South West Yorkshire Area Prescribing Committee

AZATHIOPRINE 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 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 primary care notes • Shared care should only be considered when the patient's clinical condition is stable or predictable
Indication	**Use of azathioprine as an immunosuppressant anti metabolite with steroid sparing effects to treat appropriate licensed or unlicensed non transplant conditions as initiated by rheumatology, gastroenterology, dermatology, respiratory, neurology or ophthalmology specialists**

Individual's Responsibilities	
Hospital specialist's responsibilities	➢ Record patient consent to unlicensed use in medical notes (if applicable) and confirm that this discussion has taken place in writing when requesting shared care with a primary care prescriber. ➢ Baseline monitoring and initial prescribing until the patient is established on treatment (minimum of 8 weeks). ➢ 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 ➢ Monitoring booklets are available and may be beneficial in certain circumstances, for example if the patient receives blood monitoring at a location where results are inaccessible to the clinician. In these situations the Hospital Specialist will communicate this fact to primary care at the point when prescribing and monitoring is transferred ➢ 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 Prescribers 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 ➢ Update patient's monitoring booklet as appropriate (including test dates & results, when available) ➢ All patients should be advised to have the yearly influenza vaccine. They should also have the pneumococcal vaccinations (unless contra-indicated) in accordance with the Department of Health Green Book Website: *https://www.gov.uk/government/collections/immunisation-*

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	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** • FBC • U&E • LFTs • Thiopurine methyltransferase assay (homozygous deficiency associated with serious toxicity risk) The Hospital Specialist must confirm to the primary care prescriber which stages of the maintenance monitoring have already been completed at the point when prescribing and monitoring are transferred to primary care. **Maintenance** - Repeat FBC, LFT, U&E & creatinine fortnightly for 8 weeks (0-2 months post initiation), then monthly for 4 months (2 – 6 months post initiation), then quarterly; **Following dose change of patient already established on azathioprine** - recommend fortnightly 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	Patient information leaflet and monitoring booklet (provided by hospital specialist) Hospital specialist to explain off-label use when seeking agreement from the patient for the use of this medicine (if applicable). Patients should be warned to report any unexplained bleeding, bruising, purpura, sore throat or fever. Patient should be advised to limit exposure to ultraviolet light and wear appropriate clothing and a purchase over the counter and use a high factor (30 or above) sunscreen when exposed to the sun.
Contact details	Documented in letter from specialist care to primary care

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	Target dose is usually 2-3mg/kg/day (maximum = 3mg/kg/day). Dose titration to be specified by specialist team starting treatment. Dose can be taken as single dose or divided with meals.
Serious adverse effects	Hypersensitivity reactions including malaise, fever, vomiting, diarrhoea, rash, dizziness, rigors, myalgia, hypotension, arthralgia & 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 neutropaenia)

	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	Contraindications – hypersensitivity to azathioprine or mercaptopurine, homozygous TPMT deficiency (unless under close specialist supervision), severe hepatic and renal impairment. Precautions – pregnancy considered relatively safe and benefit of continuing treatment may outweigh risk. Avoid breastfeeding
Clinically relevant drug Interactions and their management	**Allopurinol** blocks azathioprine metabolism. Concomitant administration of allopurinol and azathioprine may result in fatal toxicity: reduce azathioprine dose to one quarter (25%) of usual dose and contact specialist for advice on ongoing management. **Warfarin** – anticoagulant effect reduced by azathioprine **Aminosalicylates** (sulfasalazine, mesalazine, olsalazine, etc) and **co-trimoxazole** may enhance bone marrow toxicity Avoid live vaccines – examples could include oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster – for full details check the latest SPC before administration or the green book.

Recommended action for abnormal results

Investigation	Action
WBC <3.5 x10^9/L Neutrophils < 1.6 x10^9/L Platelets < 150 x10^9/L MCV above 105 fL	Stop azathioprine and contact appropriate specialty department immediately by phone or email for advice* 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 or AST) Greater than normal and less than 3x upper limit of lab reference range Greater than or equal to 3x upper limit of lab reference range	Repeat bloods every fortnight Ask patient about viral/bacterial infections Check that it is not due to another drug or alcohol Consider seeking specialist advice for advice on dose reduction Stop azathioprine 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 azathioprine treatment and contact appropriate specialty department immediately by phone or email*
Bruising, bleeding	Check FBC, clotting screen, LFTs, alcohol history

	• If unexplained – Stop azathioprine treatment and contact appropriate specialty department immediately by phone or email*
Malaise, flu-like symptoms	Contact specialist.
Itching	Check for other causes to confirm this is drug induced: Is this a pre-existing symptom, complications of disease, vasculitis, steroid effects, etc. Consider seeking specialist advice on dose reduction and ongoing review
Rash	Check for other causes to confirm this is drug induced: Is this a pre-existing symptom, complications of disease, vasculitis, steroid effects, etc. Mild– Consider seeking specialist advice for advice on dose reduction and ongoing review Severe– Stop treatment and contact appropriate specialty department immediately by phone or email*
Alopecia	Check FBC and LFTs Mild–Seek specialist advice for advice on dose reduction and ongoing review Severe– Stop azathioprine 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 azathioprine 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 azathioprine treatment and contact appropriate specialty department immediately by phone or email*

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