Lincolnshire Primary Care Trust

**LINCOLNSHIRE PRIMARY CARE TRUST in association with UNITED LINCOLNSHIRE HOSPITAL TRUST**

# SHARED CARE GUIDELINE: METHOTREXATE in RHEUMATOLOGY

**General Principles**

Shared Care Responsibilities:
In its guidelines on responsibility for prescribing (circular EL (91) 127) between hospitals and general practitioners, the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription. (*BNF*, 51, March 2006, p. 4)

Aims:
(1) The aim of shared care guidelines is to provide information and/or guidance to GPs and hospital staff relating to the potentially complex implications of sharing patient care for a specific drug between primary and secondary/tertiary care.

(2) Specific shared care guidance should be available for any high cost drug, high-risk drug therapy or device that may be prescribed for a patient following specialist referral. Such guidance will only be produced where shared care is considered an appropriate option.

(3) Each guideline will include a clear statement of the responsibilities of both the GP and the specialist unit within the overall provision of the treatment to the patient.

(4) Shared care guidelines will ensure that the GP has sufficient information available to undertake to prescribe a specialist treatment if s/he so wishes. It is not the intention of these guidelines to insist that GPs prescribe such treatment and any doctor who does not wish to accept clinical or legal responsibility to prescribe such a drug is under no obligation to do so. Nonetheless the development of a shared care guideline will only be undertaken within the context of a broad acceptance between the County-Wide PCT Prescribing Group and secondary/tertiary care that GP prescribing of such a treatment is appropriate within the constraints of formal shared care. Any drug approved for the development of a shared care guideline will automatically be classified as amber on the Lincolnshire Traffic Lights List and , if high-cost, will be supported financially through the High Cost Drugs Reserve. Thus there should be no financial reason why a GP should be deterred from prescribing a high cost drug under a shared care guideline.

## Further copies

Further copies of any guidelines in this series are available from PCT Prescribing Advisers.

**Date of Issue:** Jan 2007
**Review Date:** Jan 2009

**Drug Details**

Approved Name: **Methotrexate**

Brand Name: Non-proprietary

Form and Strength: 2.5mg tablets (only 2.5mg tablets are to be prescribed)

**Specialist Responsibilities**

The specialist secondary/tertiary care service will:

1. Send a letter to the GP suggesting that shared care is agreed for this patient.
2. Ensure that the patient receives supplies of methotrexate from the hospital or prescribed from the hospital on FP10HP until the GP formally agrees to share care.
3. Carry out FBC, Creatinine, LFTs, and hepatitis serology before commencing therapy, and at the appropriate intervals during the dose stabilisation period.
4. Conduct a baseline chest X-Ray and liver ultrasound.
5. Decide whether a liver biopsy is appropriate and carry it out if indicated.
6. Provide patient with Methotrexate patient treatment information leaflet.
7. Provide patient with patient-held monitoring and dosage record book and record all results in this book
8. Periodically review the patient's clinical condition.
9. Advise on dosage alterations where appropriate.

**GP Responsibilities**

The GP will:

1. Notify the consultant in writing, without undue delay, if they agree to share care.
2. Monitor the patients overall health and wellbeing.
3. Monitor the patient for adverse drug reactions and remain vigilant to the risk of potential drug interaction.
4. Prescribe the medication for the patient.
5. Carry out monitoring tests according to guidelines specified in the monitoring section, and record all results in the patient held record book.
6. Act promptly on the results of the blood tests and adjust or stop the dose if appropriate.

**If in doubt STOP the treatment and contact the Specialist – within 7 days.**

**Referral Criteria**

1. Patients will have received at least 3 months of methotrexate therapy on hospital prescription.
2. Patients will have been stabilized on a suitable dose of methotrexate. During this time it may be more convenient for the patient to have blood tests conducted at the GP surgery, but the responsibility for ensuring that the monitoring is done and the interpretation of the results remains with the specialist until the GP has agreed to take on full prescribing.
3. The specialist will have carried out an assessment of efficacy.

**Licensed Indications**
Moderate to severe active rheumatoid arthritis
**Recommended Dosage and Administration**

METHOTREXATE should be administered **ONCE A WEEK** on the same day .
5mg weekly initially, increasing progressively, usually by 2.5mg every 6 weeks, to a maintenance dose of between 10mg and 25mg once weekly.
The SC route may be considered in poor responders or when oral dose is limited by gastrointestinal side effects.
Lower doses are required in the elderly and those with renal impairment
Folic acid 5mg daily is also given on six days of the week when methotrexate is not taken to improve patient tolerance, prevent folate deficiency and reduce toxicity

**Background Pharmacology**
Methotrexate is a competitive inhibitor of dihydrofolate reductase and thus interferes in the process of DNA synthesis and cell replication. This may not account for its action in rheumatoid arthritis.
**N.B at the doses used in rheumatology, methotrexate is classed as an immunosuppresive drug and not a cytotoxic agent**.

**Preparations Available**
Methotrexate is available as tablets containing 2.5mg and 10mg of methotrexate.
Attention should be paid to the strength of methotrexate tablets and the frequency of dosing.
**Only 2.5mg tablets are to be prescribed.**

**Adverse Effects**
Hepatotoxicity: Liver fibrosis is related to the presence of psoriasis, concomitant and past alcohol consumption and (to a lesser extent) the cumulative dose. Serum Procollagen peptide 111 (PN111P) is helpful in identifying those patients at risk of liver fibrosis; however, liver biopsy is the only reliable test. If methotrexate is stopped liver fibrosis may regress.
Transient elevations in serum transaminases are common in the 1 - 3 days after a dose but they are not predictive of chronic hepatotoxicity. If the transaminases rise to above 3 times the upper limit of normal, then methotrexate should be discontinued or the dose reduced.

Haematological: Bone marrow toxicity. Macrocytic indicies without anaemia are common and do not require action. Use with extreme caution in blood disorders and avoid use if these are severe.

Gastrointestinal: Nausea and anorexia are common. Diarrhoea, vomiting and ulcerative stomatitis are less often observed but frequently necessitate cessation of treatment.

Reproductive effects: Methotrexate is a potent teratogen and abortifacient. Reversible oligospermia may occur.

Pulmonary toxicity: Acute pneumonitis is idiosyncratic and rare.

Central Nervous System: Headaches, drowsiness, dizziness and blurred vision.
Other: Hair loss (usually mild, rarely significant), fatigue, abnormal bruising, sore throat, rash, oral ulceration, photophobia.
Troublesome nausea can be treated with an anti-emetic (e.g. prochlorperazine).
Abnormal bruising/sore throat necessitate withholding of therapy until a FBC is available
Macrocytosis (MCV > 105fl) will necessitate a check of B12 and folate status and treatment if low.

**Drug Interactions**
The following drugs may interact with methotrexate and increase its activity**:**

Important: co-trimoxazole trimethoprim

Others:

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|---|---|---|
| Alcohol | furosemide | ciclosporin, |
| Aspirin | tetracyclines | probenecid |
| doxycycline | pyrimethamine | phenothiazines |
| penicillins | clozapine | retinoids, |
| ciprofloxacin | chloramphenicol | corticosteroids |
| phenytoin | dipyridamole. | NSAIDs |

**Contra-indications**
Methotrexate is contra-indicated in;
- the presence of severe**/**significant renal or significant hepatic impairment.
- liver disease including fibrosis, cirrhosis, recent or active hepatitis.
- active infectious disease.
- immunodeficiency syndrome(s).
- serious cases of anaemia, leucopenia or thrombocytopenia.

Pregnancy and Breast Feeding:
Teratogenic. Fertility may be reduced in both sexes; both men and women receiving methotrexate should use contraception throughout the treatment period and for at least 6 months after treatment has stopped.
Breast-feeding should be discontinued.

Vaccines: Live vaccinations should not be administered whilst taking methotrexate. Annual flu vaccination is recommended.

**Monitoring**

Baseline:
FBC, U&E, creatinine, LFTs, chest x-ray
Folate and serum B12 levels in the elderly > 70yrs

Thereafter
FBC (including ESR) and LFTs every 2 weeks for the first month and then monthly for the first year.
U&Es every 6 to 12 months *(more frequently if any reason to suspect deteriorating renal function).*

If during the first year the blood results have been stable then the frequency of monitoring may be reduced to three/six monthly unless there have been dose increases.
Ask patient about rash, oral ulceration, sore throat or unexplained dyspnoea or cough at each visit.

**Treatment should be stopped and advice from the supervising specialist sought if:**

Rash or oral ulceration develops
WBC falls below 4.0 x $10^9$ /l
Neutrophils fall below 2.0 x $10^9$ /l
Platelets fall below 150 x $10^9$ /l
AST or ALT shows greater than a two-fold increase
Significant reduction (20%) in renal function
New or increasing dyspnoea occurs

Patients should be advised to report any signs suggestive of an infection, especially sore throat.

**A rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.**

**Remember: if in doubt STOP the methotrexate and contact the specialist (within 7 days)**

**Indication of Likely Cost of Therapy in Primary Care**
10mg once weekly 28 day cost £3.27 (assuming 2.5mg tablets)
20mg once weekly 28 day cost £6.54 (assuming 2.5mg tablets)

**Information Given to the Patient**
Pre-treatment patient information leaflet.
Patient-held monitoring and dosage record.
Useful websites:
www.rheumatology.org.uk

www.arc.org.uk

## Contact Details

**ULHT Rheumatology Team:**
First contact the nurses help line
Rheumatology Nurses (01522) 573828 (Helpline)

Dr Carty's secretary (01522) 573413
Dr Kaushik's secretary (01522) 573036
Dr Massawi's secretary (01522) 573036

## Note:

ULHT do not provide care for all patients on Methotrexate for arthritis in Lincolnshire. The ULHT rheumatology team cannot provide advice and guidance for patients under other units.

References;

1. BNF 51 March 2006. BNF.org
2. BSR Guidelines July 2000
3. SPC (Maxtrex) Nov 2004

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