Title: Azathioprine and Mercaptopurine shared care guidelines for inflammatory bowel disease	Salford Royal NHS NHS Foundation Trust University Teaching Trust safe • clean • personal
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Document for Public Display: Yes

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.

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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 azathioprine and mercaptopurine across both primary and secondary care

Executive Summary

Azathioprine and mercaptopurine are drugs commonly used to treat inflammatory bowel disease.
Full blood counts, renal and liver function tests, are completed before treatment commences and blood tests repeated regularly (2-4 weekly) and 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 toxicity.
Azathiorpine and mercaptopurine are a safe and effective medication if taken at the right dose and with appropriate monitoring. This protocol outlines the process to ensure that patients receiving azathioprine are cared for safely.

1. Roles and Responsibilities:

The gastroenterology team and relevant Primary Care staff are responsible for ensuring that prescribing of azathioprine for patients under their care is in accordance with these guidelines
The gastroenterology team is responsible for implementing and monitoring the effectiveness of this policy, and for reviewing the guidelines on a regular basis

2. Standards

An extensive literature review has been undertaken to examine the administration of azathioprine/ 6MP. They have been developed in conjunction with:-

3. British Society of Gastroenterology guidelines for the management of IBD (Mowatt et al, 2011),
4. European Crohn's and Colitis organisation guidelines on the management of Crohn's disease (Dignass et al, 2011) and
5. NICE guidelines for the management of Crohn's disease (DH, 2012)
6. The RCN Gastroenterology Nurses forum (RCN, 2007) role descriptives of an IBD Nurse Specialist

Protocol

SHARED CARE GUIDELINES	
Patient name	
Date of Birth	
Hospital Number	

Introduction
Azathioprine and mercaptopurine are an immuno-modulatory agent that is used to induce and maintain remission in Ulcerative Colitis and Crohn's Disease. They are a pro-drug, which is cleaved rapidly in the liver to 6-mercaptopurine. Although unlicensed to treat these indications, its use is widely established in Inflammatory Bowel Disease (see BNF Section 1.5). The main toxic effect is myelosuppression, although hepatotoxicity is also well recognised.

Dose and Administration details

Azathioprine
The initial oral dose is 50mg once daily for 2 weeks, and then gradually increased in 50mg increments every 2 weeks to 2 – 2.5 mg/kg daily, if tolerated.

Mercaptopurine
The initial oral dose is 50mg once daily for 2 weeks, and then gradually increased in 25mg increments every 2 weeks to 1-1.5 mg/kg daily, if tolerated.

Clinical response can usually be expected in 6-12 weeks.

Side Effects

- Nausea, diarrhoea, vomiting anorexia, and abdominal discomfort.
- Hepatotoxicity (hepatic necrosis, biliary stasis)
- Bone marrow suppression (leucopenia, 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

See BNF 8.2.1 for comprehensive list.

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.

Cautions

- **Avoid prescribing allopurinol in patients on azathioprine/ mercaptopurine due to a clinically significant interaction that can lead to increased azathioprine toxicity.**
- Increased risk of haematological toxicity with co-trimoxazole/trimethoprim.
- Patients should avoid 'live' vaccines such as oral polio, oral typhoid, MMR, BCG and yellow fever, whilst on immunosuppressive therapy. 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 hospital specialist.
- Anticoagulant effect of warfarin possibly reduced by azathioprine/mercaptopurine.
- Careful assessment of risk versus benefit should be carried out before use during pregnancy and breastfeeding.
  Consult hospital specialist clinician or IBD nurse.
- Moderate/severe renal or liver impairment
- Significant haematological impairment
- Thiopurine methyltransferase (TPMT) deficiency
- Hypersensitivity to azathioprine/mercaptopurine

AZATHIOPRINE and MERCAPTOPURINE In Inflammatory Bowel Disease

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.

MONITORING STANDARDS BY SALFORD ROYAL NHS TRUST

Record all blood results in the patient held record book.		
Pre-treatment Monitoring	FBC, U&E's, LFT's, TPMT, varicella status.	
Subsequent Monitoring	FBC	Every week for first eight weeks of treatment.
	U&E	Every week for first eight weeks of treatment.
	LFT's	Every week for first eight weeks of treatment.
	CRP	Every week for first eight weeks of treatment.
Azathioprine will be prescribed by the gastroenterology team for the first eight weeks of treatment.		

MONITORING STANDARDS BY PRIMARY CARE		
Record all blood results in the patient held record book.		
Subsequent Monitoring	FBC UE LFT	Primary care will be responsible for blood monitoring from eight weeks onwards. Monitoring should be completed:- Monthly from weeks 12 to 26. Three monthly thereafter.
The ongoing prescribing of the azathioprine will be the responsibility of the patients GP.		

ACTION AND ADVICE FOR GP'S IN RESPONSE TO BLOOD MONITORING/SIDE-EFFECTS	
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 azathioprine/ mercaptopurine** and contact IBD nurse or hospital specialist clinician **immediately.**
Symptoms Action	
Rash (significant new) Stop azathioprine and check FBC.	If FBC abnormal contact IBD nurse or hospital specialist clinician. Wait until rash resolved and consider restarting at reduced dose, providing no blood dyscrasias.
Severe or persistent infections, fever, chill.	**Stop azathioprine / mercaptopurine**, **check FBC** and contact IBD nurse or hospital specialist.

Persistent sore throat	Do not restart until results of FBC known. For sore throat throats, take FBC, hospital specialist.
Abnormal bruising or bleeding	**Stop azathioprine/ mercaptopurine 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	Advise patient to divide dosage and take with food. If no improvement, reduce dosage or stop and contact IBD nurse or hospital specialist clinician if reducing dose ineffective

SHARED CARE RESPONSIBILITIES

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. Provide a patient held monitoring 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.

Contact Details	
Consultants **Dr Robinson** **Dr Paine** **Dr Lal** **Dr Shaffer** **Dr Babbs** **Dr Al-Rifahi**	 **01612064560** **01612065794** **01612065147** **01612065147** **01612065994** **01612065994**
IBD Nurses	**01612064023**
Email	**ibd@srft.nhs.uk**

7. Policy Implementation Plan

The advanced practitioner will have overall responsibility for the implementation of the protocol.

The nursing protocols for the monitoring and administration of azathioprine/ 6MP for IBD patients have been approved by Consultant Gastroenterologist, the clinical lead for gastroenterology clinical governance committee and the ADNS for medicine. They are subject to annual review.
However, if there are any significant changes to any of the supporting policies and guidelines, which directly affect the implementation of this protocol, the author will consider reviewing the document earlier than the planned review date. The author is responsible for ensuring the dissemination to nursing and medical colleagues at a local review for information and implementation. The protocol will be held on synapse.

5. Monitoring and Review

The author and authorising Consultant Gastroenterologist will regularly monitor the effectiveness of this protocol.
Annual service review report will be developed

References

British Society of Gastroenterology guidelines for the management of IBD (Mowatt et al, 2011),
European Crohn's and Colitis organisation guidelines on the management of Crohn's disease (Dignass et al, 2011) and
Forbes A. A clinician's guide to inflammatory bowel disease. Chapman and Hall Medical. London.
NICE guidelines for the management of Crohn's disease (DH, 2012)
Sandborn W. 2004. Azathioprine or mercaptopurine for induction of remission in Crohn's Disease. Cochrane Database of Systematic reviews, 2, 2004

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

You must Complete

Endorsed by:		
Name of Lead Clinician/Manager or Committee Chair	**Position of Endorser or Name of Endorsing Committee**	**Date**
Andrew Robinson	Clinical director - gastroenterology	June 2013
Selwa Elrouby/ John MacDonald	Medicines Management Group	June 2013

You must complete if appropriate

Record of Changes to Document - Issue number: 3				
Changes approved in this document by - Corporate Governance and Risk Management			Date: 18/03/2014	
Section Number	Amendment (***shown in bold italics)***	Deletion	Addition	Reason
	Change of title from Azathioprine shared care guidelines		Change of title Change of title from Azathioprine shared care guidelines	

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 azathioprine 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: **1/6/2013**