Royal Berkshire NHS
NHS Foundation Trust

PRESCRIBING GUIDANCE
METHOTREXATE for the treatment of INFLAMATORY BOWEL DISEASE (IBD)

For the latest information on interactions and adverse effects, always consult the latest version of the Summary of Product Characteristics (SPC), which can be found at: http://www.medicines.org.uk/

Approval and Authorisation

Approved by	Job Title	Name	Date
BW APC	CHAIR	A.PENN	04/05/16
RBFT DTC	CHAIR	S.HUSSEIN	01/06/16

Change History

Version	Date	Author	Reason
V1.0	2014	Surrey PCT	Shared care
V1.1	2016	A Scott	Adaptation of Surrey guidance

Introduction

Methotrexate is a folic acid antagonist and is classified as an antimetabolic cytotoxic immunosuppressant agent. It is used to induce and maintain remission in Ulcerative Colitis and Crohn's Disease and although unlicensed to treat these indications, its use is widely established in Inflammatory Bowel Disease (see BNF Section 1.5, Feagan et al, 2000).

This information sheet does not replace the SPC, which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.
Link to the relevant SPC website: www.medicines.org.uk

Dose

The usual dose of methotrexate is 10-15mg **once a week on the same day**, although doses of up to 25mg can be given during flares of the disease pathway.

Clinical response to treatment can usually be expected in 6-12 weeks

Folic Acid

The patient must be prescribed 5mgs of folic acid to be taken orally the day after their methotrexate. Clinical trials have shown that supplementation with folic acid reduces the gastro-intestinal side effects of methotrexate by up to 80%. Folic acid must not be taken on the day of treatment as efficacy of the treatment will be impaired.

Cautions

- Patients should try to avoid contact with people who have active chickenpox or shingles and should report any such contact to their GP or hospital specialist.
- Due to diminished hepatic and renal function and decreased folate stores, methotrexate should be used with extreme caution in elderly patients, a reduction in dosage should be considered and these patients should be closely monitored for early signs of toxicity.
- Obese patients may have prolonged excretion of methotrexate

Contraindications

- Known sensitivity
- Significantly impaired hepatic function (LFT's x2 of normal values)
- Significantly impaired renal function
- Pre-existing blood dyscrasias, such as bone marrow hypoplasia, significant anaemia, leucopenia, or thrombocytopenia
- Alcoholism
- Severe acute or chronic infections and immunodeficiency syndrome
- Pregnancy and breast-feeding
- Pleural effusion/pleural fibrosis.

Side effects

- Gastro-intestinal disturbances - Nausea, vomiting, diarrhoea, anorexia and abdominal discomfort
- Hepatotoxicity (hepatic necrosis, biliary stasis)
- Bone marrow suppression (leucopoenia, thrombocytopenia) and therefore increased risk of infection
- Oral ulceration, rarely gastrointestinal ulceration
- Hypersensitivity reactions (fever, rigors, rash, myalgia, arthralgia, hypotension, dizziness)
- Rarely pancreatitis, interstitial nephritis
- Alopecia

At the beginning of treatment the patient should be advised to report any signs of bone marrow suppression (i.e. infection, fever, unexplained bruising or bleeding) to the IBD nurse. This should then be reported to the Consultant and GP.

Interactions

Precautions should be taken with concurrent administration of methotrexate and: Aspirin, NSAIDS, diuretics, hypoglycaemics, tetracycline, chloramphenicol, phenytoin, probenicid, penicillin.
Trimethoprim and co-trimoxazole increase the risks of toxicity
Ciclosporin increases the toxicity of both the methotrexate and ciclosporin

Criteria for Use

RESPONSIBILITIES and ROLES

Specialist responsibilities	
1	Initiate treatment and prescribe until the GP formally agrees to share care (as a minimum supply the first two weeks of treatment or until patient is stabilised).
2	Carry out baseline and subsequent monitoring until the GP agrees to share care
3	Send a letter to the GP requesting shared care for the patient.
4	Routine clinic follow-up on a regular basis.
5	Send a letter to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated.
6	Evaluation of any reported adverse effects by GP or patient.
7	Advise GP on review, duration or discontinuation of treatment where necessary.
8	Inform GP of patients who do not attend clinic appointments.
9	Ensure that backup advice is available at all times

General Practitioner responsibilities	
1	Monitor patient's overall health and well being.
2	Prescribe the drug treatment as described
3	Report any adverse events to the hospital specialist, where appropriate
4	Monitor blood results (FBC, U&E's, LFT's & CRP) in line with recommendations below
5	Help in monitoring the progression of disease.

<table>
<tr><th colspan="4">Monitoring requirements and actions</th></tr>
<tr><td colspan="4">• Pre-treatment FBC, U&Es, LFT's, CRP, ESR
• Subsequent Monitoring
▪ LFT's, FBC & U&E's - Every week for 4 weeks after dose optimisation: then if stable 2 monthly thereafter.</td></tr>
<tr><td rowspan="2">FBC</td><td>WBC</td><td><4.0 x 10^9/L</td><td rowspan="3">Stop next scheduled dose and contact IBD nurse team or consultant for further advice.</td></tr>
<tr><td>Platelets</td><td>< 80 x 10^9/L</td></tr>
<tr><td>LFT's</td><td colspan="2">> 2 fold rise in AST, ALT (from upper limit of reference range)</td></tr>
</table>

Symptoms and actions	
Dry Cough/dyspnoea	• Stop methotrexate • Contact the IBD nurses/consultant • Will need a chest x-ray to assess for damage
Rash (significant new)	• Stop methotrexate and check FBC • If FBC abnormal contact IBD nurse or consultant/registrar • Wait until rash resolved and consider restarting at reduced dose, providing no blood dyscrasias
Severe or persistent infections, fever, chill	• Stop methotrexate • Check FBC and contact IBD nurse or Consultant/Registrar • Do not restart until results of FBC known
Abnormal bruising or bleeding	• Stop methotrexate until recovery and check FBC • Do not restart if blood test abnormal • Contact IBD nurse or Consultant/Registrar
Varicella	• If in contact with the virus, contact consultant/registrar or IBD nurse
Nausea	• Advise patient to take dose with food or prior to going to bed • If no improvement, reduce dose or stop • Contact IBD nurse or consultant/registrar if reducing dose ineffective

Patient's / Carer's role
1 Ask the specialist or GP for information, if he or she does not have a clear understanding of the treatment. 2 Tell the specialist or GP of any other medication being taken, including over-the-counter products. 3 Read the patient information leaflet included with your medication and report any side effects or concerns you have to the specialist or GP

BACK-UP ADVICE AND SUPPORT

Contact details	Specialist	Telephone No.	Email address:
IBD Nurses:	Rebecca Merrick/Charlotte King/Jessica Aparo/Tiago Almeida	(0118) 322 8914	Ibd.nurses@royalberkshire.nhs.uk