SHARED CARE PRESCRIBING GUIDELINE METHOTREXATE (ORAL AND SUBCUTANEOUS) IN ADULT PATIENTS WITH RHEUMATOID ARTHRITIS

DOCUMENT DETAILS

Document type	*Shared Care Prescribing Guideline*
Document name	*Shared Care Prescribing Guideline: Methotrexate (Oral and Subcutaneous) in Adult Patients with Rheumatoid Arthritis*
Document location	*Intranet*
Version	*V1*
Effective from	*04 June 2010*
Review date	*04 June 2012*
Owner	Dr Sophia Steer Chair RA NICE Implementation Subgroup 4 (DMARD's)
Approved by	*Drug & Therapeutics Committees (DTC)* *Guy's & St Thomas' NHS Foundation Trust* *King's College Hospital NHS Foundation Trust* *NHS Lambeth* *NHS Southwark*
Related documents	*NICE National Clinical Guideline: Rheumatoid Arthritis, February 2009*
Key words	*Shared, care, prescribing, methotrexate, Metoject, DMARD, guideline, rheumatology, rheumatoid, arthritis, NICE*
Relevant external law, regulation, standards	
Comments on this document to:	*Clinical Governance Pharmacist* *c/o Pharmacy Department, Guy's Hospital*

CHANGE HISTORY

Date	*Change details*	*Approved by*

Methotrexate
Rheumatoid Arthritis

NOTES to the GP

The information in the shared care guideline has been developed in consultation with Primary Care and it has been agreed that it is suitable for shared care.
This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing this drug.

The questions below will help you confirm this:

- Is the patient's condition predictable or stable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.
If the answer is NO to any of these questions you should contact the requesting consultant or your local PCT medicines management team. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Prescribing should follow requirements in the South East London Interface Prescribing Policy
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount

Date shared care guideline prepared: 8/3/2009

Approved by: PCT Medicines Management Committee
NHS Lambeth 3/5/2010
NHS Southwark 29/3/2010

Approved by DTC or equivalent Date approved:
Guy's & St Thomas' 23/3/2010
King's College 24/5/2010

Review date: 4/6/2012

Prepared by:

Scott Mercer
Principal Medical Pharmacist
Guy's & St Thomas' NHS Foundation Trust

Dr Sophia Steer
Consultant Rheumatologist
King's College NHS Foundation Trust

Manisha Madhani
Pharmacy Team Leader
General and Emergency Medicine
King's College NHS Foundation Trust

Co-authors:

Dr Terence Gibson
Consultant Rheumatologist
Guy's & St Thomas' NHS Foundation Trust

Professor Andrew Cope
Consultant Rheumatologist
Guy's & St Thomas' NHS Foundation Trust

AGREEMENT TO PARTICIPATE IN SHARED CARE

METHOTREXATE (ORAL & SUBCUTANEOUS) IN ADULT PATIENTS WITH RHEUMATOID ARTHRITIS

Consultant Name:	**Patient name:**
Consultant signature:	**Patient Hospital Number:** **Patient NHS Number:**
Date completed: **Hospital:**	**Patient Agreement** ☐ **Patient agrees to shared care** ☐ **Patient does not agree to shared care**
GP Name	**Specialist Rheumatology Nurse Name**
GP Signature	**Specialist Rheumatology Nurse Signature**
Date completed:	**Date completed:**

ACTION

1. Consultant Rheumatologist

- Explain shared care to patient and obtain agreement.
- Indicate requesting hospital.
- Complete and sign agreement.
- Fax full shared care guideline (including signed agreement to GP) - fax numbers at **http://www.nhs.uk**.
- Place original in notes.

2. General Practitioner

- If **in agreement** to participate in shared care, sign and fax back to Rheumatology Department:
  - Guy's & St Thomas': 020 7407 7532
  - King's College: 020 3299 1734
- If **not in agreement** to participate in shared care, contact consultant and local PCT medicines management team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the local PCT Medicines Management team should be informed.
- Once decision reached file copy in patient's notes.

3. Specialist Rheumatology Nurse

- Once received completed agreement by Consultant and GP, sign to confirm awareness that the patient will be under shared care.
- Take any necessary actions prior to shared care commencing (changing of appointments etc).
- Original to be filed in Patient's clinical record.

Attach patient addressograph or enter: Patient name Patient hospital number Patient NHS number Date of Birth

Methotrexate 2.5mg Tablets or Metoject® Injection

1. CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the consultant and the GP are in agreement that the patient's condition is stable or predictable.
- The hospital will provide the patient with a supply of therapy until the patient is stable.

2. AREAS OF RESPONSIBILITY

Consultant	GP
▪ Establish or confirm diagnosis and assess patient suitability for treatment ▪ Baseline monitoring FBC, U&E's, Creatinine, LFT's, ESR, CRP, chest x-ray (+/- lung function tests) ▪ Discuss treatment with patient (adverse effects (including rash/sore throat), once weekly administration and need for folic acid) and ensure they have a clear understanding of it. Where appropriate obtain signed consent. ▪ Provide patient with Arthritis Research Campaign Patient information leaflet on methotrexate and NPSA pre-treatment leaflet. ▪ Prescribe **methotrexate** (for **tablets** use only **2.5mg strength**) **once a week** and monitor treatment according to local guideline or formulary until patient's condition is stable or predictable ▪ Prescribe **folic acid 5mg once a week** (usually the day after methotrexate) ▪ For methotrexate injection, follow local procedures to ensure patient is trained and demonstrates competence on injection technique, disposal of sharps and use of cytotoxic spillage kit ▪ Enter blood results in patient held monitoring booklet ▪ Once the patient's condition is stable or predictable fax the signed shared care guideline to GP for consideration ▪ Continue to monitor all patients on biologic therapy. Shared care will not be sought for biologic therapy (anti-TNF's, rituximab). ▪ Ensure contact details (section 4) are up to date ▪ Confirm patient is not pregnant, if any doubt perform pregnancy test. Continued on next page *After agreement to shared care* ▪ Inform GP when patient is stable ▪ Inform GP of abnormal monitoring results and any changes in therapy ▪ Evaluate adverse events reported by GP or	▪ Consider shared care proposal within 2 weeks of receipt ▪ If named GP is not available over the next week pass request to a GP colleague ▪ If in agreement to shared care take over prescribing responsibility, confirm agreement by faxing a signed copy of page 3 back to the Rheumatology Department. ▪ If not in agreement to share care discuss with requesting consultant or local PCT medicines management team within 2 weeks of receipt of shared care request *After agreement to shared care* ▪ Prescribe methotrexate as recommended in most recent clinic letter and patient held monitoring book ▪ Prescribe **methotrexate once a week (for tablets use only 2.5mg strength)** ▪ Prescribe **folic acid 5mg once a week** (usually the day after methotrexate) ▪ Monitor general health of patient (discuss with rheumatologist if concerned) and check adverse effects as appropriate ▪ Reinforce to patient that methotrexate is taken once a week, the number of 2.5mg methotrexate tablets to be taken, folic acid is to be taken once a week on a different day (as stated in monitoring booklet) and rash/sore throat. ▪ Inform specialist consultant of suspected adverse effects ▪ Report suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk ▪ Stop treatment on advice of specialist or immediately if urgent need arises ▪ Check compatibility interactions when prescribing new or stopping existing medication ▪ Carry out monitoring and follow up according to shared care guideline ▪ Enter blood results in patient held monitoring booklet

patient ▪ Report suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk ▪ Carry out ongoing monitoring and follow up accordingly to shared care guidelines including continued need for therapy.	▪ Discuss any abnormal results with specialist consultant and agree any action required ▪ Only ask specialist to take back prescribing should unmanageable problems arise. Allow an adequate notice period.

3. PATIENT'S RESPONSIBILITIES

- Attend all hospital and GP appointments
- Take medicines as agreed
- Keep a medicines monitoring booklet and show it to any healthcare professional that treats them
- Understand that methotrexate is taken weekly and the number of 2.5mg tablets to be taken
- Understand that folic acid 5mg is taken once a week usually the day after the methotrexate
- If self administering methotrexate injections, understand how to inject, how to dispose of needles and syringes, how to use a cytotoxic spillage kit and how to contact the specialist nurse if necessary.
- Report any adverse effects to GP, hospital doctor or specialist nurse immediately
- Do not share medicines
- Inform hospital and GP of any changes in address or telephone numbers
- Avoid self administration of over-the-counter aspirin or ibuprofen

4. COMMUNICATION AND SUPPORT

Hospital contacts

Kings College Hospital

Rheumatology Consultants:	0203 299 9000 Telephone (Secretary)
Dr E. Choy	Ext 1732
Dr P. Gordon	Ext 1735
Professor Scott	Ext 1731
Dr S. Steer	Ext 1733
Locum	Ext 5611

Rheumatology Nurse Specialist Advice Line (Monday to Friday 09:00 – 17:00)
Tel: 020 3299 8568 Fax: 020 3299 1734

Rheumatology Specialist Registrar via hospital switchboard 020 3299 9000

Pharmacist:
For Drug Information queries: 0203 299 9000 ext 3007

Guys and St Thomas's Hospital

Rheumatology Consultants:
Dr T Gibson, 020 7188 5867 or pager 881870 via switchboard.
Prof A. Cope 020 7188 5884
Dr B. Kirkham 020 7188 5884
Dr S. Agarwal 020 7188 5867

Rheumatology Nurse Specialist Advice Line (Monday to Friday 09:00 – 17:00)
Tel: 020 7188 5896 Fax: 020 7407 7532

Rheumatology Registrar via hospital switchboard 020 7188 7188 (Monday to Friday 09:00 – 17:00)

Rheumatology Consultant oncall available via hospital switchboard 020 7188 7188

Medicines Information 020 7188 5008 (St Thomas'), 020 7188 8748 (Guy's)

Attach patient addressograph or enter: Patient name Patient hospital number Patient NHS number Date of Birth

Methotrexate 2.5mg Tablets or Metoject® Injection

5. CLINICAL INFORMATION

Indication(s):	Rheumatoid Arthritis
Place in Therapy:	Disease modifying anti-rheumatic drug
Dose & route of administration:	Oral or subcutaneous: 7.5mg – 25mg **once a week.** **Only prescribe 2.5mg tablets or the appropriate strength of Metoject pre-filled syringes.** Concomitant **folic acid 5mg once a week** (usually the day after methotrexate - not to be taken on day methotrexate is taken.
Duration of treatment	Indefinitely if patient is responding well to treatment and in absence of significant side effects
Criteria for stopping treatment	Failure to respond to treatment or adverse effects necessitating withdrawal. **If blood results fall into the parameters below or the patient reports an adverse drug reaction listed below, withhold and discuss with Rheumatologist (oncall if necessary – see section 4).** WBC < 3.5 x 10^9/l Neutrophils < 2.0 x 10^9/l Platelets <150 x 10^9/l AST, ALT > twice upper limit of reference range MCV > 105 fL Unexplained fall in serum albumin (in absence of active disease) New or increasing dyspnoea or dry cough – stop immediately and urgent discussion with rheumatologist Unexplained acute widespread rash – withhold and discuss with rheumatologist. Oral ulceration (if severe), nausea (if severe) or vomiting, diarrhoea, dark urine or abdominal pain. Severe sore throat/abnormal bruising Renal Impairment (GFR < 50 ml/min)

Monitoring Requirements including frequency:	**Consultant:** **<u>Baseline</u>** Full blood count, urea, electrolytes, creatinine, liver function tests, erythrocyte sedimentation rate, C-reactive protein, chest X-ray (unless done in the last 6 months) +/- lung function tests **<u>Ongoing</u>** Full blood count, urea and electrolytes, creatinine and liver function tests 2 weekly for 6 weeks or until target dose is achieved, then monthly for one year. Shared care will be sought after 3 months providing the patient has been stable for 6 weeks. After one year the frequency of monitoring can be reduced to every 2 – 3 months but this is based on the clinical judgement of the Consultant Rheumatologist. **<u>Following dose changes</u>** Full blood count and liver function tests two weekly after dose increases for 6 weeks then if stable back to monthly thereafter. Shared care will be sought 6 weeks after the dose change providing the patient is stable. Ask patient about any rashes or oral ulceration at each visit. **GP:** Monthly blood tests for one year. After one year a reduced frequency of monitoring (every 2 – 3 months) may be appropriate depending on the clinical judgement of the Consultant Rheumatologist with consideration for patient specific risk factors (i.e. age, renal function, alcohol intake) and co-morbitidies (e.g. diabetes).
Follow up arrangements	**Consultant Rheumatologist** Subject to individual patient response: 3 monthly, 6 monthly or 12 monthly if well controlled and disease activity stable. At each clinic attendance update the patient held monitoring booklet. Remind patient of signs and symptoms of methotrexate toxicity and check patient understanding of once weekly administration and need for folic acid. Ask patient about any rashes or oral ulceration at each visit. Report suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk Within 2 weeks of each clinic attendance, write/fax or telephone GP to advise on: • review, duration or discontinuation of treatment • recent blood test results • frequency of monitoring • any adverse effects experienced and consequent actions • non-attendance and any consequent actions

	GP Blood tests as outlined in monitoring section. At each appointment update the patient held monitoring booklet. Request patient seen earlier if: • disease flare • adverse effects experienced • recurrent infections Remind patient of signs and symptoms of methotrexate toxicity and check patient understanding of once weekly administration and need for folic acid. Ask patient about any rashes or oral ulceration at each visit.
Practical issues including other relevant advice/information:	**Adverse Effects / Abnormal laboratory Parameters** MCV > 105 - if B12, folate and TSH abnormal treat any underlying abnormality. If B12, folate and TSH normal discuss with rheumatologist. Nausea/dizziness/headache – if tolerable continue. Severe symptoms may require dose reduction or cessation of treatment. Consider using an antiemetic if nausea is severe. Discuss ongoing nausea with rheumatologist. Abnormal bruising or severe sore throat – Check FBC immediately and withhold until results available. Discuss with rheumatologist. New onset shortness of breath or dry cough – stop methotrexate immediately and discuss with rheumatologist. Pneumonitis is more likely to occur in first year of treatment but can occur at any time. Unexplained acute widespread rash – withhold and discuss with rheumatologist. Severe oral ulceration – withhold and discuss with rheumatologist. **Pregnancy, breastfeeding and contraception** Methotrexate is contraindicated in pregnancy and breast feeding. Whilst taking methotrexate and for at least 3* months stopping, both men and women must use reliable contraception. For patients considering family planning, discuss with rheumatologist. Women must wait at least 3 full menstrual cycles (or 3* months) after stopping methotrexate before conceiving. Men should continue to use contraceptives for 3* months after stopping methotrexate. ***NOTE: Some manufacturers recommend using reliable contraception for 6 months after cessation of methotrexate therapy. Always consult the Summary of Product Characteristics for the product being prescribed (www.medicines.org.uk)** Methotrexate may be excreted in breast milk so breast feeding must be avoided.

	Vaccinations Patients must not receive immunisations with live vaccines such as oral polio, MMR, BCG or yellow fever. Seasonal and pandemic influenza vaccination and Pneumovax are safe and recommended. Patients exposed to Chicken Pox / shingles should receive passive immunisation with VZIG (varicella-zoster immunoglobulin), if they are varicella-zoster virus (VZV) susceptible (VZV IgG undetectable on blood testing). **Risk factors for hepatotoxicity** Obesity, diabetes and alcohol excess increase the likelihood of methotrexate induced liver damage. Alcohol consumption should be well within National guidelines and should be in the region of 4-6 units a week. **Methotrexate Injection (Metoject)** For methotrexate injection, each Acute Trust to follow local procedures to ensure patient is trained and demonstrates competence on injection technique, disposal of sharps and use of cytotoxic spillage kit. Guy's & St Thomas' protocol available on intranet and copies available from specialist nurses. Nurses also hold copies of competency assessments. **Clinically Significant Drug Interactions** (refer to BNF for full list) ▪ **Co-trimoxazole, trimethoprim, sulphonamides** (avoid - may increase anti folate effect and lead to increased risk of marrow aplasia) ▪ **NSAIDs** (monitor for signs/symptoms of toxicity – excretion of methotrexate probably reduced by NSAIDs). Patients should be advised to avoid self-medication with over-the-counter **aspirin** or **ibuprofen**. Discuss with rheumatologist before commencing patients on newly prescribed NSAIDs. ▪ **Neomycin** (monitor efficacy – possible reduced absorption of methotrexate) ▪ **Ciprofloxacin** (monitor for signs/symptoms of toxicity – excretion of methotrexate possibly reduced) ▪ **Doxycycline/tetracycline** (increased risk of toxicity) ▪ **Penicillins** (increased risk of toxicity) ▪ **Clozapine** – (avoid methotrexate as increased risk of agranulocytosis) ▪ **Ciclosporin** (increased risk of toxicity) ▪ **Leflunomide** (increased risk of toxicity)
Information provided	Arthritis Research Campaign Leaflet: Methotrexate NPSA pre-treatment patient information leaflet Monitoring Booklet
Evidence Base for treatment and Key references:	NICE National Clinical Guideline: Rheumatoid Arthritis, February 2009 BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in conjunction with the British Association of Dermatologists. 2008. BSR/BHPR DMARD quick reference guideline November 2009. British National Formulary 58 Summary of Product Characteristics – Goldshield, Metoject, Hospira, Maxtrex Renal Drug Handbook, 3rd Edition, Radcliffe Publishing.

NB: for full details of adverse effects and drug interactions refer to latest Summary of Product Characteristics