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# Shared Care Guideline

## Mercaptopurine – inflammatory bowel disease

### Executive Summary

- Unlicensed indication, but widely established use of mercaptopurine.
- Dosing: 25mg daily for two weeks, then 1-1.5mg/kg daily.
- Clinical response can usually be expected within 6-12 weeks.
- GP to monitor FBC & LFTs as set out within this document.
- The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document [here](#)

Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use. Further information about the general responsibilities of the hospital specialist and GP can be found [here](#)

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## 1. Scope

Prescribing and monitoring by General Practitioners.

## 2. Aim

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

## 3. Introduction

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 or NICE guidelines CG152 & CG166). The main toxic effect is myelosuppression, although hepatotoxicity is also well recognised.

## 4. Abbreviations

- BNF- British National Formulary
- NICE- National Institute for Health and Care Excellence
- Mg- milligrams
- Kg- Kilograms
- MMR- Measles, Mumps & Rubella
- BCG- Bacillus Calmette-Guérin
- GP- General Practitioner
- IBD- Inflammatory Bowel Disease
- TPMT- Thiopurine methyltransferase
- FBC- Full Blood Count
- LFT- Liver Function Test
- U&Es- Urea & Electrolytes
- CRP- C-Reactive Protein
- AST- Aspartate transaminase
- ALT- Alanine transaminase

## 5. Dose and Administration

### Mercaptopurine

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- The initial oral dose is 25mg once daily for two weeks, and then increased to 1-1.5mg/kg daily, if tolerated.
  - Clinical response can usually be expected in 6-12 weeks.

Further information can be found in the Summary of Product Characteristics  
<http://www.medicines.org.uk/emc/medicine/24688>

## 6. Adverse Effects

### **Common (≥ 1 in 100 and < 1 in 10)**

- Nausea, diarrhoea, vomiting, anorexia, and abdominal discomfort and headaches.

### **Uncommon (≥ 1 in 1000 and < 1 in 100)**

- Rash
- Skin photosensitivity
- Signs of bone marrow suppression (leukopenia, thrombocytopenia) and therefore increased risk of infection ie fever, sore throat, oral ulceration, abnormal bruising or bleeding.
- Hypersensitivity reactions (fever, rigors, rash, myalgia, arthralgia, hypotension, dizziness)
- Hepatotoxicity (hepatic necrosis, biliary stasis, cholestatic jaundice)
- Alopecia
- Severe diarrhoea in inflammatory bowel disease population.

### **Rare (≥ 1 in 10000 and < 1 in 1000)**

- Skin cancer and other malignancies
- Pneumonitis (reversible)
- Pancreatitis.

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## 7. Cautions

- Careful assessment of risk versus benefit should be carried out before use during pregnancy, in patients likely to become pregnant and breastfeeding.
- Thiopurine methyltransferase (TPMT) homozygous deficiency
- The patient should be advised to report any signs of bone marrow suppression or hypersensitivity (i.e. infection, fever, chills, cough, unexplained bruising or bleeding, fatigue, hypotension, myalgia, dizziness) to the GP; this should then be reported to the hospital specialist clinician or specialist nurse
- Patients should be advised to limit exposure to ultraviolet light and sunlight and to wear high factor sun creams and/or protective clothing to limit risk of photosensitivity and skin cancer.
- 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.
- If a pre-treatment check of varicella zoster serology reveals no previous exposure then Varilix® is considered safe to administer provided the last dose of vaccine is at least 4 weeks before the start of mercaptopurine therapy.
- Patients with no history of exposure to varicella zoster virus (VZV) or who are serology negative should be advised 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 mercaptopurine.
- Renal or hepatic impairment

## 8. Contraindications

- Allergy/hypersensitivity to azathioprine or mercaptopurine
- Moderate/severe renal or liver impairment
- Significant haematological impairment
- Avoid prescribing allopurinol in patients on mercaptopurine due to a clinically significant interaction that can lead to increased mercaptopurine toxicity, unless advised by specialist gastroenterologist.
- Avoid prescribing mercaptopurine with co-trimoxazole or trimethoprim due to increased haematological toxicity.
- Avoid prescribing mercaptopurine with febuxostat
- Avoid prescribing mercaptopurine with clozapine due to increased risk of agranulocytosis

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## 9. Interactions

- Live vaccinations
- Allopurinol (see above)
- Febuxostat (see above)

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- Co-trimoxazole or trimethoprim (see above)
- Warfarin (enhanced anticoagulant effect)
- Patients taking mercaptopurine along with other immunosuppressive therapy, including steroids are at increased risk of secondary infections.
- If a pre-treatment check of varicella zoster serology reveals no previous exposure then the hospital specialist will write to the GP practice asking that the patient be given varicella zoster vaccine (2 doses of Varilrix® with an interval of 6 weeks between doses). After confirmation that these doses have been administered then the hospital specialist will consider initiation of mercaptopurine at least 4 weeks after the last dose of vaccine.
- Contact hospital specialist for advice on any other vaccinations if required.
- Yearly influenza vaccine is recommended in patients on mercaptopurine therapy.

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## 10. Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

Pre-treatment monitoring		
<b>Record all blood results in the patient held record book.</b>		
<b>Pre-treatment Monitoring</b>	<ul style="list-style-type: none"> <li>• TMPT testing</li> <li>• Hospital to perform FBC, U&amp;E's, LFT's, assessment of renal function, hepatitis B&amp;C status, Epstein Barr status.</li> <li>• Check varicella zoster serology in patients where is an unclear history of chicken pox or shingles.</li> </ul>	
<b>Subsequent Monitoring</b>	<b>FBC</b>	Every 2 weeks for 2 months then monthly for 4 months, then if stable 3 monthly thereafter.
	<b>LFTs</b>	Every 2 weeks for 2 months then monthly for 4 months, then if stable 3 monthly thereafter.
	<b>CRP</b>	3 monthly to assess response to treatment.

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	<b>Renal function and U+Es</b>	Every 6 months (more frequently if there is any reason to suspect deteriorating renal function).
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Note: Exact frequency of monitoring of above parameters may differ according to clinical discretion or specialist advice”.

Note: If a pre-treatment check of varicella zoster serology reveals no previous exposure then the hospital specialist will write to the GP practice asking that the patient be given varicella zoster vaccine (2 doses of Varilrix® with an interval of 6 weeks between doses). After confirmation that these doses have been administered then the hospital specialist will consider initiation of mercaptopurine at least 4 weeks after the last dose of vaccine.

<b>Abnormal blood test results</b>	
<b>Blood Test Results</b>	<b>Action</b>
<b>Lymphocytes</b> <0.5 x 10 <sup>9</sup> /L	Discuss with IBD nurse or specialist hospital clinician.
<b>Neutrophils</b> < 2.0 x 10 <sup>9</sup> /L  < 1.5 x 10 <sup>9</sup> /L	Discuss with IBD nurse or specialist hospital clinician. Stop and discuss with IBD nurse or hospital specialist clinician.
<b>Platelets</b> < 150 x 10 <sup>9</sup> /L	Discuss with hospital IBD nurse or hospital specialist clinician.
<b>Liver function tests</b> >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 mercaptopurine and contact IBD nurse or hospital specialist clinician immediately.
<b>Abnormal symptoms</b>	
<b>Symptoms</b>	<b>Action</b>
<b>Rash (significant new)</b>	Stop 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.

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<b>Severe or persistent infections, fever, chill.</b>  <b>Persistent sore throat</b>	Stop mercaptopurine, check FBC and contact IBD nurse or hospital specialist. Do not restart until results of FBC known. For sore throat, take FBC, contact hospital specialist.
<b>Abnormal bruising or bleeding</b>	Stop mercaptopurine until recovery and check FBC. Do not restart if blood test abnormal, contact IBD nurse or hospital specialist clinician.
<b>Varicella</b>	If in contact with the virus, contact hospital specialist clinician or IBD nurse.
<b>Nausea</b>	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.

## 11. Shared Care Responsibilities

### a. Hospital specialist:

- Send a letter to the GP requesting shared care for the patient.
- Inform GP of patients who do not attend clinic appointments.
- To provide any advice to the patient/carer when requested.
- Initiate treatment and prescribe the first month of treatment.
- 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.
- Ensure that backup advice is available at all times.

### b. General Practitioner:

- Agreement to shared care guideline by the GP.
- Report any adverse events to the hospital specialist, where appropriate.
- Request advice from the hospital specialist when necessary.
- Monitor patient's overall health and well-being.
- Prescribe the drug treatment as described.
- Monitor blood results (FBC, U+E's and LFT's, CRP) in line with recommendations from hospital specialist.
- Help in monitoring the progression of disease.
- Complete blood monitoring details in Patient Held Record Book/appropriate electronic record.

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**c. Patient or parent/carer:**

- Report to the hospital specialist or GP if they do not have a clear understanding of their treatment.
- Patients must not exceed the recommended dose.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Must inform other clinical staff that they are receiving treatment.
- Report any adverse effects to the hospital specialist or GP.

**12. Contact numbers for advice and support**

<b>Cambridge University Hospital NHS Foundation Trust</b>		
<b>Specialist</b>	<b>Post</b>	<b>Telephone</b>
<b>Inflammatory Bowel Disease Helpline for Patients</b>		01223 257212 (voice mail)
Dr Miles Parkes	Consultant Gastroenterologist	01223 216389
Dr Jeremy Woodward	Consultant Gastroenterologist	01223 596231
Dr Stephen Middleton	Consultant Gastroenterologist	01223 216226
Dr Timothy Raine	Consultant Gastroenterologist	01223 348456
Dr Ewen Cameron	Consultant Gastroenterologist	01223 348718
Dr Gareth Corbett	Consultant Gastroenterologist	01223 348716
Prof Arthur Kaser	Consultant Gastroenterologist	Ext 768308
Sr Allison Nightingale	Inflammatory Bowel Disease Nurse Specialist	01223 217990 <b>(for GPs to contact for advice)</b>

**13. Monitoring compliance with and the effectiveness of this document**

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

**14. Equality and Diversity Statement**

This document complies with the Cambridge University Hospital NHS Foundation Trust service Equality and Diversity statement.

**15. Disclaimer**

It is your responsibility to check that this printed out copy is the most recent issue of this document.

**16. Document management**

<b>Document ratification and history</b>	
Approved by:	Cambridge University Hospitals NHS Foundation Trust Joint Drug and Therapeutics Committee
Date approved:	20 February 2018
Approved by:	Cambridgeshire and Peterborough Joint Prescribing Group

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Date approved:	18 January 2018
Date placed on CPJPG website:	March 2018
Review date:	20 February 2020
Obsolete date:	20 May 2020
Supersedes which document?	Version 1, April 2015
Authors:	Narinder Bhalla, Consultant Pharmacist – Medication Safety
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File name:	Mercaptopurine SCG Version2 February 2018.doc
Version number:	2
CUH Document ID:	6194

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 Summary of Product Characteristics <http://www.medicines.org.uk/emc/medicine/24688>

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