

Shared care guideline for 6-mercaptopurine for inflammatory bowel disease in adults

General Principles

This agreement outlines suggested ways in which the responsibilities for managing the prescribing of the drug treatment and clinical indication listed in the table below can be shared between the Specialist and General Practitioner (GP). The Specialist(s) is responsible for initiating treatment, prescribing the drug and monitoring of therapy until such a time as when the patient is deemed to be stable. If GPs are not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the Specialist.

If a Specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, the GP and the patient. The intention to undertake shared care should be explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients on 6-mercaptopurine are under regular follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

Indications

6-mercaptopurine (6-MP) is used as a steroid-sparing agent in both Ulcerative Colitis and Crohn's disease. It is an effective treatment in the management of inflammatory bowel disease to induce and maintain remission in patients intolerant of azathioprine.

6-mercaptopurine is an effective maintenance therapy for Crohn's disease for up to 4 years, following which treatment should be reviewed by the patient's hospital team.

6-mercaptopurine is licensed for a variety of leukaemias. **This shared care guideline, however, will only cover the treatment of adults \geq 18 years of age with inflammatory bowel disease.** Although unlicensed to treat the above indications, its use is widely established in inflammatory bowel disease.

In the UK patients are often given azathioprine first and switched to 6-MP if they are intolerant of azathioprine. As 6-MP is given at half the dose of azathioprine, it is important to be certain as to which agent is being prescribed to avoid potential serious dosing errors.

Mercaptopurine is an anti-metabolite interfering with nucleic acid synthesis. It is metabolised by the enzyme thiopurine methyltransferase (TPMT). Patients with intermediate or low TPMT activity and are at greater risk of adverse drug reactions on standard doses and are at risk of suffering life-threatening complications even when treated with low doses of azathioprine. It is recommended as best practice that the hospital consultant should check the TPMT activity for any deficiencies before prescribing mercaptopurine.

Presentation/Dose/Administration

Oral:

6-mercaptopurine is administered orally and is available as 50mg tablets.

- The usual dose of 6-mercaptopurine is **1-1.5mg/kg daily**. However, some patients may respond to lower doses.
- After any dose change, the patient should be transferred back to hospital led care where they will be the responsibility of the consultant/hospital team until shared care is re-requested.

Responsibility for monitoring 6-Mercaptopurine			
MONITORING	RESPONSIBILITY	CONDITIONS	TESTS
Pre-treatment	Hospital team	All	FBC , LFTs, U&Es, CRP, TPMT levels, and Varicella Zoster status Results to be known before drug is commenced
Initiation to stabilisation	Hospital team	All	FBC, LFT, U&Es At initiation and after any increase in dose - Every week for 4 weeks until stabilised
Ongoing	GP	All	FBC, LFT 3 monthly U&E's Annually

Criteria for managing events & symptoms occurring during 6-Mercaptopurine therapy in primary care		
LABORATORY EVENTS	VALUES	ACTION
Elevation in liver enzymes (AST, ALT)	> 2 fold rise in AST, ALT (from upper limit of reference range)	Contact Consultant or Specialist team
	> 3 fold rise in AST, ALT	Stop 6-mercaptopurine and contact Consultant immediately
Mild-to-moderate renal impairment	Mild: GFR 20 to 50 mL/min Moderate: GFR 10 to 20 mL/min	
Lymphocytes < 0.5 x 10 ⁹ /L	< 0.5 x 10 ⁹ /L	Discuss with Consultant or Specialist team
Neutrophils	< 2.0 x 10 ⁹ /L	Discuss with Consultant or Specialist team
	< 1.0 x 10 ⁹ /L	Stop and discuss with Consultant.
Platelets	< 150 x 10 ⁹ /L	Discuss with Consultant or Specialist team

SYMPTOMS	MANAGEMENT
Rash	Stop 6-mercaptopurine and check FBC. If FBC is abnormal, contact specialist nurse or consultant. Wait until rash resolved and consider restarting at reduced dose, providing no blood dyscrasias
Severe or persistent infections, fever, chills, sore throat	Stop 6-mercaptopurine, check FBC and contact Specialist nurse or Consultant. Do not restart until FBC results are known. For sore throats, take the FBC and contact the Consultant
Abnormal bruising or bleeding	Stop 6-mercaptopurine until recovery and check FBC. Do not restart if blood test is abnormal & seek advice from specialist
Varicella	If in contact with the virus, contact the specialist team.
Nausea	Advise patient to divide dosage and take with food. If no improvement, reduce dose or stop and contact the specialist team if dose reduction is ineffective.

Key adverse drug reactions (ADRs)

- Gastrointestinal disturbances (nausea, vomiting, anorexia).
- Bone marrow suppression (leucopenia, thrombocytopenia) and therefore an increased risk of infection.
- Oral mucositis (sore mouth).
- Hypersensitivity reactions (fever, rash, myalgia, dizziness).
- Hepatotoxicity (hepatic necrosis, biliary stasis).
- Rarely pancreatitis.
- Rarely alopecia .

NB. Patients should be advised to report any mouth ulcers, sore throat, fever, epistaxis, unexpected bruising or bleeding and any unexpected illness or infection and should be seen URGENTLY for a full blood count, liver function tests, urea and electrolytes.

This document only lists the key important ADRs. For comprehensive information on adverse drug reactions, cautions, contra-indications and interactions, please refer to the current British National Formulary and Summary of Product Characteristics.

Contraindications & Precautions

- **Pregnancy:** 6-mercaptopurine is known to be teratogenic, especially during the 1st trimester. Its use should be avoided whenever possible during pregnancy. Adequate contraceptive precautions should be advised if either partner is receiving 6-mercaptopurine. Ideally, therapy of 6-mercaptopurine should be withdrawn in advance of the intention to start a family, however this may not be appropriate in the individual and the risk/benefit balance should be considered
- **Breastfeeding:** Patients receiving 6-mercaptopurine should **discontinue breastfeeding.**
- Moderate/severe renal or hepatic impairment.
- TPMT deficiency.
- Severe anaemia, leucopenia or thrombocytopenia.
- Active infection or immunodeficiency.
- Known allergic hypersensitivity to 6-mercaptopurine.
- Hepatic impairment – may need dose reduction.
- Renal impairment – reduce dose.
- **Immunisation using a live organism vaccine has the potential to cause infection in immunocompromised hosts. Therefore, immunisations with live organism vaccines are not recommended. Contact the hospital specialist for advice on any vaccinations if required.**

Drug interactions

- **Allopurinol** – enhanced effects and increased toxicity of 6-mercaptopurine when concomitantly given. **BNF states that the dose of 6-mercaptopurine should be reduced to one quarter of its usual dose.**
- **Febuxostat** - use is not recommended in patients concomitantly treated with 6 –mercaptopurine.
- **Anticoagulants** – 6-mercaptopurine possibly reduces the anticoagulant effect of coumarins.
- **Trimethoprim, co-trimoxazole:** avoid concomitant use with 6-mercaptopurine as there is an increased risk of haematological toxicity.
- Avoid concomitant use of 6-mercaptopurine with **clozapine** as there is an increased risk of agranulocytosis

See [BNF](#) and manufacturer's SPC [Home - electronic Medicines Compendium \(eMC\)](#) for up-to-date advice

Consultant /Specialist responsibilities

- Identify those patients who will benefit from treatment with 6-mercaptopurine.
- Undertake pre-treatment monitoring of FBC, U&Es, LFTs and TPMT levels and Varicella Zoster status
- Ensure that the patient/carer is an informed recipient in therapy, provide necessary education on their treatment regimen and any monitoring or follow up that is required and issue local patient information leaflets.
- Provide patients with a patient held record book; undertake pre-treatment monitoring of FBC, LFTs, U&Es, creatinine, and recording varicella status in the record book.
- Initiate mercaptopurine and stabilise patient on a therapeutic dose of mercaptopurine before referral to the GP.
- Send a letter to the GP requesting a formal agreement to share care, prescribing and transfer care to GP only after receipt of a completed and signed agreement from the GP.
- Ensure prior dissemination of sufficient information to patient's GP and other carers.
- Inform the GP that mercaptopurine has been commenced, the dose and future plans for dose changes in keeping with the shared care agreement.
- Clinical and laboratory supervision of the patient by blood monitoring and routine clinic follow-up on a regular basis.
- Send a letter/results notification to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated.
- Where the GP is not performing the phlebotomy, the blood test form MUST be annotated to request that blood results are also copied to the GP
- Evaluation of any reported adverse effects by GP or patient.
- Advise GP on review, duration or discontinuation of treatment where necessary. Where urgent action is required following tests the hospital team will telephone the patient and inform GP.
- Inform GP of patients who do not attend clinic appointments.
- Counsel the patient on contraception and what to do if pregnancy occurs. Document in the notes.
- Provide access to backup advice and support facilities at all times.
- Ensure, where timing is appropriate, that the patient has received a flu vaccine prior to commencing treatment that is likely to cause immunosuppression. Document this in the patient notes and inform the GP it has been given

GP responsibilities

- Reinforce the patient's understanding of the nature, effect and potential side effects of the drug before prescribing it as part of the shared care programme and contact the Specialist for clarification where appropriate.
- Prescribe mercaptopurine at the dose recommended by the hospital Specialist once the patient is stabilised on treatment and side effects have been excluded as far as possible by the hospital. Any decision to alter treatment should usually be taken by the hospital Specialist
- Monitor blood results (FBC, LFT U&E) in line with recommendations in this document.
- Check for possible drug interactions when newly prescribing or stopping concurrent medication.
- Monitor patient's overall health and well-being.
- Report any adverse events to the Consultant/Specialist, where appropriate.
- Report any adverse events to the CSM, where appropriate.
- Stop mercaptopurine if serious adverse drug effect/reaction and contact Specialist team
- Help in monitoring the progression of disease.
- **Refer the patient back to the hospital team after 4 years of 6-mercaptopurine treatment.**

CCG responsibilities

- To provide feedback to trusts via South West Essex Medicines Management Committee.
- To support GPs to make the decision whether or not to accept clinical responsibility for prescribing.
- To support trusts in resolving issues that may arise as a result of shared care.

Patient/ Carer responsibilities

- Report any adverse effects to their GP and/or Specialist
- Ensure they have a clear understanding of their treatment.
- Report any changes in disease symptoms to GP and/or Specialist
- Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy.
- Take/ administer the medication as prescribed.
- Undertake any monitoring as requested by the GP and/or Specialist.

Contact details

Consultant, medical staff and nurse practitioners at the Basildon and Thurrock University Hospitals NHS Foundation Trust (BTUH) are available to give advice and can be contacted either through the main hospital switchboard or direct:

Department / Specialist	Contact Telephone Number
Hospital switchboard – ask for Specialist or On-Call Specialist (Gastroenterologist)out-of-hours	01268 524900
Gastroenterology	

Document Control	
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Shared Care Guidelines are also available electronically via: to insert website link after approval	
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MERCAPTOPURINE PATIENT INFORMATION LEAFLET

This form will be completed by the Hospital Specialist and given to the patient once stabilised and a fax back has been received from the GP accepting the transfer of responsibility to primary care.

You have been prescribed **Mercaptopurine** tablets

for.....

This **treatment** will continue until stopped by your doctor

Your GP has been given all the necessary information regarding your condition and treatment.

The date for your next hospital appointment is

The success and safety of your treatment also depends on you.

- You will have been given information, which tells you about your treatment and condition.
- Avoid excessive alcohol consumption.
- Do not take any over-the-counter medicines, herbal, complementary or alternative medicines and treatments without getting advice from your doctor.
- Avoid contact with chicken pox or shingles.
- Avoid driving and hazardous work until you have learned how Mercaptopurine affects you, as this drug can occasionally cause dizziness.
- Mercaptopurine can increase the skin's sensitivity to sunlight and the risk of developing some forms of skin cancer. Use sun block and wear a hat and light clothing when out in strong sunshine.
- Do **not** use sunlamps or sun beds.
- You will need to have blood tests at least every three months.
- Your GP/ Practice Nurse needs to see you everymonths

If you experience any of the following side-effects, urgently see your GP:

- Mouth ulcer, sore throat, sore mouth.
- Feeling generally unwell.
- Feeling sick, upset stomach, diarrhoea.
- Rashes – new rash or severe itching anywhere on the body.

Stop treatment and get immediate medical advice if you develop:

- An infection with fever and or chills or a severe sore throat.
- Sudden shortness of breath (breathlessness).
- The whites of your eyes or skin become yellow.
- Severe itching of the skin.
- New unexplained bleeding or bruising.
- Severe and continuing abdominal pain or diarrhoea or vomiting.
- If you think you are pregnant contact the SPECIALIST nurse or Specialist
- If you have any concerns about your treatment contact your GP or the hospital.

The direct-dial telephone numbers for the department are.....

GP MERCAPTOPYRINE SHARED MONITORING AGREEMENT 1ST LETTER

Name of GP

Address

Drop code of GP.....

Dear Dr

Re: Patient's name.....

Date of birth.....

Hospital number.....

NHS number.....

I have seen this patient and believe that he/she is suitable for treatment with Mercaptopurine for:

.....

I have initiated the patient on **Mercaptopurine 50mg tablets**

Take..... tablets (.....mg) times per day.

I will be prescribing and monitoring this patient at our clinic until such a time that the patient is deemed stable, which is likely to be in the region of months.

I would like to seek your agreement to take over the prescribing and monitoring of this patient's treatment after this stabilisation period as per agreed shared care guideline which is enclosed for your information.

Please complete, sign and fax back the form below to stated safe haven fax.

I thank you in anticipation.

Yours sincerely

Dr
(Consultant)

MERCAPTOPURINE SHARED CARE GP/PRACTICE FAX BACK FORM

Patient name..... Hospital number.....

Dear GP

You will take over monitoring of the patient including responsibility for organising blood tests and other tests required in accordance with the shared care guidance (enclosed). You will be responsible for reviewing underlying disease including complications and efficacy of therapy.

PLEASE COMPLETE, SIGN AND FAX BACK TO CLINIC/HOSPITAL:

I agree to take over the prescribing and monitoring of this medication and disease.

Signed by (GP).....

Name of GP

Address

or

I am not willing to undertake shared care for this patient because.....
.....
.....

Signed by (GP).....

Name of GP

Address

Please return to

Or Faxback to:.....

References:

1. NHS ONEL and BHRuT NHS Trust Shared Care Guidelines: Mercaptopurine & Azathioprine in Inflammatory Bowel Disease. Approved September 2013, review date November 2015.
2. City & Hackney NHS AND Homerton University Hospital: Mercaptopurine shared care guideline. Approved January 2010.
3. BNF 70
4. 6-Mercaptopurine (Aspen) Summary of Product Characteristics accessed on Electronic Medicines Compendium (eMC). Last Updated on eMC 31 March 2015. Last accessed November 13, 2015.
5. NICE Clinical Knowledge Summaries: DMARDs (<https://cks.nice.org.uk/dmards>). Last accessed November 17, 2016.