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 GP • The GP must reply in writing to the request for shared care as soon as practicable if unwilling to participate. • The responsibility for prescribing and monitoring must be documented clearly in the patient's hospital and GP notes • Shared care should only be considered when the patient's clinical condition is stable or predictable
Indication	**Licensed indications** - rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis and polymyositis, auto-immune hepatitis **Unlicensed indications** - systemic vasculitis, inflammatory bowel diseases (Crohn's Disease, Ulcerative Colitis, Microscopic Colitis)

Individual's Responsibilities	
Hospital specialist's responsibilities	➢ Baseline monitoring and initial prescribing until the patient is established on treatment (minimum of 8 weeks). ➢ Monitoring disease progression and treatment response ➢ Supporting and advising GPs ➢ 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 the GP at the point when prescribing and monitoring is transferred ➢ Ensure that the patient has an adequate supply of medication until GP 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 GP. ➢ Provide patient with rheumatology nurse helpline contact number
General Practitioner's responsibilities	➢ Ensure hospital is notified if unwilling to undertake prescribing and monitoring when requested ➢ 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) ➢ Encourage influenza and pneumococcal vaccination as per green book ➢ Ensure no drug interactions with concomitant medicines ➢ To inform Rheumatology Team if patient repeatedly does not attend routine blood monitoring.
Monitoring required	**Baseline** - FBC, U&E, creatinine, LFT, TPMT assay (homozygous deficiency associated with serious toxicity risk) The Hospital Specialist must confirm to the GP which stages of the maintenance monitoring have already been completed at the point when prescribing and monitoring are transferred to the GP. **Maintenance** - Repeat FBC, LFT, U&E & creatinine fortnightly for 8 weeks,

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	monthly for 4 months, then quarterly;
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) 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 high factor (30 or above) sunscreen when exposed to the sun
Contact details	Documented in letter from specialist care to GP

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 & 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 www.medicines.org.uk/emc/ 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. **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

Recommended action for abnormal results

Investigation	Action
WBC <3.5 x10^9/L Neutrophils < 2 x10^9/L Platelets < 150 x10^9/L	Stop and contact appropriate specialty department immediately by phone or email*
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) < 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 dose reduction
> 3x upper limit of lab reference range	Stop and contact appropriate specialty department immediately by phone or email*
MCV above 105 fL	Check TFT, B12 and folate, alcohol history

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 treatment and contact hospital specialist
Malaise, flu-like symptoms	Contact specialist to consider switch to mercaptopurine.
Itching	Check for other causes, reduce dose and review
Rash	Check for other causes: complications of disease, vasculitis, steroid effects, etc. Mild – reduce dose Severe – stop*
Alopecia	Stop and contact hospital specialist
Oral ulcers, stomatitis	Stop treatment and contact hospital specialist* Check WBC Check for candida & treat accordingly Mild - mouthwash and good dental hygiene
Diarrhoea	Check for other causes Mild -treat symptomatically and/or reduce dose if persistent. Contact hospital specialist. Stop if severe.*

***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.**