Shared Care Guideline:
6-Mercaptopurine

NHS County Durham and Darlington NHS Foundation Trust

NHS County Durham and Darlington Area Prescribing Committee

Overview	6-mercaptopurine is an immunosuppressant drug. It is sometimes used where treatment with azathioprine has failed due to mild side effects such as nausea
Indication	Unlicensed • Ulcerative colitis • Crohn`s disease
Dose	Initial dose • 1 to 1.5 mg/kg/day If starting at 1mg/kg/day this can be increased to 1.5mg/kg after ONE week. Lower doses may be appropriate for patients who have had previous haematological side effects related to azathioprine or 6-mercaptopurine and who can be maintained in remission using a lower dose
Specialist's Responsibilities	**Initial investigations:** • Full Blood Count (FBC), Liver Function Tests (LFTs), Erythrocyte Sedimentation Rate (ESR) /C-Reactive Protein(CRP) • Check Thiopurine Methyltransferase (TPMT) status • Check Varicella Zoster status if there is an uncertain history and recent exposure to the virus. It is the responsibility of the specialist to arrange vaccination should the patient be found to not have immunity In addition the following may also be requested; Weight, Height and Blood Pressure (BP) and calculated Creatinine clearance (CrCl) / Glomerular Filtration Rate (GFR), **Initial prescribing until stable:** **Prescribing responsibility and monitoring to stay with the specialist until patient has been on a stable dose for at least 6 weeks at which point shared care is requested.** Specialist to issue a prescription for enough medication to last until shared care is accepted by GP. This will usually be a minimum of 28 days. **Communication and Documentation to GP:** • Obtaining agreement of GP to participate in shared-care arrangement for 6-mercaptopurine therapy. This will be by sending a completed copy of the shared care request letter (appendix 1) to the GP • The specialist must ensure that the GP is aware when the next blood monitoring is required. • The GP Must be made aware of any additional monitoring requirements specific to the patient • Prompt communication with the GP regarding the patient's progress, any reassessment and changes in treatment. • Provide additional information and advice to the GP on actions he/she may need to take e.g. on dosage adjustment, other changes in therapy and management of adverse effects, as required.
GP's Responsibilities	**Maintenance prescription:** Prescribe 6-mercaptopurine in accordance with the specialist's recommendations as outlined in the shared care agreement.

Clinical monitoring:

Continue to clinically monitor patient in line with this shared care agreement and referral letter from specialist (as described in clinical monitoring section below)

Criteria Requiring Specialist contact:

- Failure to attend for review or undertake blood tests
- Intolerance of drugs
- Communications failure

Documentation to specialist:

- Accepting or rejecting request for shared care within 28 days, if rejecting please state concerns and reasons Blood results to specialist via use of patient-held record.

Clinical monitoring:

FBC, LFTs and ESR/CRP
Optional calculated CrCl /GFR

Frequency:

Weekly until on stable dose for FOUR weeks, review in clinic (and blood tests) after SIX to EIGHT weeks then clinical monitoring monthly for THREE months
After THREE months reduce frequency of monitoring to THREE monthly

<u>After dose increase</u>

Repeat FBC, LFTs, calculated CrCl /eGFR TWO weeks after dose increase, then monthly for THREE months, then THREE monthly thereafter

For patients heterozygote for low TPMT activity, monitoring should continue at <u>monthly</u> intervals as a minimum.

NOTE – this guideline sets out the standard monitoring requirements, however it is essential that each patient is considered on an individual basis and monitoring frequency should reflect this. The GP should be made aware of any deviations.

Safety monitoring:

Please refer to Summary of Product Characteristics (SPC) or BNF /eBNF for full details of adverse effects, contraindications, cautions and drug interactions.

- Monitoring for response and adverse drug reactions (ADRs)
- Ask about the following at each visit
    - sore throat
    - bruising or bleeding
    - rash
    - oral ulceration

Adverse Events

Adverse event	Action to be taken
WBC less than 3.5 x 10^9/L	Withhold and discuss with specialist team
Neutrophils less than 1.5 x 10^9/L	Withhold and discuss with specialist team
Platelets less than 120 x 10^9/L	Withhold and discuss with specialist team
More than a TWO fold rise in Alanine transaminase (ALT) / Aspartate aminotransferase (AST) from upper limit of normal	Withhold and discuss with specialist team
Rash, oral ulceration	Withhold and discuss with specialist team
Mean Cell Volume (MCV) more than 105	Withhold, check B12, folate, TFT and discuss with specialist team
Abnormal bruising or sore throat	Withhold, check FBC and discuss with specialist team

	Please note: Any rapid fall or consistent downward trend for blood counts or rapid rise or consistent upward trend for liver enzymes should prompt caution. Action may be required even if values are within normal range. If in doubt please contact specialist team. • Bone marrow suppression characterised by sore throat, infection, fever, malaise, cough, unexplained bruising or bleeding, fatigue, hypotension/ hypertension, myalgia, dizziness and rash • GI side effects including Nausea, vomiting and diarrhoea • Arthralgia • Alopecia • Jaundice • Pancreatitis • Hepatotoxicity All suspected serious reactions should be reported to the specialist and the MHRA
Contra-indications	• Known hypersensitivity to azathioprine or 6-mercaptopurine. • Homozygote for low TPMT activity
Cautions	• Heterozygote for low TPMT activity • Renal insufficiency – use doses at lower end of the normal range and monitor carefully for toxicity. • Hepatic impairment – monitor carefully for hepatic or haematological toxicity and reduce dose if signs of toxicity occur
Drug Interactions	• Avoid co-prescribing 6-mercaptopurine with Allopurinol due to an increased risk of toxicity, unless advised by specialist clinician. If co-prescribed the dose of 6-mercaptopurine must be reduced to 25% of the original dose. • Anticoagulant effect of warfarin is inhibited by 6-mercaptopurine. • Concomitant use with co-trimoxazole or trimethoprim can cause life threatening haematoxicity. • Aminosalicyclates i.e sulfasalazine, mesalazine, olsalazine, balsalazide, may contribute to bone marrow toxicity.
Other Information	**Vaccinations** • “Live” vaccines (including Oral Polio, Oral Typhoid, measles, mumps and rubella (MMR), bacillus Calmette-Guérin (BCG) and yellow fever) are not recommended whist on treatment • Seasonal influenza vaccination is recommended annually. • Pneumococcal vaccination is recommended in line with current guidance **Fertility, Pregnancy and Breast-feeding** • Careful assessment of risk versus benefit should be carried out before use during pregnancy, in patients likely to become pregnant and breastfeeding • European Crohn´s and Colitis Organisation (ECCO) supports the use of 6 - mercaptopurine in some circumstances the benefit to the mother may outweigh the risk to the unborn child. The decision to continue should be made jointly by the specialist team and the obstetric team. Dose reduction at 32 weeks gestation may prevent neonatal leucopenia. • ECCO guidance suggests that women treated with 6-mercaptopurine can continue to breast feed.

	General • 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) • Patients with no history of exposure to varicella zoster virus 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.
Contact Details	Thank you for sharing the care of this patient. If you have any concerns or queries, please contact the Consultant, secretary or call the appropriate helpline below. UHND Gastroenterology Helpline: 0191 3332333 DMH Gastroenterology Helpline: 01325 743434

NHS
County Durham and Darlington
NHS Foundation Trust

Department of Gastroenterology
County Durham and Darlington Foundation Trust

GP name
GP address

Dear Dr ……

Request for Shared Care of 6-MERCAPTOPURINE Date:

Re: Patient's name DOB:
Address Hospital Number:

This patient has been prescribed 6 Mercaptopurine via the ORAL route for the management of
- Ulcerative colitis
- Crohn's Disease

The patients' current dose is ……per day

The patient was commenced on this drug on ……..and has been stable on the current dose since……..

I would now like to ask you to take over the responsibility for prescribing this medication for this patient, as agreed by your CCGs and the Area Prescribing Committee.

The shared care document lists the monitoring requirements for this medication. Can I ask that any problems are reported back into secondary care.

The next blood monitoring is due on …… and should be continued in line with the shared care guideline.

In addition, the following patient specific monitoring is required for this patient

……..

This is part of the shared care guideline approved by the Area Prescribing Committee, available at http://medicines.necsu.nhs.uk/guidelines/durham-darlington/.

The patient will remain under regular clinical review by his or her usual consultant/ specialist nurse as described in the shared care agreement.

Please send back the second part of this letter, with 28 days, so we know that we have your agreement to this arrangement. If you are not happy to accept this patient or have any concerns, then please contact my secretary as soon as practically possible

Yours sincerely

Consultant name
Contact details

GP Agreement

Patient's Name:
DOB:
Hospital No:

I agree to take over the prescribing and monitoring of 6-Mercaptopurine in line with the approved shared care document as found at http://medicines.necsu.nhs.uk/guidelines/durham-darlington/

Dose to be prescribed ……..

Dated ……/……/

Signed: …….

GP's Name:

GP contact details

Please return to Consultant's secretary. You may wish to keep a copy for your records.