dose and trend of results remain stable. If dose changes occur then monitoring should resume every 2 weeks as above.

Patients should be monitored more frequently if there is a reason to suspect deteriorating renal function.

The blood tests should not be taken within 3 days of administration of methotrexate.

Monitoring parameter	Recommended response
WBC < 4.0 x 10 ⁹ /l	withhold until discussed with specialist team
Neutrophils <2.0 x 10 ⁹ /l	withhold until discussed with specialist team
Platelets <150 x 10 ⁹ /l	withhold until discussed with specialist team
>2 fold rise in AST, ALT (from upper limit reference range)	withhold until discussed with specialist team
MCV> 105 fl	Check serum folate and B12 & TSH . Withhold until results are available and discuss with specialist team
Albumin-unexplained fall (in absence of active disease)	withhold until discussed with specialist team
Renal function-significant deterioration (or Creatinine > 150 micromol/L)	withhold until discussed with specialist team
New or increasing dyspnoea or dry cough	withhold and discuss urgently with specialist team
Rash, oral ulceration, nausea & vomiting, diarrhoea	withhold until discussed with specialist team
Abnormal bruising or severe sore throat	withhold until FBC results available & discuss with the specialist team

9. Information to patient

Explain current dose of ONCE WEEKLY methotrexate and dose of folic acid. Inform patient of expected response to treatment and possible side effects.

Patients should be told to go to their GP immediately if they experience any fever, rash, bruising, bleeding, sore throat, oral ulceration, shortness of breath, dry cough, jaundice or infection.

As per NPSA recommendations patients should be given a pre-treatment patient information leaflet and a patient held monitoring booklet.

10. Responsibilities of clinicians involved

Stage of Treatment	Hospital Specialist	General Practitioner
Initiation	<p>Assess the patient following referral by GP</p> <p>Carry out baseline full blood count, differential WCC, platelets, U&Es and LFTs PIIINP, Hep B Hep C, HIV AND VZV.</p> <p>Perform baseline chest x-ray (where not performed within last 6 months).</p> <p>Ensure patient is competent to self administer doses, or arrange administration by practice / district nursing.</p> <p>Supply a cytotoxic waste bin and advise patient on safe disposal of waste products.</p> <p>Give patient NPSA Methotrexate booklet and fill in.</p> <p>Recommend appropriate treatment to the GP by approved DMARDs clinic letter</p>	Prescribe on FP10
Maintenance	<p>Assess clinical response to treatment</p> <p>Provide adequate advice and support for the GP</p> <p>Provide information to GP on frequency of monitoring if doses are changed</p> <p>Fill in patient NPSA Methotrexate booklet where relevant.</p>	<p>FBC (including platelets, differential white cell), U&Es, LFTs (including AST or ALT) should be checked every 1-2 weeks until therapy stabilised, and provided it is stable monthly thereafter. (Frequency may reduce further on specialist advice).</p> <p>Fill in patient NPSA Methotrexate booklet, including any dose changes and results.</p>

Contact Details:

During office hours

Contact the relevant consultant's secretary via HEY switchboard (01482 875875)

Specialist pharmacists :

Interface Pharmacist – Antonio Ramirez	01482 674306
Neurology - Jane Morgan	01482 674411
Renal Medicine – Aaron Acquaye	01482 674043
Rheumatology – Emily Hardaker	01482 674043

Out of hours – Contact on-call Registrar for specialty via HEY switchboard.

APPROVAL PROCESS

Written by:	Marie Miller, Interface Pharmacist; Updated by Jane Morgan, Senior Pharmacist – Medicines Information (May 17); Antonio Ramirez, Interface Pharmacist (June 18)
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