Shared care guideline for methotrexate in rheumatoid arthritis and severe psoriasis in adults

General Principles

This agreement outlines suggested ways in which the responsibilities for managing the prescribing of the drug treatment and clinical indication listed in the table below can be shared between the Specialist and General Practitioner (GP). The Specialist(s) is responsible for initiating treatment, prescribing the drug and monitoring of therapy until such a time as when the patient is deemed to be stable. If GPs are not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the Specialist.
If a Specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.
Sharing of care assumes communication between the Specialist, the GP and the patient. The intention to undertake shared care should be explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients on methotrexate are under regular follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

Indications

Methotrexate is a disease modifying agent licensed for a wide variety of neoplastic diseases and used for several unlicensed indications. This document, however, will only cover the treatment of adults with methotrexate for:
Licensed indications:
Rheumatoid arthritis (RA) and severe psoriasis

Presentation/Dose/Administration

Oral:
2.5mg tablets
(10mg tablets available, use only 2.5mg tablets to avoid confusion and potential overdose).

Subcutaneous :
7.5mg to 30mg pre-filled syringes (Metoject®).

Rheumatoid arthritis:

Initial dose is 7.5mg to 15mg once a week which can be increased up to 25mg once a week according to the secondary care physicians assessment of response and side effects.

Severe Psoriasis

Initial dose 2.5 mg to 10 mg once a week, increased according to response in steps of 2.5 – 5 mg at intervals of at least 1 week; usual dose 7.5 – 15 mg once weekly. Max dose 30 mg once a week.

- **BOTH ORAL AND SUBCUTANEOUS DOSES SHOULD ONLY BE GIVEN ONCE A WEEK ON THE SAME DAY OF THE WEEK**

- When switching from oral to subcutaneous administration, use the same dose or the nearest lower dose that matches the strengths of the available pre-filled syringes**.**

Folic acid supplement

Folic acid 5mg once weekly is co-prescribed with methotrexate to counteract its anti-folate side-effects, to be taken on a different day to methotrexate. If necessary the folic acid may be increased to 5mg daily, apart from the day of taking methotrexate. **FOLIC ACID SHOULD BE TAKEN ON A DIFFERENT DAY OF THE WEEK TO METHOTREXATE.**

Responsibility for monitoring methotrexate

- **The patient will be given a patient held booklet for recording results in by the hospital.**
- **Record all blood results in the methotrexate patient held record book**

MONITORING	RESPONSIBILITY	CONDITIONS	TESTS
Pre-treatment	Hospital team	All	FBC, U&Es, electrolytes, LFTs, CXR Pulmonary Function Tests in selective high risk cases. Varicella status – record history of chickenpox or VZV IgG immunity status in patient booklet. (BTUH to vaccinate if necessary)
Initiation to stabilisation	Hospital team	All	FBC, LFTs and U&Es **every two weeks until dose and monitoring/blood tests stable for 6 weeks.**
Ongoing	GP	All	FBC, LFTs and U&Es monthly until dose and disease is stable for 1 year. Thereafter, monitoring may be reduced in frequency, based on clinical judgement, and following discussion with specialist team, to every 2-3 months

Criteria for managing events & symptoms occurring during methotrexate therapy in primary care

LABORATORY EVENTS	VALUES	ACTION
Elevation in liver enzymes AST, ALT or falling albumin	Serial rise over 3 visits **or** >2 times upper limit of reference range.	**Stop treatment and seek advice from Specialist team**. *(See relevant telephone number(s) on page 6)*
Declining renal function	Significant deterioration/mild to moderate renal Impairment.	
WBC	< 3.5 x 10^9/L	
Neutrophils	< 2.0 x 10^9/L	
Platelets	< 150 x 10^9/L	
Serial falls in WBC and / or Platelets	>10% on 3 occasions	
MCV	> 105 fl	Withhold and check vitamin B_{12}, folate and TSH. If abnormal, treat any underlying abnormality. If normal, discuss with the specialist team.

SYMPTOMS	MANAGEMENT
Rash	**Stop drug** and discuss with specialist team. ***(See relevant telephone number(s) on page 6)***
Severe sore throat, abnormal bruising or bleeding	**Stop drug** and repeat FBC immediately. Follow relevant course of action from table above.
Cough, dyspnoea or fever	**Stop drug** and seek advice from specialist team.
Oral ulceration and stomatitis	May be overcome by low-dose folate (e.g. increase from 5mg one a week to 6 times a week). If persistent, seek advice.
Dyspepsia, diarrhoea, nausea, vomiting	May be overcome by low-dose folate and/or taking tablets with evening meal or increasing the fluid intake over 24 hours prior to taking methotrexate. If persistent, seek advice.

Key adverse drug reactions (ADRs)

- Hepatotoxicity eg liver cirrhosis, fibrosis, acute hepatitis.
- Pulmonary toxicity. Interstitial pneumonitis often associated with eosinophilia, causing dry unproductive cough, dyspnoea and fever, rarely pulmonary fibrosis. Can occur in first year of treatment and later.
- Gastrointestinal disturbances eg ulcerative stomatitis, dyspepsia, anorexia, nausea, diarrhoea and vomiting, rarely gastrointestinal ulceration.
- Bone marrow suppression, leucopaenia, thrombocytopenia, anaemia.
- CNS disturbances eg headache, tiredness, drowsiness, blurred vision.
- Hypersensitivity reactions eg fever, rigors, rash, pruritus.
- Renal failure and uraemia.

NB. Patients should be advised to report any mouth ulcers, sore throat, fever, epistaxis, unexpected bruising or bleeding and any unexpected illness or infection and should be seen URGENTLY for a full blood count, liver function tests, urea and electrolytes.

This document only lists the key important ADRs. For comprehensive information on adverse drug reactions, cautions, contra-indications and interactions, please refer to the current British National Formulary and Summary of Product Characteristics.

Contraindications & Precautions

Contraindications

- Severe/significant renal or significant hepatic impairment. Liver disease including fibrosis, cirrhosis, recent or active hepatitis
- Pre-existing blood dyscrasias, such as bone marrow hypoplasia, significant anaemia, leucopenia, or thrombocytopenia
- Severe acute or chronic infections and immunodeficiency syndrome
- Alcohol abuse
- Pregnancy and breast-feeding. Methotrexate is teratogenic to ova and sperm. Therefore, patients of either sex should be counselled about contraception during treatment and for at least 3 months after stopping methotrexate.
- Hypersensitivity to methotrexate or any of the excipients
- **Vaccinations**: live vaccines should be AVOIDED (i.e. oral polio, MMR, BCG and yellow fever and oral typhoid). **Annual flu and pneumococcal vaccination is recommended.**

Precautions

- Patients who have never had chickenpox or shingles may be at risk of severe infection whilst being treated with methotrexate. Patients should be advised to avoid close contact with people who have active chickenpox or shingles (especially if they do not have a known history of chickenpox or they know they do not have VZV IgG antibody) and should report any such contact (or if they develop chickenpox or shingles) to their GP or specialist for further advice (also see Consultant and GP responsibilities).
- Surgery – Patient to inform anaesthetist that they are on methotrexate.
- Dentist– Patient to inform dentist that they are on methotrexate.

Drug interactions

- Phenytoin: Antifolate effect of methotrexate is increased.
- Methotrexate is extensively protein bound and may be displaced by certain drugs such as salicylates, hypoglycaemics, diuretics, ciprofloxacin, sulphonamides, diphenylhydantoins, tetracyclines, chloramphenicol and p-aminobenzoic acid, and the acidic anti-inflammatory agents, so causing a potential for increased toxicity when used concurrently.
- Probenecid, penicillin, NSAIDs: Methotrexate excretion is reduced (clinically significant interaction between NSAID and methotrexate is rare, although patients should be advised to avoid self-medication with over the counter aspirin or ibuprofen).
- Concomitant use of other drugs with nephrotoxic, myelotoxic or hepatotoxic potential such as leflunomide, azathioprine, sulphasalazine, retinoids and alcohol should be avoided.
- Tolbutamide: Serum concentration of methotrexate may be increased.
- Co-trimoxazole (Septrin®) and trimethoprim should be avoided: Antifolate effect of methotrexate is increased and greatly increases the risk of marrow aplasia.
- Retinoids: Plasma concentration of methotrexate increased by acitretin, also increased risk of hepatotoxicity-avoid concomitant use.
- Patients must not receive immunisations with live vaccines. Pneumococcal and annual influenza vaccines are recommended. In patients exposed to chickenpox or shingles, passive immunisation should be carried out using VZIG.

See BNF and manufacturer's SPC Home - electronic Medicines Compendium (eMC) for up-to-date advice

Consultant /Specialist responsibilities

- Identify those patients who will benefit from treatment with methotrexate.
- Provide patients with a patient held record book, undertake pre-treatment monitoring of FBC, LFTs, U&Es, creatinine, chest x-ray and record varicella status in the record book.
- Ensure that the patient/carer is an informed recipient in therapy, provide necessary education on their treatment regimen and any monitoring or follow up that is required and issue local patient information leaflets. http://www.nrls.npsa.nhs.uk/resources/?entryid45=59800
- Initiate methotrexate and stabilise patient on a therapeutic dose of methotrexate before referral to the GP.
- Send a letter to the GP requesting a formal agreement to share care and transfer care to GP only after receipt of a completed and signed agreement from the GP.
- Ensure prior dissemination of sufficient information to patient's GP and other carers.
- Inform the GP that methotrexate has been commenced, and the dose and future plans for dose escalation in keeping with the shared care agreement.
- Clinical and laboratory supervision of the patient by blood monitoring and routine clinic follow-up on a regular basis.
- Send a letter/results notification to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated.
- Evaluation of any reported adverse effects by GP or patient.

- Advise GP on review, duration or discontinuation of treatment where necessary. Where urgent action is required following tests the hospital team will telephone the patient and inform GP.
- Inform GP of patients who do not attend clinic appointments.
- Counsel the patient on contraception and what to do if pregnancy occurs. Document in the notes.
- Provide access to backup advice and support facilities at all times.
  Ensure, where timing is appropriate, that the patient has received a flu vaccine prior to commencing treatment that is likely to cause immunosuppression. Document this in the patient notes and inform the GP it has been given

GP responsibilities

- Reinforce the patient's understanding of the nature, effect and potential side effects of the drug before prescribing it as part of the shared care programme and contact the Specialist for clarification where appropriate.
- Prescribe methotrexate at the dose recommended by the hospital Specialist once the patient is stabilised on treatment and side effects have been excluded as far as possible by the hospital. Any decision to alter treatment should usually be taken by the hospital Specialist, including nurse practitioner.
- Check for possible drug interactions when newly prescribing or stopping concurrent medication
- Monitor blood results (FBC, LFT, U&E, ESR and/or CRP) in line with recommendations in this document.
- Monitor patient's overall health and well-being.
- Report any adverse events to the Consultant/Specialist, where appropriate.
- Report any adverse events to the CSM, where appropriate.
- Stop methotrexate if serious adverse drug effect/reaction and contact Specialist team.
- Help in monitoring the progression of disease.
- Encourage patients to carry an up-to-date monitoring and record booklet and information sheet as provided by the hospital http://www.nrls.npsa.nhs.uk/resources/?entryid45=59800

CCG Responsibilities

- To provide feedback to trusts via South West Essex Medicines Management Committee.
- To support GPs to make the decision whether or not to accept clinical responsibility for prescribing.
- To support trusts in resolving issues that may arise as a result of shared care.

Patient/ Carer responsibilities

- Report any adverse effects to their GP and/or Specialist.
- Ensure they have a clear understanding of their treatment.
- Report any changes in disease symptoms to GP and/or Specialist.
- Alert GP and/or Specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy.
- Take/ administer the medication as prescribed.
- Undertake any monitoring as requested by the GP and/or Specialist.

Dispensing Pharmacist responsibilities (Hospital or Community)

- Check patient held monitoring record prior to dispensing.
- Dispensing should meet the NPSA requirements for safe dispensing.

Contact details

Consultant, medical staff and nurse practitioners at the Basildon and Thurrock University Hospitals NHS Foundation Trust (BTUH) are available to give advice and can be contacted either through the main hospital switchboard or direct:

Department / Specialist	Contact Telephone Number
Hospital switchboard – ask for Specialist or On-Call Specialist(Rheumatologist/Dermatologist/ Gastroenterologist) out-of-hours	01268 524900
Rheumatology	
Dermatology	
Gastroenterology	

Document Control	
Version:	Draft v0.12
Shared Care Guidelines are also available electronically via: to insert website link after approval	
Approved by:	South West Essex Medicines Management Committee
Date of issue	November 2016
Next Review Date:	November 2018

METHOTREXATE PATIENT INFORMATION LEAFLET

This form will be completed by the Hospital Specialist and given to the patient once stabilised and a fax back has been received from the GP accepting the transfer of responsibility to primary care.

You have been prescribed **methotrexate 2.5 mg tablets*** or **methotrexate syringes** (delete as applicable)

for.....

This **weekly treatment** will continue until stopped by your doctor

Either as,

Methotrexate 2.5mg tablets (delete as applicable)

Take.....tablets (.....mg) on .....each week

Or

Methotrexate ..... Injection (delete as applicable)

Contents of one syringe (.....mg) to be given intramuscularly / subcutaneously (delete as applicable)

on .....each week

Your GP has been given all the necessary information regarding your condition and treatment.

The date for your next hospital appointment is .....

The success and safety of your treatment also depends on you.

- You will have been given a monitoring booklet, which tells you all about methotrexate, what it is used for and all about its side effects. It is important that you read this booklet and take it with you to all GP and hospital appointments; you should also show it to the pharmacist when you collect your prescription.
- Avoid excessive alcohol consumption.
- Do not take ibuprofen or aspirin without getting advice from your doctor.
- Avoid contact with chicken pox or shingles.
- Your GP/ Practice Nurse needs to see you every .....

If you experience any of the following side-effects see your GP:

- Mouth ulcer, sore throat, sore mouth.
- Feeling generally unwell.
- Feeling sick, upset stomach, diarrhoea.
- Rashes – new rash or severe itching anywhere on the body.

Stop treatment and get immediate medical advice if you develop:

- An infection with fever and or chills or a severe sore throat.
- Sudden shortness of breath (breathlessness).
- The whites of your eyes become yellow.
- Severe itching of the skin.
- New unexplained bleeding or bruising.
- Severe and continuing diarrhoea or vomiting.
- If you think you are pregnant.

If you feel you have any concerns about your treatment contact your GP or the hospital. The direct-dial telephone numbers for the department are.....

The NPSA booklet is freely available and was compiled by the NPSA in June 2006
http://www.nrls.npsa.nhs.uk/resources/?entryid45=59800

GP METHOTREXATE CONTINUING CARE AGREEMENT 1ST LETTER

Name of GP .....

Address .....

Drop code of GP.....

Dear Dr
Re: Patient's name.....
Date of birth.....
Hospital number.....
NHS number.....

I have seen this patient and believe that he/she is suitable for treatment with Methotrexate for:

.....

I have initiated the patient on either

Methotrexate 2.5mg tablets (delete as applicable)

Take.....tablets (.....mg) on .....each week

Or

Methotrexate ..... Injection (delete as applicable)

Contents of one syringe (.....mg) to be given intramuscularly / subcutaneously (delete as applicable)

on .....each week

I will be prescribing and monitoring this patient at our clinic until such a time that the patient is deemed stable, which is likely to be in the region of ..... months.

I would like to seek your agreement to take over the prescribing and monitoring of this patient's treatment after this stabilisation period based on the continuing care document enclosed for your information.

Please complete, sign and fax back the form below to stated safe haven fax. I thank you in anticipation.

Yours sincerely

Dr
(Consultant)

METHOTREXATE CONTINUING CARE GP/PRACTICE FAX BACK FORM

Patient name..... Hospital number.....

Dear GP

You will take over monitoring of the patient including responsibility for organising blood tests and other tests required in accordance with the shared care guidance (enclosed). You will be responsible for reviewing underlying disease including complications and efficacy of therapy.

PLEASE COMPLETE, SIGN AND FAX BACK TO CLINIC/HOSPITAL: .....

I agree to take over the prescribing and monitoring of this medication and disease.

Signed by (GP).....

Name of GP .....

Address .....

or

I am not willing to undertake shared care for this patient because.....
.....
.....

Signed by (GP).....

Name of GP .....

Address .....

Please return to .....

Or Faxback to:.....

References:

1. NHS ONEL and BHRuT NHS Trust Shared Care Guidelines: Methotrexate Rheumatoid arthritis, Psoriasis, Crohn's Disease & Ulcerative colitis. Approved November 2011. Review date April 2013
2. City & Hackney NHS and Homerton University Hospital: Methotrexate shared care guideline. Approved January 2010
3. Mid Essex Locality and Mid-Essex Hospital NHS Trust: Methotrexate shared care Guideline. Approved May 2010. Review date: May 2012
4. BNF 70
5. Metoject Pen® (Medac GmbH) Summary of Product Characteristics accessed on Electronic Medicines Compendium (eMC). Last Updated on eMC 19-Jun-2014. Last accessed November 06, 2015
6. NEL Commissioning Support Unit: Therapeutics Advisory group (TAG) for CCGs and NHS trusts in Norfolk and Waveney: Shared care prescribing information for oral and subcutaneous Methotrexate for the Treatment of Rheumatoid Arthritis, Juvenile Arthritis, Connective Tissue Disease, Felty's Syndrome, Psoriasis and Inflammatory Bowel Disease. July 2015.
7. NICE Clinical Knowledge Summaries: DMARDs (https://cks.nice.org.uk/dmards). Last accessed November 17, 2016.