Shared Care Protocol

Oral methotrexate 2.5mg tablets in dermatology/gastroenterology/rheumatology patients

NHS Somerset

Specialist Details

Name: _____

Location: _____

Telephone no: _____

Date: _____

Patient Identifier
(please include NHS number as minimum)

This shared care protocol (SCP) sets out details for the sharing of care for dermatology/gastroenterology/rheumatology patients prescribed oral methotrexate. It should be read in conjunction with the Summary of Products Characteristics (SPC, available at www.emc.medicines.org.uk)

As outlined in NHS Circular 1992 (Gen 11), when a consultant considers a patients' condition is stable he/she may seek the agreement of the patients' GP to "share" the patients' care. This document provides information on drug treatment for the shared commitment between the consultant and GP concerned. GPs are invited to participate. If the GP is 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. The doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as is practical.

Introduction

Methotrexate is a folic acid antagonist and is classified as an antimetabolite cytotoxic agent. It is used in the treatment of severe, active rheumatoid arthritis; severe, uncontrolled psoriasis; and to produce regression in a wide range of neoplastic conditions.

Indications

- Adults with moderate to severe, active rheumatoid arthritis who are unresponsive or intolerant to conventional therapy.
- Severe, uncontrolled psoriasis (acute, generalised or pustular psoriasis; psoriatic erythroderma; extensive chronic plaque psoriasis), unresponsive or intolerant to conventional therapy.
- (Unlicensed) Unresponsive or chronically active Crohn's disease.
- (Unlicensed) Dermatomyositis; psoriatic arthritis; connective tissue disease (SLE, myositis and vasculitis); blistering conditions; sarcoidosis; lymphomatoid papulosis.

Contra-indications

- Hypersensitivity to methotrexate or excipients of the formulation
- Severe or significant renal impairment
- Significant hepatic impairment, or liver disease including fibrosis, cirrhosis, recent or active hepatitis
- Active infectious disease e.g. tuberculosis
- Overt or laboratory evidence of immunodeficiency syndrome(s)
- Serious cases of anaemia, leucopoenia or thrombocytopenia and active peptic ulceration
- Concurrent treatment with clozapine (Clozaril®) due to the substantial potential for causing agranulocytosis
- Pregnancy (following administration to a man or woman conception should be avoided for at least 3 months)
- Breast feeding

Methotrexate should not be used concomitantly with drugs with anti-folate properties, e.g. co-trimoxazole (Septrin®).

Dose
Initially 5mg - 7.5mg orally **once weekly**, maintenance dose 7.5mg - 25mg per week. Dosage should be determined by a secondary care clinician responsible for shared care of the patient - they may recommend exceptions to these restrictions.

Methotrexate dose is usually titrated at regular intervals until target dose / response is achieved.
Maximum weekly dose should not exceed 25mg unless prior agreement between consultant and GP.

Methotrexate must be used with caution in renal failure or hepatic impairment; elderly patients should be given a smaller test dose and titrated at a slower rate.

Folic acid Dose
Folic acid 5mg to be taken **once a week** on the day after methotrexate to limit side effects,
e.g. gastrointestinal and haematological toxicity.

Special warnings and precautions
Methotrexate should be used with extreme caution in patients with haematological depression, renal impairment, diarrhoea, ulcerative disorders of the GI tract, and psychiatric disorders.
Methotrexate is immunosuppressive and may therefore reduce immunological response to concurrent vaccination. Severe antigenic reactions may occur if a live vaccine is given concurrently.

CSM advice; in view of reports of blood dyscrasias (including fatalities) and liver cirrhosis with low-dose methotrexate, the CSM has advised:

- Full blood count and renal and liver function tests before starting treatment and repeated weekly until therapy stabilized, thereafter patients should be monitored every 2-3 months
- Patients should be advised to report all symptoms and signs suggestive of infection, especially sore throat

Adverse effects
The incidence and severity of adverse effects are considered to be dose related

Commonly these include: nausea, stomach pains, mucositis / stomatitis mouth ulcers
Rarely these include: vomiting, diarrhoea, loss of appetite, headache, tiredness, dizziness, blurred vision, eye irritation, fever, chills, joint / muscle pain, allergic reaction, rash, acne, mood changes

Serious adverse effects include:

Blood	Bone marrow depression – leucopoenia, thrombocytopenia and anaemia
Skin	Stevens-Johnson Syndrome, epidermal necrolysis, erythematous rashes, pruritus, urticaria, photosensitivity, pigmentary, changes, alopecia, ecchymosis, telangiectasia, acne, furunculosis
Lungs	Acute or chronic interstitial pneumonitis, acute pulmonary oedema, pulmonary fibrosis
Liver	Hepatic toxicity / significant elevations in LFTs (> 2-3 times ULN), fibrosis or cirrhosis
Kidney	Renal failure and uraemia
Neurological	Aphasia, paresis, hemiparesis, and convulsions
Other	Malignant lymphomas

Drug interactions
Do **not** prescribe concomitant **trimethoprim** or **co-trimoxazole (Septrin®)** due to risk of pancytopenia.
Do **not** prescribe concomitant **clozapine (Clozaril®)** due to the substantial potential to depress bone marrow function.

Haematological toxicity	Increased by	Clozapine, corticosteroids
Pulmonary toxicity	Increased by	Cisplatin
Plasma level	Increased by	Acitretin, theophylline
Anti-folate effect	Increased by	Sulphonamides, trimethoprim, co-trimoxazole, nitrous oxide, pyrimethamine, phenytoin
Renal elimination	Reduced by	Aspirin, NSAIDs, quinolones, tetracyclines, penicillins, probenecid, ciclosporin, omeprazole

Patient Information
Patients should be advised to avoid alcohol & self-medicating with aspirin or ibuprofen. Patients should report all symptoms and signs suggestive of infection especially sore throat. Elderly patients should be warned to omit their methotrexate dose whenever they are at risk of acute dehydration e.g. acute fever, vomiting or diarrhoea. Patients should be advised to check with their pharmacist on the safety of any new drug prescription they receive.

Pregnancy and Lactation
Because methotrexate is both abortifacient and teratogenic it is strictly contraindicated in pregnancy and during breastfeeding. Adequate contraceptive measures must be taken by women of childbearing potential during methotrexate therapy, and for **6 months** after treatment discontinued. Although methotrexate is not mutagenic, the drug may affect spermatogenesis. It is customary to advise men to avoid fathering children during therapy and for at least **6 months** after stopping.

Monitoring
As per the Somerset PCT document “Primary Care Development: 4.3.4 Enhanced Service Specification for Near Patient Testing Service”, which is in line with BSR 2008 guidance and NICE CG 79.

FBC, U&E, LFTs prior to treatment
Urinalysis prior to treatment
Chest X-ray, unless done in last 6 months. Pulmonary function tests in selected patients.

FBC, U & E, LFTs every 2 weeks until dose and monitoring stable for 6 weeks.
Thereafter, monthly until dose and disease is stable for 1 year.
Thereafter, frequency of monitoring may be decreased based on clinical judgment.

CRP	3 monthly	(to assess response to therapy)
ESR	monthly	(to assess response to therapy)

Cost
BNF No. 58, September 2009
28 x 2.5mg methotrexate tablets = £3.27
28 x 5mg folic acid tablets = £0.88

Shared Care Responsibilities

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to, and accepted by, the patient. This provides an opportunity to discuss drug therapy.

The clinician who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Consultant responsibilities

- Compliance with NPSA Alerts for methotrexate.
- Assessing the need for methotrexate.
- When initiating treatment the patient must receive counseling in verbal and written form (this includes providing and completing the **Methotrexate patient information and monitoring booklet**)
- Completing relevant baseline investigations.
- Following the patient's response to treatment at the out- patient clinic.
- Communicating advice to the patient's GP re monitoring requirements.
- Decision to switch to sub-cutaneous administration of methotrexate when appropriate.
- Issuing the first prescription for 4 weeks Methotrexate and requesting the GP commence blood monitoring during this initiation phase, taking and monitoring bloods 2 weeks after initiation then ongoing as specified.
- At any stage of treatment, advising GP of concerns about monitoring or potential adverse effects of treatment.

General Practitioner responsibilities

- Compliance with NPSA Alerts for methotrexate.
- Prescribing methotrexate 2.5mg tablets at a weekly dose under the shared care of the hospital consultant.
- Any abnormality in tests should be discussed with the consultant **before** treatment is continued.
- Ensuring the patient has received counseling in verbal and written form (including, if necessary, providing and completing the **Methotrexate patient information and monitoring booklet)**
- Reporting any suspected adverse reactions to the hospital.
- Report any significant events relating to methotrexate therapy to the PCT.
- Liaising with the hospital consultant regarding any complications of treatment.
- Monitoring the general health of the patient.
- Monitoring for specific side effects as detailed in "Monitoring" section.

Withhold methotrexate and contact consultant if:

- WCC $< 4 \times 10^9$/L
- Neutrophils $< 2 \times 10^9$/L
- Platelets $<150 \times 10^9$/L
- AST/ALT > 2 times upper limit of normal (minor elevations are common in rheumatology patients)
- Creatinine > 2 times the baseline result
- Acute infection; acute respiratory disease; acute renal insufficiency; folate deficiency (MCV > 105 fl, check B_{12}, folate, TFT)
- Oral ulceration/sore throat, unexplained rash or unusual bruising

Note: a rapidly increasing or decreasing trend in any values should prompt caution and extra vigilance.

Patient/carer responsibilities

- Following counseling, to be willing to administer the methotrexate as directed at home.
- To report any concerns in relation to treatment with methotrexate.
- To report any other medication being taken, including over-the-counter products.
- To report any adverse effects or warning symptoms whilst taking methotrexate.

Further support

- Medicines Information department, Musgrove Park Hospital: 01823 342253
- Medicines Information department, Yeovil District Hospital: 01935 384327
- Prescribing & Medicines Management Team, NHS Somerset: 01935 384123

Version:	1.1	Date
Approved by:	Somerset Prescribing Forum, NHS Somerset	Jan 2010
	Drug & Therapeutics Committee, Taunton & Somerset NHS FT	Jan 2010
	Drug & Therapeutics Committee, East Somerset NHS FT	
	Drug & Therapeutics Committee, Somerset Partnership NHS FT	N/A
Reformatted by:	Matt Brindley, Specialist Pharmaceutical Advisor, NHS Somerset	July 2010
Review required by:		Jan 2012

References:

- Summary of Product Characteristics, Maxtrex 2.5mg tablets, Pharmacia Ltd, September 2008
- British National Formulary, No. 58, September 2009
- Somerset Primary Care Trust; Specification for a National Enhanced Service; 2.3 Provision of near–patient testing; Protocol Number SPCT5