Health and Social Care Board

Interface Pharmacist Network Specialist Medicines

Mercaptopurine

Gastroenterology shared care guideline.

Specialist details	Patient identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

Introduction

This shared care guideline refers to the use of mercaptopurine in the treatment of **NON-CANCER CONDITIONS ONLY.**

Unlicensed indications: Crohn's disease, ulcerative colitis, autoimmune hepatitis.

Adult dosage and administration

A typical dose regimen is 1 - 1.5mg/kg daily. Some patients may respond to lower doses.
Dosage may need to be reduced in renal or hepatic impairment.
To avoid potential dose confusion, the use of the term '6-Mercaptopurine' should be avoided.

Preparations available:

- Mercaptopurine 50mg tablets (unlicensed 10mg preparations may also be available)
- Mercaptopurine liquid 20mg/ml (Xaluprine®)
- Liquid and tablets preparations are not bioequivalent and haematological monitoring is advised when switching formulations.

Hospital specialist responsibilities

- Agree shared care with patient's GP.
- Provide the patient/carer with relevant (preferably written) information on use, side effects and need for monitoring of medication.
- If the liquid formulation is used, provide training on safe handling, storage, spillage and waste disposal (provide a cytotoxic spill kit and cytotoxic sharps box if necessary).
- Provide shared care monitoring record booklet if required.
- Undertake baseline tests as indicated in monitoring table.
- Review results of safety monitoring and request additional tests as required.
- Monitor disease, response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required.

Monitoring table		Hospital specialist	GP			Hospital specialist
Test	Indication	Pre-treatment baseline	During treatment			Annual review
			Until on stable dose for 6 weeks	Next 3 months	Thereafter	
FBC	Baseline assessment, dose adjustment	✓	Every 2 weeks	Every month	Every 3 months	As part of annual review or as clinically indicated
LFTs						
U&Es, eGFR						
ESR/CRP	Disease activity scoring	✓	Every 3 months			
Height & weight	Baseline assessment	✓	Not routinely required			If clinically indicated
Blood pressure	Baseline assessment, respiratory and TB screening	If clinically indicated				
Chest x-ray						
PFTs, TB screening if indicated						
TPMT	To assess suitability for treatment	✓				
Ask about oral ulceration, sore throat, unexplained rash or unusual bruising/bleeding		✓	At every consultation			✓
If a further DMARD is added as combination therapy, or the dose is increased, the initial starting schedule should be reinstated. There may be clinical circumstances where the frequency of monitoring may vary and this should be specified by the initiating specialist						

GP responsibilities

- Prescribe mercaptopurine.
- Arrange and record ongoing monitoring as advised by specialist (see monitoring table), ensuring practice systems are in place to recall patients for monitoring blood tests.
- Prevent ongoing prescription if patient is not compliant with monitoring. Liaise with specialist if appropriate.
- Report any adverse drug reactions to the initiating specialist and the usual bodies (eg. MHRA/CHM).
- Ensure no drug interactions with other medicines.
- Administer inactivated influenza vaccine annually unless otherwise advised by the initiating specialist.
- Check patient has had ONE DOSE of pneumococcal vaccine (revaccination is not recommended except every five years in patients whose antibody levels are likely to have declined more rapidly eg. asplenia), see BNF or Green Book.
- Passive immunization using varicella immunoglobulin (VZIG) should be considered in non-immune patients if exposed to chickenpox or shingles. Contact Regional Virus Laboratory, Royal Group of Hospitals, duty virologist 07889 086 946 for advice if exposure is suspected. For other queries eg. those concerning exposure, infection or any recommendations relating to healthy susceptible household contacts, consult the Green Book and/or take additional advice from Regional Virus Laboratory, Royal Group of Hospitals.
- Ask about oral ulceration, sore throat, unexplained rash or unusual bruising/bleeding at every consultation.

Withhold mercaptopurine and contact specialist if:

- WCC < 3.5 x 10^9/L
- Neutrophils < 1.6 x 10^9/L
- Unexplained eosinophilia > 0.5 x 10^9/L
- Platelets < 140 x 10^9/L
- MCV > 105fL, (check B12 & folate & TFT)
- AST/ALT > 3 times the upper limit of normal (for results between 2 – 3 x ULN, continue mercaptopurine, repeat bloods and seek specialist advice) Minor elevations of AST/ALT are common
- If renal impairment develops
- Unexplained fall in serum albumin
- Oral ulceration / sore throat
- Unexplained rash / abnormal bruising
- New or increasing dyspnoea or dry cough.

Normal reference range may vary slightly between labs.
Results should be recorded in the patient's shared care monitoring record booklet (where in use).
Please note an unusual fall or rise or a consistent downward or upward trend in any value should prompt review of the patient and extra vigilance. Some patients may have abnormal baseline values, specialist will advise.

Adverse effects, precautions and contraindications

Contraindications include:

- Hypersensitivity to azathioprine or mercaptopurine
- TPMT deficiency - avoid if deficient or reduce dose if low levels.

General signs of malaise such as dizziness, diarrhoea, rash, myalgia and arthralgia occur infrequently. If severe or persistent refer to the initiating specialist.
Infection. Immunosuppressants can increase susceptibility to infection. It is advisable not to commence or continue treatment with mercaptopurine when patients have an established local or systemic infection. It is advisable to recommence once the infection has been treated. Precise period of discontinuation depends on the nature and severity of infection and the activity of the underlying disease.
Nausea can occur initially but can be reduced by taking the tablets after food.
Blood disorders: leucopenia, anaemia and thrombocytopenia. GPs should be alert to any oral ulceration, sore throat, unexplained rash or abnormal bruising or bleeding.
Abnormal liver function can occur.
Pancreatitis has been reported in a small percentage of patients.
Pregnancy / contraception: women of childbearing potential and men receiving mercaptopurine should be advised to use effective contraception. Patients discovered to be or planning to become pregnant should be referred to the initiating specialist at the earliest opportunity without discontinuing mercaptopurine.
Breastfeeding. Women being treated with mercaptopurine should seek specialist advice.
Cancer risk. Patients receiving long-term immunosuppressive drugs are at increased risk of developing a malignancy. The most frequently occurring types are lymphoma and skin malignancy. The avoidance of excessive exposure to the sun, and the use of high factor sunscreen and protective clothing are advised. Adherence to population screening programmes is particularly important in this population.
Live vaccines. Consult the Green Book and take additional advice from initiating specialist if required.

Common drug interactions

Allopurinol: prolongs activity of mercaptopurine and increases risk of severe myelosuppression. If must be given concomitantly, it is essential that only a quarter of the usual dose of mercaptopurine is given.
Aminosalicylates (eg. Sulfasalazine) increase risk of haematological toxicity. Increased monitoring may be required.
Clozapine: avoid concomitant use.
Febuxostat: avoid concomitant use.
Trimethoprim or **co-trimoxazole**: increased risk of haematological abnormalities.
Warfarin effect may be reduced requiring an increased dose of warfarin.

Communication

For any queries relating to this patient's treatment with mercaptopurine, please contact the specialist named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC or the BNF

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