Gastroenterology

Shared Care Guideline

6-Mercaptopurine - In Inflammatory Bowel Disease

1 Scope

Prescribing and monitoring by General Practitioners.

2 Purpose

To provide advice on safe prescribing and monitoring of 6-mercaptopurine for use in the management of inflammatory bowel disease.

3 Introduction

6-mercaptopurine is used as a disease-modifying agent to induce and maintain remission of Crohn's Disease and Ulcerative Colitis in patients intolerant of azathioprine.

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.

4 Dose and administration

6-Mercaptopurine

- The initial oral dose is 25mg – 50mgs once daily for two weeks, and then gradually increased in 25mg increments every two weeks to 1mg/kg daily, if tolerated.
- Clinical response can usually be expected in 6-12 weeks.

5 Adverse effects

- Nausea, diarrhoea, vomiting and anorexia and abdominal discomfort
- Bone marrow suppression (leucopenia, thrombocytopenia) and therefore increased risk of infection
- Hepatotoxicity (hepatic necrosis, biliary stasis)
- Oral ulceration, rarely gastrointestinal ulceration
- Hypersensitivity reactions (fever, rigors, rash, myalgia, arthralgia, hypotension, dizziness)

• Rarely pancreatitis

• Alopecia.

See BNF 8.1.3 for comprehensive list.
The patient should be advised to report any signs of bone marrow suppression (ie infection, fever, unexplained bruising or bleeding) to the GP, this should then be reported to the hospital specialist clinician or IBD nurse.

6 Cautions

• **Avoid prescribing allopurinol in patients on 6-mercaptopurine due to a clinically significantinteraction that can lead to increased 6-mercaptopurine 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 the 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 urgently to their GP or specialist.

• Anticoagulant effect of warfarin possibly reduced by 6-mercaptopurine.

• Careful assessment of risk versus benefit should be carried out before use during pregnancy and breast-feeding. Consult hospital specialist clinician or IBD nurse.

7 Contraindications

• Moderate/severe renal or liver impairment

• Significant haematological impairment

• Thiopurine methyltransferase (TPMT) deficiency

• Hypersensitivity to 6-mercapotopurine.

See BNF (8.2.2) or summary of product characteristics for mercaptopurine for full list.

8 Monitoring standards for 6-Mercaptopurine at Peterborough and Stamford Hospitals NHS Foundation Trust

Record all blood results in the patient held record book.		
Pre-treatment Monitoring	FBC, U&Es, LFTs, TPMT phenotype, varicella status. Hep B,C, HIV, EBV	
Subsequent Monitoring	FBC	Every week for 2 months then monthly for 4 months, then if stable 3 monthly thereafter.
	U&Es	Every 6 months (more frequently if there is any reason to suspect deteriorating renal function).
	LFTs	Every week for 2 months then monthly for 4 months, then if stable 3 monthly thereafter.
CRP		3 monthly to assess response to treatment.

9 Action and advice for GPs in response to blood monitoring and 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 6-mercaptopurine** and contact IBD nurse or hospital specialist clinician **immediately.**
Symptoms	**Action**
Rash (significant new)	**Stop 6-mercaptopurine 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, chills. Persistent sore throat	**Stop 6-mercaptopurine**, **check FBC** and contact IBD nurse or hospital specialist. Do not restart until results of FBC known. For sore throat throats, take FBC, hospital specialist.
Abnormal bruising or bleeding	**Stop 6-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.

10 Shared care responsibilities

10.1 Consultant and/ or IBD Nurse

- Initiate treatment and prescribe the first month of treatment or until patient is stabilised.
- Send a letter to the GP requesting shared care for this patient. Agreement to shared care will be assumed unless GP advises otherwise.
- Routine clinic follow-up on a regular basis.
- Send a letter to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated.
- Evaluation of any reported adverse effects by GP or patient.
- Advise GP on review, duration or discontinuation of treatment where necessary.
- Inform GP of patients who do not attend clinic appointments.
- Ensure that backup advice is available at all times.

10.2 General practitioner

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

11 Contact numbers for advice and support

Specialist	**Post**	**Telephone**
Inflammatory Bowel Disease Helpline for Patients		01733 673876 (voice mail)
Dr Sunny Nair	Consultant Gastroenterologist	01733 678509
Dr Tapas Das	Consultant Gastroenterologist	01733 677524
Dr Naveen Kumar	Consultant Gastroenterologist	01733 677524
Dr Mo Thoufeeq	Consultant Gastroenterologist	01733 677525
Dr Mary Ninkovic	Consultant Gastroenterologist	01733 678510
Mrs Gill Anderson Mrs Eliane Marsden	Inflammatory Bowel Disease Nurse Specialists	017330678000 bleep 1698

12 Monitoring compliance with and the effectiveness of this guideline

Gastroenterology will regularly review their incidents and feedback from GPs with regard to the use of this drug and update the guideline accordingly.

Equality and diversity statement

This document complies with the Peterborough and Stamford Hospitals NHS Foundation Trust service equality and diversity statement.

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Owning department:	Gastroenterology		
Author(s):	Miles Parkes and Narinder Bhalla , Adapted for Peterborough and Stamford NHS trust by Sunny Nair and Gill Anderson		
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