Title: Methotrexate shared care guidelines	Salford Royal NHS NHS Foundation Trust University Teaching Trust safe • clean • personal
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Authors Division: Salford Health Care	
Departments/Groups This Document Applies to: Gastroenterology	
Scope: Trust wide	**Classification: Shared care guidelines**
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To be read in conjunction with the following documents: **BSG guidelines for the management of IBD.**	

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Document for Public Display:

Required NHSLA Evidence **Y/N**

If this policy is required for NHSLA evidence, then this document must have been checked against the current standards for compliance. If this is not known by the author, confirmation should be sought from the Risk and Health and Safety Department.

Contents Page

Policy Statement

The Inflammatory Bowel Disease (IBD) service is well extablished service within Salford Royal Hospitals NHS Trusts.. The IBD National standards (RCP, 2009) outlines that services should have shared care guidelines in palce to support care delivery and raising the standard of care patients with IBD receive. The following document outlines the shared care guidelines for patients receiving methotrexate across both primary and secondary care

Executive Summary

Methotrexate is a disease-modifying drug indicated in the treatment of severe Crohn's disease and ulcerative colitis, for which it is unlicensed. For these conditions it is prescribed as a single low-dose is administered once a week. Full blood counts, renal and liver function tests are required before treatment commences and blood tests repeated regularly (2-4 weekly) until therapy is stabilised. Thereafter it is essential that blood tests are
repeated at 1-3 monthly intervals to clinically evaluate and monitor the patient, and prevent methotrexate toxicity.
Oral methotrexate is a safe and effective medication if taken at the right dose and with appropriate monitoring. However, over the last fifteen years there have been over a hundred patient safety incidents in England alone including 25 deaths as a result of prescribing, dispensing, administration or monitoring incidents. The National Patient Safety Agency (NPSA) issued a safety alert concerning the use of oral methotrexate in June 2006..

Protocol

Patient name	
Date of Birth	
Hospital Number	

Introduction
Methotrexate is an immuno-modulatory agent used to induce and maintain remission of Crohn's Disease and Ulcerative Colitis in steroid refractory or steroid dependent disease. Methotrexate inhibits the enzyme dihydrofolate reductase, essential for the synthesis of purines and pyrimidines. Although unlicensed to treat Inflammatory Bowel Disease methotrexate is widely used in Crohn's Disease (BNF Section 1.5) and less commonly used in Ulcerative Colitis. The predominant toxic effects are myelosuppression and rarely pneumonitis. Methotrexate is excreted by the kidney and is therefore contraindicated in patients with significant renal impairment.**D**
OSE

AND ADMINISTRATION

1. Oral administration, initially 15mg ***once a week*** as a single dose, increasing to 20mg once a week after 2 weeks and up to a maximum of 25mg once a week after a further 2 weeks as tolerated according to response. A lower starting dose may be required for the elderly or frail or those with renal impairment. Clinical response is usually evident in 4-6 weeks.
2. Folic acid tabs 5mg once a week, 2-3 days after the methotrexate dose is useful in nausea, abdominal discomfort, diarrhoea or anorexia associated with methotrexate is a problem.
3. Metoclopramide may be used to prevent nausea; 10mg, 30 minutes before methotrexate.

There are 2 strengths of methotrexate tablets available. To avoid confusion and reduce the risk to patients, **methotrexate should be prescribed and dispensed as 2.5 mg tablets**. All communication (letters, Patient Held Record Books etc), discharge prescriptions and FP10's should normally carry the following details:-

- **Weekly dose** (methotrexate usually taken once a week).
- **Day of the week** dose taken (always same day each week).
- **Usual strength of tablets the patient takes**

(e.g. if patient takes 10mg per week on Mondays as four 2.5mg tabs, this should be clearly indicated on the prescription.

Common:-

- Gastrointestinal disturbances (anorexia, nausea, vomiting, diarrhoea, ulcerative stomatitis (oral ulceration), rarely gastrointestinal ulceration).
- Alopecia (usually minor).
- CNS disturbances (headache, drowsiness, blurred vision).

Less Common

- Hypersensitivity reactions (fever, rigors, rash)
- Bone marrow suppression (leucopoenia, thrombocytopenia, anaemia).

Rare

- Hepatotoxicity (liver cirrhosis reported).
- Pulmonary toxicity (interstitial pneumonitis often associated with eosinophilia, rarely pulmonary fibrosis).

BNF Section 10.1.3 & 13.5.3 for more details.

The patient should be advised to report any signs of bone marrow suppression (i.e. infection, fever, unexplained bruising or bleeding) to the GP, this should then be reported to the hospital specialist clinician or IBD nurse.

Patients should avoid live vaccines such as oral polio, oral tyhoid, MMR, BCG and yellow fever whilst on methotrexate. Contact hospital specialist for advice on any vaccinations if required.

- Patients should try to avoid contact with people who have active chickenpox or shingles and should report any such contact to their GP or specialist for further advice.
- Alcohol consumption in moderation, e.g. the occasional glass of wine, is not contra-indicated.
- Excretion of methotrexate reduced by NSAID's, with possible increased toxicity. Avoid over the counter NSAID's.
- Concomitant administration of a folate antagonist e.g. Septrin (cotrimoxazole) and trimethoprim, have been reported to cause acute megaloblastic pancytopenia. Hence concomitant use with methotrexate should be avoided.
- Other antibacterials such as tetracyclines, penicillins or ciprofloxacin may increase methotrexate toxicity.

See BNF section 10.1.3 for more details and see BNF Appendix 1 for further details of interactions

The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent British National formulary.

CONTRAINDICATIONS

- Liver impairment (any abnormality of LFT's before therapy or during therapy if LFT's do not normalise after 2 weeks).
- Moderate to severe renal impairment.
- Methotrexate is contra-indicated in pregnancy and breast-feeding. Both male and female patients should wait 6 months after stopping methotrexate before trying to conceive a child.
- Active infection and immunodeficiency syndromes.
- Severe haematological impairment or profound deterioration
- If Pneumonitis suspected.
- If stomatitis develops.

HOSPITAL RESPONSIBILITIES

Record all blood results in the patient held record book.		
Pre-treatment Monitoring	FBC, U&E's, LFT's, varicella status and chest x-ray	
Subsequent Monitoring	FBC	Every week for 2 months
	U&E	Every week for 2 months
	LFT's	Every week for 2 months
	CRP	Every month for 2 months
	Chest X-ray and lung function tests if symptoms occur	
	Consider liver biopsy if persistently abnormal	

PRIMARY CARE RESPONSIBILITIES

Record all blood results in the patient held record book.		
Subsequent Monitoring	FBC	Monthly from three months to six months Three monthly thereafter.
	U&E	Every 6 months (more frequently if there is any reason to suspect deteriorating renal function).
	LFT's	Monthly from three months to six months Three monthly thereafter
Referral to hospital team if respiratory symptoms or blood abnormalities are		

noted.

If a GP has taken blood tests for the general medical management of a patient and blood test results fall into the categories below or the patient reports one of the adverse events below, these are recommendations as regards the next step:-

Blood Test Results Action	
Lymphocytes **<0.5 x 10^9/L**	Discuss with IBD nurse or specialist hospital clinician
Neutrophils **< 2.0 x 10^9/L** **< 1.5 x 10^9/L**	 Discuss with IBD nurse or specialist hospital clinician. Stop and discuss with IBD nurse or hospital specialist clinician.
Platelets < 150 x 10^9/L.	Discuss with hospital IBD nurse or hospital specialist clinician
Liver function tests >2 fold rise in AST, ALT (from upper limit of reference range) > 4 fold rise in AST, ALT	 Contact IBD nurse or hospital specialist clinician. **Stop methotrexate** and contact IBD nurse or hospital specialist clinician **immediately.**
Symptoms Action	
Oral ulceration/stomatitis.	If FBC abnormal contact IBD nurse or hospital specialist clinician. Wait until rash resolved and consider restarting at reduced dose, providing no blood dyscrasias.
New or increasing dyspnoea or persistent cough (with no other obvious cause – suspected pneumonitis).	**Stop methotrexate**, **check FBC** and contact IBD nurse or hospital specialist. Do not restart until results of FBC known.

Persistent sore throat	For sore throat throats, take FBC, AND contact hospital specialist.
Abnormal bruising or bleeding	**Stop methotrexate until recovery** and check FBC. Do not restart if blood test abnormal, contact IBD nurse or hospital specialist clinician.
Varicella	If in contact with the virus, contact hospital specialist clinician or IBD nurse.
Nausea, abdominal discomfort, diarrhoea, anorexia	Add folic acid 5mg once weekly, 2-3 days after methotrexate dose. If not effective reduce dose or stop methotrexate and contact hospital specialist.

[redacted]

Consultant and/or IBD Nurse

1. Initiate treatment and prescribe until the GP formally agrees to share care (as a minimum, supply the first month of treatment or until patient is stabilised).
2. Send a letter to the GP requesting shared care for this patient.
3. Routine clinic follow-up on a regular basis.
4. Supply of shared care patient held booklet.
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

1. Monitor patient's overall health and well being.
2. Prescribe the drug treatment as described.
3. Monitor blood results (FBC, U+E's and LFT's, CRP) in line with recommendations from hospital specialist.
4. Report any adverse events to the hospital specialist, where appropriate.
5. Help in monitoring the progression of disease.
6. Complete blood monitoring details in Patient Held Record Book.

Consultants **Dr Robinson** **Dr Paine** **Dr Lal** **Dr Shaffer** **Dr Babbs** **Dr Al-Rifahi**	 **01612064560** **01612065794** **01612065147** **01612065147** **01612065994** **01612065994**
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References

British Society of Gastroenterology guidelines for the management of IBD (Mowatt et al, 2011),

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Forbes A. A clinician's guide to inflammatory bowel disease. Chapman and Hall Medical. London.

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Explanation of Terms Used
FBC – full blood count
U&E – urea and electrolytes
LFT – liver function tests
CRP – c reactive protein
GP – general practitioner
IBD – inflammatory bowel disease

Endorsed by:		
Name of Lead Clinician/Manager or Committee Chair	**Position of Endorser or Name of Endorsing Committee**	**Date**
Andrew Robinson	Clinical director	June 2013
John MacDonald/ Selwa Elroeby	Medicine management	June 2013

Record of Changes to Document - Issue number: 3				
Changes approved in this document by - Corporate Governance and Risk Management			Date: 7/7/05	
Section Number	Amendment (***shown in bold italics)***	Deletion	Addition	Reason

Screening Equality Analysis Outcomes (Policies/Procedures)

The Trust is required to ensure that all our policies/procedures meet the requirements of its service users, that it is accessible to all relevant groups and **furthers the aims of the Equality Duty for all protected groups by age, religion/belief, race, disability, sex, sexual orientation, martial status/civil partnership, pregnancy/maternity, gender re-assignment. Due consideration may also be given to carers & socio/economic.**

Have you been trained to carryout this assessment? YES **If 'no' contact Equality Team 62598 for details.**	
This Section must be completed **Name of policy or document :shared care guidelines for methotrexate** **Key aims/objectives of policy/document** **(impact on both staff & service users):** **To outline the key responsibilities of the primary and secondary care in the administration and monitoring of methotrexate prescribed to patients with IBD.**	
1) a) Whom is this document or policy aimed at?	1a) trust wide, primary and secondary health care teams involved in the administration of methotrexate to patients with IBD
2) a) Is there any evidence to suggest that your 'end users' have different needs in relation to this policy or document; (e.g. health/employment inequality outcomes) (**NB If you do not have any evidence you should put in section 8 how you will start to review this data)**	2a) no
3) a) Does the document require any decision to be made which could result in some individuals receiving different treatment, care, outcomes to other groups/individuals?	3a) no
b) If yes, on what basis would this decision be made? **(It must be objectively justified)**	3b)
4) a) Have you included where you may need to make reasonable adjustments for disabled users or staff to ensure they receive the same outcomes to other groups ?	4a)
5) a) Have you undertaken any consultation/involvement with service users or other groups in relation to this document?	5a) yes

b) If yes, what format did this take? face/face or questionnaire? (please provide details of this)	5b) review at patient panel
c)Has any amendments been made as a result?	5c) no
6) a) Are you aware of any complaints from service users in relation to this policy?	6a) no
b) If yes, how was the issue resolved? Has this policy been amended as a result?	6b)

7) a) To summarise; is there any evidence to indicate that any groups listed below receive different outcomes in relation to this document?

	Yes		No	unsure
	Positive	**Negative***		
Age			x	
Disability			x	
Sex			x	
Race			x	
Religion & Belief			x	
Sexual orientation			x	
Pregnancy & Maternity			x	
Marital status/civil partnership			x	
Gender Reassignment			x	
Carers *1			x	
Socio/economic2**			x	

1: That these two categories are not classed as protected groups under the Equality Act.
2: Care must be taken when giving due consideration to socio/economic group that we do not inadvertently discriminate against groups with protected characteristics

Negative Impacts

*If any negative impacts have been identified you must either a) state below how you have eliminated these within the policy or b) conduct a full impact assessment:

8) How will the future outcomes of this policy be monitored?
Annual review and audit of compliance with protocol.

9) **If any negative impact has been highlighted by this assessment, you will need to undertake a full equality impact assessment:**

Will this policy require a full impact assessment? Yes/No (delete)
(if yes please contact Equality Team, 62598/67204, for further guidance)

High/Medium/Low signed **Cath Stansfield**
date: **01/06/2013**