East Lancashire Medicines Management Board Shared Care agreement for weekly Methotrexate therapy in long term conditions

This shared care agreement outlines the responsibilities for managing the prescribing and monitoring of methotrexate therapy in long term conditions (e.g. rheumatoid arthritis, psoriasis) between the specialist and general practitioner (GP) in East Lancashire. If the GP is unable to undertake these roles, then he or she is 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.

Contents: *Areas of responsibility for the sharing of care, Monitoring Arrangements, Aspects of care for which the consultant is responsible, Aspects of care for which the GP is responsible, Ancillary products, Monitoring requirements, Patient Information materials, The Patients' Role, Parenteral Therapy, Local Contact details, Prescribing information, References.*

Areas of responsibility for the sharing of care

The specialist must inform the GP in writing of the intention to transfer responsibility for prescribing and blood monitoring to primary care for this drug in every patient.
If the arrangement is unacceptable to the GP then the GP must contact the specialist in writing to make this clear.
The intention to share care must be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients taking methotrexate are under regular follow-up in secondary care, where it is expected that baseline tests will be taken, before care is transferred to the GP.
A patient held Drug Monitoring Record Book (DMRB) is the fundamental communication tool for recording dosing and monitoring information. Results of monitoring blood tests and changes of dose must be recorded promptly in the DMRB and the DMRB must be viewed and checked by all prescribers prior to issue of a prescription for methotrexate.
Where the prescribing role is transferred to primary care, the monitoring of blood indices should ideally also occur in primary care. If however monitoring is maintained in specialist clinic, the DMRB must be updated at that clinic.
The doctor who prescribes the medication assumes legal clinical responsibility for the drug and the consequences of its use.

Monitoring Arrangements This table describes the monitoring responsibilities

	Consultant	Usual GP
FBC Prior to treatment	Yes	
LFTs Prior to treatment	Yes	
U&E's Prior to treatment	Yes	
Chest X-Ray Prior to treatment	Yes	
FBC, LFTs (ALT only), U&Es **fortnightly for the** first 6 weeks after the last dose change; thereafter **monthly** until stabilised. Monitoring frequency can be reduced further, in discussion with the patient, to **3 monthly** if the dose and trend remains stable. *	Yes until GP takes on responsibility for blood monitoring.	Yes, in accordance with advice from specialist
Ask patient at each consultation if they have dyspnoea	Yes	Yes

- The frequency of monitoring is ***not*** based on evidence but from practical *experience* published by learned colleagues.

Aspects of care for which the consultant is responsible

- Have read and implemented the recommendations of the NPSAs Methotrexate Safety Alert July 2004 (see below). Links to supporting documents are found below.
- Discuss the benefits and side effects of treatment with the patient using the Arthritis Research Campaign (ARC) or British Association of Dermatologists (BAD) patient information leaflet. Ensure that the patient understands that dosing is at WEEKLY.
- Perform baseline tests (FBC, LFTs, U&E's, creatinine, chest X-ray). Continue monitoring until responsibility for monitoring is assumed by the GP.
- Initiate and titrate treatment with methotrexate
- Provide the patient with the East Lancashire Hospitals patient held Drug Monitoring Record Book and a copy of the patient information leaflet (see above).
- Invite the GP to participate in shared care and provide written monitoring guidelines.
- Ensure availability of baseline test results and recommend frequency of monitoring.
- Initiate folic acid 5mg WEEKLY, the day after the methotrexate dose.
- Periodically review the patient's condition and communicate promptly by letter with the GP when treatment is changed or if the patient fails to attend clinic.
- Advise the GP on when to adjust the dose, stop treatment, or consult with specialist.
- Prescribe only 2.5mg strength tablets wherever practical. New patients will be commenced on 2.5mg tablets and given a minimum two week supply. The dose and number of 2.5mg tablets to be taken must be specified.
- View and check the Drug Monitoring Record Book prior to issue of all prescriptions for methotrexate.
- Report adverse events to the CSM via the yellow card scheme and to the GP.
- Ensure that clear backup arrangements exist for GPs to obtain advice and support.
- Ensure the patient is not pregnant.
- Ensure the patient is counselled on not becoming a parent during, and for 3 months after treatment.
- Complete and forward Incident Reports (IR1) for incidents relating to methotrexate

Aspects of care for which the GP is responsible

- Have read and implemented the recommendations of the NPSAs Methotrexate Safety Alert July 2004. Links to supporting documents are found below.
- Prescribe methotrexate generically as 2.5mg strength tablets ONCE A WEEK where possible. (Not to prescribe as directed but use specific dose and directions).
- Prescribe folic acid 5mg ONCE A WEEK the day after the methotrexate dose.
- Ensure the patient has a patient held monitoring and dosage card and patient information leaflet given by the hospital.
- Ensure compatibility with other concomitant medication.
- Ensure that the patient understands that dosing is at weekly intervals, and which warning symptoms to report. (See appendix 1 Patient Information Leaflet)
- Monitor blood counts, hepatic and renal function at recommended frequencies, and refer if abnormal.
- Blood test results should be interpreted in line with the table in this document.
- Ensure that any test results or changes in therapy are recorded in the patient held monitoring and dosage card.
- To be aware of patients attending with other symptoms; signs of methotrexate toxicity or intolerance may present as breathlessness, dry persistent cough, vomiting and diarrhoea.
- Adjust or stop treatment on the advice of the specialist team or immediately if an urgent need to stop treatment arises
- Report adverse events to the specialist team and CSM via the yellow card system.
- View and check the Drug Monitoring Record Book prior to issue of all prescriptions for methotrexate.
- Review and sign repeat prescriptions for methotrexate separately from routine repeat prescriptions
- Complete and forward Incident Reports (IR1) for incidents relating to methotrexate

Whoever prescribes the methotrexate must ensure blood tests are performed and that results are recorded in the patients'` monitoring and dosage record.

Ancillary products which may need to be prescribed in primary care

Folic acid at a dose of 5mg **ONCE weekly,** preferably the day ***after*** the methotrexate, is the typical dose for this drug in prevention of minor adverse effects. (Folic acid can be given any day as long as it is **NOT** on the same day as methotrexate). A Pneumovax II vaccination and annual influenza vaccination is also recommended.

Monitoring requirements

Symptoms	Action required
New or increasing dyspnoea or cough	Withhold and urgently discuss with member of specialist team
Rash or oral ulceration, nausea, vomiting or diarrhoea.	Withhold until discussed with member of specialist team
Abnormal bruising or severe sore throat	Immediate FBC and withhold until the result of FBC is available.

Changes in blood results	Action required
MCV>105fl	Investigate and check serum $B_{12,}$ folate and TFTs. If B_{12} or folate low start appropriate supplementation. Discuss with specialist team if necessary.
Significant deterioration in renal function	Withhold until discussed with member of specialist team
Unexplained fall in albumin	Withhold until discussed with member of specialist team
WBC < 3.5 or 4.0 $x10^9$ /l	Withhold until discussed with member of specialist team
Neutrophils < 2.0 $x10^9$/l	Withhold until discussed with member of specialist team
Platelets <150$x10^9$ /l	Withhold until discussed with member of specialist team
ALT >2 fold rise (from the upper limit of reference range) (observing for successive increases).	Withhold until discussed with member of specialist team

Baseline Laboratory Values.

Laboratory values	Normal range
WBC	4.0-10.0$x10^9$/L
Neutrophils	2.0-7.5$x10^9$/L
Platelets	150-450$x10^9$/L
ALT*	7-56

* Observing for successive increase

Patient Information materials

- **Patient Information Leaflet** (ARC/BAD) – available from the specialist clinic (*see references*)
- The **Drug Monitoring Record Booklet** – available from specialist clinics, ELHT hospital Pharmacies or PCT medicines management teams.

The Patients' Role

- To bring the DMRB to all appointments or consultations with a health professional
- To report to the specialist team or GP if he or she has any concerns in relation to treatment with methotrexate.
- To inform specialist team or GP of any other medication being taken, including over-the-counter products.
- To report any adverse effects or warning symptoms (i.e. infection, fever, chills, unexplained bruising or bleeding) to the specialist team or GP whilst taking methotrexate.

Parenteral Therapy

Occasionally patients may require subcutaneous or intra-muscular treatment with methotrexate and in this case the responsibility for prescribing and monitoring will remain with the hospital specialist.

Contact details for local specialist advice

Specialist Area	Name	Telephone
Rheumatology	Dr L S The (Secretary) Dr J Brockbank (Secretary) Dr Burke (Secretary) Dr Ariyaratnam (Sectretary) Elaine Doyle Bridget Jepson Ann Gooden Liz Mahomed	01254 734428 01254 734604 01282 804436 01282 804820 01282 474047 01254 734491 01254 734510 01254 734431
Dermatology	Dr M B Daly (Secretary) Dr I H Coulson (secretary) Dr C Owen (Secretary)	01254 734093 01282 804819 01254 734364
East Lancashire Hospitals NHS Trust Pharmacy Dept	Medicines Information	01254 732254
Other specialists	Via hospital switchboard	01254 263555

This document has been approved by East Lancashire Drug and Therapeutics Committee and applies to the following organisations:
Blackburn with Darwen PCT, East Lancashire PCT, East Lancs Hospitals NHS Trust.

Document prepared by Vince Goodey Review Date 26th November 2009

NPSA METHOTREXATE ALERT – JULY 2004

http://www.npsa.nhs.uk/web/display?contentId=3107

This alert sets out the actions for NHS organisations in England and Wales to reduce the risks associated with oral methotrexate.

The NPSA has also issued an update about producing patient information, following queries and concerns raised by clinical groups. Patients with concerns about taking oral methotrexate to treat arthritis are advised to contact the Arthritis Research Campaign on 0870 850 5000. Patient information from ARC is also available at http://www.arc.org.uk

Methotrexate Prescribing Information (for long term conditions)

Indications: (Licensed) Rheumatoid arthritis, psoriasis.
(Unlicensed) psoriatic arthritis, Crohn's disease, connective tissue disease (SLE, Myositis & Vasculitis) & Felty's syndrome.

Dosing
A typical dose regimen may be: 7.5mg to 25 mg **ONCE weekly**; **starting dose** may vary depending on the severity of the condition and patient characteristics such as age, renal function & other co-morbid conditions. The initial dose may be 5-10mg once weekly, increasing by 2.5- 5mg every 4-6 weeks until stabilised. Rarely the maximum dose can be 30mg per week. Lower doses should be considered for frail elderly persons who often have poor renal reserve. If maximum oral dose is not effective or causes intolerance, consider alternative route of administration before discontinuation of the drug

Cautions
1. Patients with clinically significant renal impairment from any cause (pre renal, renal or post renal).
2. Localised or systemic infection including hepatitis B&C and history of TB (also see contra-indications section)
3. Unexplained anaemia and or cytopaenia associated with marrow failure (also see contra-indications section).
4. Live immunisations should be avoided (Pneumo vac & Flu vac can be given) **Elective Surgery:** Therapy can be continued. Caution for early detection of infection and complications.

Drug interactions:
a. Phenytoin, co-trimoxozole, trimethoprim: Antifolate effect of methotrexate is increased. Folate antagonists such as trimethoprim and co-trimoxazole should not be given concomitantly.
b. Probenecid, penicillin, azapropazone, NSAID: Methotrexate excretion is reduced. (Clinically significant interaction between NSAID & methotrexate is rare)
c. Tolbutamide: serum concentration of methotrexate may be increased
Alcohol: patients receiving methotrexate to limit their alcohol intake to a minimal amount, ***well within national limits .***
NSAIDS: Most NSAIDS can be continued as long as *monitoring is regularly undertaken*. Special cautions need to be exercised if significant abnormalities are noted in liver enzymes. All patients should be ***regularly advised*** to ***avoid over the counter medications*** including aspirin and ibuprofen 12 without the knowledge of the specialist team

Contra-indications:
a. Pregnancy & breast feeding
All patients, male & female, should be advised against conception and pregnancy during treatment with methotrexate as it is an abortificient as well as a teratogenic drug. If patients become pregnant inadvertently it is appropriate to refer the patient to an Obstetrician. Breast-feeding should not be allowed as the drug may be excreted in the breast milk. Patients should be advised to continue contraception for at least 3 months after stopping methotrexate.

b. Suspected local or systemic infection
In contrast to many immunosuppressive therapies, methotrexate is ***relatively safe*** and has a much lower risk of infection associated with its use. However infections are still reported and such infections need to be diagnosed at an early stage to prevent systemic dissemination. Methotrexate should ***be stopped immediately,*** if infection is suspected. If infection is associated **with dehydration and pre-renal failure**, consider ***folinic acid rescue (seek specialist advice).*** The infections can be due to a range of organisms from viral and bacterial to rare opportunistic infections. One recent short-term observational study (over 6 months) showed a high death rate (33%) in patients with pulmonary infections. Significant mortality and morbidity can be associated with ***viral infections due to Herpes Zoster / varicella***. Patients with ***history of contacts*** with such viral infections or even vaccination need special advice.

c. Bone marrow failure with unexplained anaemia and cytopaenia
Significant drop in cellular counts can occur as a result of *Methotrexate induced* ***Bone marrow suppression***. It is particularly likely in the elderly and in patients with significant ***renal impairment*** or in patients with ***concommitant administration of anti folate drugs***. A significant drop in cellular count should be treated immediately by:
a. ***Withdrawing*** the methotrexate therapy
b. Giving ***folinic acid rescue*** therapy
c. Consider ***immediate*** discussion with ***supervising specialist***

Possible side effects of treatment
Low-dose methotrexate may be associated with a number of serious adverse effects, including: hepatotoxicity, pulmonary toxicity and bone marrow toxicity. Other common non-life-threatening adverse effects of low dose methotrexate are those affecting the gastrointestinal system (nausea, diarrhoea and stomatitis), and the central nervous system (headaches, drowsiness, mood alteration, blurred vision).

References

Arthritis and Rheumatology Council Methotrexate Patient Information Leaflet: http://www.arc.org.uk/arthinfo/patpubs/6247/6247.asp

National Guidelines for the Monitoring of Second Line Drugs. British Society for Rheumatology & British Association of Dermatologists. July 2006.
National Patient Safety Agency. www.npsa.nhs.uk
Wyeth Pharmaceuticals. Methotrexate sodium tablets 2.5 mg. Summary of Product Characteristics 2003.
ESCA: Methotrexate for the treatment of moderate to severe active rheumatoid arthritis. Midland Therapeutic Review and Advisory Committee (MTRAC)
Committee of Safety of Medicines. Current problems in pharmacovigalence. Medicines Control Agency. Current problems Volume 23 September 1997. Blood dyscrasias and other ADRs with low dose methotrexate.