South West Yorkshire Area Prescribing Committee

Mercaptopurine Shared Care Guideline

Introduction	
General statements	• The patient will receive supplies of the drug from the hospital until the transfer of shared care is agreed between consultant and the primary care prescriber. • The primary care prescriber must reply in writing to the request for shared care as soon as practicable if unwilling to participate conveying the clinical reason for this. • The responsibility for prescribing and monitoring must be documented clearly in the patient's hospital and general practice notes • Shared care should only be considered when the patient's clinical condition is stable or predictable
Indication	Inflammatory Bowel Disease: unresponsive and frequently relapsing cases of Crohn's Disease and Ulcerative Colitis.

Individual's Responsibilities	
Hospital specialist's responsibilities	• Document in the patient's medical notes and advise the primary care prescriber that you have reached agreement with the patient on the unlicensed use of this medicine and that an appropriately licensed medicine would not meet the patient's needs. • Baseline monitoring and initial prescribing until the patient is established on treatment (minimum of 8 weeks). Patient is only transferred to primary care prescriber once stabilised. • Baseline screening for HIV, Hepatitis B and C, varicella zoster virus immunoglobulins and Epstein barr virus antibodies prior to initiation (if indicated). • Monitoring disease progression and treatment response • Supporting and advising primary care prescribers • Give patient information leaflet • Ensure that the patient has an adequate supply of medication until primary care prescriber supply can be arranged. • Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the primary care prescriber. • Provide patient with the specialist clinic helpline contact number
Primary care prescriber's responsibilities	• Ensure hospital is notified in writing if unwilling to undertake prescribing and monitoring when requested conveying the clinical reason for this. • Prescribing following written request from specialist care • Ensure monitoring is undertaken according to shared care guideline and only continue prescribing if patient is compliant with monitoring, blood test results are satisfactory, and no adverse or unwanted side effects.* • Follow guidance in the event of reaction or abnormality, record it and report back to specialist • All patients should be advised to have the yearly influenza vaccine and pneumococcal vaccinations (unless contra-indicated) in accordance with the Department of Health Green Book Website: *https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book* (note specialist groups may have specific advice on certain vaccinations).

	• Ensure no adverse drug interactions with concomitant medicines • To inform the hospital specialist if patient repeatedly does not attend routine blood monitoring.
Monitoring required	**Baseline** • Full blood count • Urea and electrolytes • Liver function tests • Thiopurine methyltransferase assay (homozygous deficiency associated with serious toxicity risk) **Maintenance** - Repeat FBC, LFT fortnightly for 8 weeks, then monthly for 4 months, then quarterly; U&Es 6-monthly **Following dose change of patient already established on mercaptopurine** - recommend 2-weekly blood test for 4 weeks and the recommencement of the usual monitoring schedule.
When and how to discontinue treatment	Loss of efficacy, intolerable or serious side effects, abnormal blood monitoring – please see overleaf for detailed guidance as regards reducing dose or stopping treatment.*
Information given to the patient	Hospital specialist to explain off-label use when seeking agreement from the patient for the use of this medicine (if applicable). Patient information leaflet. Patients should be warned to report any unexplained bleeding, bruising, purpura, sore throat or fever to their prescriber.
Contact details	Documented in letter from specialist care to primary care prescriber.

Product Information

The information in this Shared Care Guideline should be used in conjunction with the latest edition of the BNF and Summary of Product Characteristics

Dosage and administration	The usual dosage is **1 - 1.5mg/kg/day** taken as a **single daily dose** or in **2-3 divided doses** and should be adjusted within these limits. Remember mercaptopurine tablets are 50mg & scored. Dose is dependent on the clinical response and haematological tolerance. Therefore some patients may respond to lower doses. Consideration should be given to reducing the dosage in patients with impaired renal/hepatic function.
Serious adverse effects	Hypersensitivity reactions including malaise, fever, vomiting, diarrhoea, rash & interstitial nephritis. Pancreatitis. Bone marrow toxicity (anaemia, leukopaenia, thrombocytopaenia) - patients should be advised to report unexplained bruising, bleeding, or severe sore throat. Alopecia. Increased risk of some cancers (skin and haematological). Opportunistic infections (potentially fatal if associated with neutropenia) Refer to the current BNF and the summary of product characteristics (SPC) online via https://products.mhra.gov.uk/product/ for complete and up to date information.
Precautions and contra-indications	Refer to the current BNF and the summary of product characteristics (SPC) online via https://products.mhra.gov.uk/product/ for complete and up to date information.

	Precautions – pregnancy considered relatively safe and benefit of continuing treatment may outweigh risk. Patient should discuss this with specialist.
Clinically relevant drug Interactions and their management	**Allopurinol** blocks mercaptopurine metabolism. Concomitant administration of allopurinol and mercaptopurine may result in fatal toxicity: reduce mercaptopurine dose to one quarter (25%) of usual dose and contact specialist for advice on ongoing management. **Warfarin** – anticoagulant effect reduced by mercaptopurine **Aminosalicylates** (sulfasalazine, mesalazine, olsalazine, etc.) and **co-trimoxazole** may enhance bone marrow toxicity **Live vaccines are contra-indicated** However flu vaccines and Pneumovax are safe and recommended. Refer to the green book for further information or seek specialist advice if unsure. This is not a comprehensive list, please Refer to the current BNF and the summary of product characteristics (SPC) online via https://products.mhra.gov.uk/product/ for complete and up to date information.

Recommended action for abnormal results

Investigation	Action
WBC <3.5 x10^9/L Neutrophils < 2 x10^9/L Platelets < 150 x10^9/L	Stop mercaptopurine and contact appropriate specialty department immediately by phone or email for advice*
MCV above 105 fL	Check TFT, B12 and folate, alcohol history
Hb fall >1g in 4 weeks or below 10g	Check for increased disease activity Ask about NSAID use and symptoms of GI blood loss or dyspepsia and stop NSAIDS if implicated. Check MCV and iron studies Consider endoscopy
Deranged liver function tests (ALT) ALT greater than normal but < 3x upper limit of lab reference range	Repeat bloods every 2 weeks Ask patient about viral/bacterial infections Check that it is not due to another drug or alcohol Consider seeking specialist advice regarding potential dose reduction
ALT > 3x upper limit of lab reference range	Stop mercaptopurine and contact appropriate specialty department immediately by phone or email for advice*
Deterioration of Us & Es from baseline	Consider seeking specialist advice regarding potential dose reduction

Recommended action for adverse effects

Adverse Event	Action

Hypersensitivity, pancreatitis	Stop treatment and contact appropriate specialty department immediately by phone or email*
Bruising, bleeding	Check FBC, clotting screen, LFTs, alcohol history • If unexplained – Stop mercaptopurine treatment and contact appropriate specialty department immediately by phone or email*
Malaise, flu-like symptoms	Contact specialist.
Itching	Check for other causes. Consider seeking specialist advice on dose reduction and ongoing review
Rash	Check for other causes: complications of disease, vasculitis, steroid effects, etc. Mild– Consider seeking specialist advice for advice on dose reduction and ongoing review Severe– Stop mercaptopurine treatment and contact appropriate specialty department immediately by phone or email*
Alopecia	Check FBC and LFTs Mild –Seek specialist advice for recommendation on dose reduction and ongoing review Severe– Stop mercaptopurine treatment and contact appropriate specialty department immediately by phone or email*
Oral ulcers, stomatitis	Check WBC Check for candida & treat accordingly Mild - mouthwash and good dental hygiene Severe– Stop mercaptopurine treatment and contact appropriate specialty department immediately by phone or email*
Diarrhoea	Check for other causes Mild -treat symptomatically and/or Consider seeking specialist advice for advice on dose reduction and ongoing review Severe– Stop mercaptopurine treatment and contact appropriate specialty department immediately by phone or email*

***If the decision is made in primary care to stop treatment with mercaptopurine please contact the relevant department immediately to let the patient's specialist team know that disease-modifying treatment has been stopped.**