Shared Care Guideline: *Azathioprine*

County Durham and Darlington NHS
NHS Foundation Trust

NHS
County Durham and Darlington
Area Prescribing Committee

Overview	Azathioprine is an immunosuppressant drug
Indication	Licensed • Rheumatoid arthritis • Pemphigus vulgaris • Ulcerative colitis • Crohn`s disease • Severe Refractory eczema • Autoimmune hepatitis (NOTE that the patient MUST BE under the care of a specialist hepatologist, either in CDDFT or tertiary centre (Freeman Road Hospital (FRH) / James Cook University Hospital (JCUH) Unlicensed • Psoriatic arthritis • Systemic vasculitis • Sarcoidosis • Idiopathic pulmonary fibrosis
Dose	Initial dose of one of the following regimes • 1 to 2mg/kg/day increasing after a minimum of ONE week, as necessary to 2 to 3mg/kg/day. • 3mg/kg/day
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 azathioprine 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 e.g. Weight, Height BP CrCl/GFR • 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 azapthioprine in accordance with the specialist's recommendations as outlined in the shared care request letter **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:** **Gastroenterology patients** Weekly for FOUR weeks, then in clinic review at week SIX to EIGHT weeks. If stable, patients can be transferred to THREE monthly. If unstable, repeat after a further MONTH, then THREE monthly monitoring thereafter **Rheumatology and dermatology patients** Fortnightly until on stable dose for SIX weeks then monthly for THREE months After THREE months reduce frequency of monitoring to THREE monthly <u>After dose increase (all specialities)</u> Repeat TWO weeks after dose increase, then if stable revert back to THREE monthly thereafter. If unstable repeat after a further MONTH before reverting back to THREE monthly monitoring. **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 2.0 x 10^9/L	Withhold and discuss with specialist team
Platelets less than 150 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	Check B12, folate, Thyroid Function Tests(TFTs) 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
- Rigours
- Rash
- Alopecia
- Jaundice
- Pneumonitis
- Hypertension
- Pancreatitis

All suspected serious reactions should be reported to the specialist and the MHRA

Contra-indications

- Known hypersensitivity to azathioprine or 6-mercaptopurine.
- Concomitant ribavirin
- Homozygote for low TPMT activity
- Lesch - Nyhan syndrome

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 Azathioprine with Allopurinol due to an increased risk of azathioprine toxicity, unless advised by specialist clinician. If co-prescribed the dose of azathioprine must be reduced to 25% of the original dose.
- Anticoagulant effect of warfarin is inhibited by azathioprine.
- Concomitant use with co-trimoxazole or trimethoprim can cause life threatening haematoxicity.

Other Information	**Vaccinations** • Live vaccines can be considered in patients on a dose of up to 3mg per Kg daily after careful consideration of the risks and benefits in conjunction with the patient; please discuss with the appropriate specialist • Seasonal influenza vaccination is recommended annually. • Pneumococcal vaccination is recommended every FIVE years **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 • The European Crohn´s and Colitis Organisation (ECCO), The British Association of Dermatologists (BAD) and the British Society for Rheumatology (BSR) support the use of azathioprine 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 and should not exceed 2mg/kg per day. Dose reduction at 32 weeks gestation may prevent neonatal leucopenia. • ECCO, BAD and BSR guidance suggests that women treated with azathioprine can continue to breast feed. More information on use of azathioprine in pregnancy and breastfeeding can be found on the BSR and BAD websites **https://www.guidelines.co.uk/BSR/RA-in-pregnancy-and-breastfeeding/252703.article** http://www.bad.org.uk **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 should be advised to limit exposure to ultraviolet light and sunlight and to wear high factor sun creams and/or protective clothing to limit risk of photosensitivity and skin cancer. • 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 Rheumatology Helpline: 0191 3332763 DMH Rheumatology Helpline: 01325 743881 UHND Gastroenterology Helpline: 0191 3332333 DMH Gastroenterology Helpline: 01325 743434 Note : there is no dedicated Dermatology Helpline

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Department of ……
County Durham and Darlington Foundation Trust

GP name
GP address

Dear Dr ……

Request for Shared Care of AZATHIOPRINE **Date:**

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

This patient has been prescribed **Azathioprine via the ORAL route** for the management of

□ Rheumatoid arthritis □ Pemphigus vulgaris □ Ulcerative colitis
□ Autoimmune Hepatitis □ Severe Refractory Eczema □ Crohn's Disease
□ Idiopathic pulmonary fibrosis (unlicensed) □Sarcoidosis (unlicensed) □ Systemic Vasculitis (unlicensed)
□ Psoriatic arthritis (unlicensed)

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 Azathioprine 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