BNSSG Shared Care Guidance

Section 1: Heading

Drug	Azathioprine
Amber *one month*	
Indication	Autoimmune rheumatologic conditions including inflammatory arthritis, connective tissue diseases and vasculitis. Ocular inflammation Interstitial lung disease (not IPF)
Speciality / Department	Rheumatology Ophthalmology Respiratory
Trust(s)	University Hospitals Bristol & Weston Foundation Trust
	North Bristol Trust, Southmead Hospital

Section 2: Treatment Schedule

Usual dose and frequency of administration	Azathioprine is given daily by mouth and is available as 25mg, 50mg and 100mg tablets. It is recommended that the activity of TPMT (thiopurine methytransferase, the key enzyme metabolizing azathioprine) is measured prior to treatment, to identify those patients likely to experience serious adverse effects. A typical dose regimen is to commence 50 to 100mg orally daily and to increase by 50mg every 2 weeks to a maximum dose of 2.5mg per kg per day (usually 150 to 200mg daily).
Route and formulation	Oral
Duration of treatment	This should be continued as long as clinically indicated unless there is a serious side effect or the drug becomes ineffective.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate
Pre-treatment assessment: This will be performed by the rheumatology/ophthalmology/respiratory department. Height, weight, blood pressure, FBC, renal function/GFR, LFT's, TPMT and screening for viral infection (HIV, Hep B, Hep C) will be done prior to commencing azathioprine. Screening for lung disease (including pulmonary function tests and appropriate imaging) will be done if indicated at the discretion of the specialist (the extent of this screen may vary between departments). Any patient currently smoking should be offered access to smoking cessation services.
Subsequent tests - where appropriate
Monitoring: This will be performed primarily by the patient's GP, with support from the specialist team in the event of abnormal results (see below) Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks. Once on stable dose, **monthly** FBC, creatinine/calculated GFR, ALT and/or AST and albumin for 3 months; thereafter, FBC, creatinine/calculated GFR, ALT and/or AST and albumin **at least every 12 weeks**. More frequent monitoring is appropriate in patients at higher risk of toxicity. Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule. Note that a rise in alkaline phosphatase may reflect disease activity rather than drug toxicity. Similarly a low WCC may be a feature of the underlying disease e.g. SLE. If in doubt please contact the patient's specialist.

Section 4: Side Effects

Please list the most common side effects and management. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	The most common side effects are nausea, vomiting, diarrhoea and heartburn. These can be reduced by taking the drug with meals and an H2-blocker or proton pump inhibitor may also be helpful. Rashes, hepatitis and alopecia may also occur. The most serious side effect is bone marrow suppression. Chicken pox/shingles infection - stop and commence aciclovir.
Referral back to specialist	**Actions to be taken by patient's GP:** Azathioprine should be WITHELD if any of the following occur: Abnormal bruising or sore throat- Stop drug and check FBC WCC <3.5 $x10^9$/L Neutrophils <1.6 $x10^9$/L Platelets <100 $x10^9$/L Unexplained eosinophilia >0.5 $x10^9$/L Mean cell volume >105 f/l ALT and or AST >twice upper limit of reference range Unexplained reduction in albumin

	Renal impairment: Creatinine increase >30% over 12 months and/or unexplained reduction in calculated GFR: stop drug if acute change. If gradual may need dose reduction Rash or oral ulceration **Please repeat monitoring bloods in 1 week and if still low/high then discuss with the specialist team. Falling trends may also prompt discussion.**

Section 5: Drug Interactions

Please list clinically significant drug interactions (eMC link please click here)

Significant Drug Interactions	Allopurinol: azathioprine has increased toxicity. Therefore the azathioprine dose should be reduced to a quarter of the usual dose. Aminosalicylates: may increase the risk of leukopaenia when given with azathioprine. Warfarin: azathioprine reduces anticoagulant effect of warfarin. Co-trimoxazole and trimethoprim: can cause life threatening haematotoxicity when co-prescribed with azathioprine. ACE-inhibitors: increased risk of anaemia or leukopenia Febuxostat: avoidance of azathioprine advised by the manufacturer of febuxostat. Live vaccines (e.g. yellow fever vaccination): risk of generalised infections Pneumonia and flu vaccinations are recommended.
Reminder to ask patient about specific problems	Nil

Section 6: Contra-indications, Cautions and Special Recommendations

Please list

Cautions:

- Reduced TPMT activity (heterozygous state): may be associated with delayed haematotoxicity
- Sunscreens and protective covering should be encouraged to reduce sunlight exposure
- Localised or systemic infection
- Azathioprine is compatible throughout pregnancy and with breast feeding at ⩽2 mg/kg/day
- Patients should avoid contact with people who have active chickenpox or shingles and report any contact to their GP and hospital specialist. If immunosuppressed patients are exposed to chickenpox or shingles, they will need to be assessed for susceptibility and the need for aciclovir post exposure prophylaxis, see: UKHSA guidance: Guidelines on post-exposure prophylaxis (PEP) for varicella/shingles and the Green Book Chapter 34.

Contraindications:

- Absent TPMT (homozygous state): avoid, can be fatal.
- Very low TPMT activity
- Lesch-Nyhan syndrome

Section 7: Advice to the patient

Advice for prescribing clinician to inform patient

1. Discuss potential benefits and side-effects of treatment with the Specialist and/or GP.
2. Share any concerns they have in relation to their treatment.

3. To report any side-effects to the Specialist and/or GP (see individual drug fact sheet for specific information).
4. To ensure that the patient held record is presented at every consultation (in primary or secondary care).
5. To agree to and attend for the monitoring of therapy (including having blood tests carried out at agreed intervals) and assessment of outcomes, to assist health professionals to provide safe, appropriate treatment.
6. To inform GP/Specialist/pharmacist of all medicines (including OTC preparations) that they are currently taking.

Section 8: Responsibilities for Secondary Care

Core responsibilities

1. Confirm diagnosis and indication for drug treatment
2. Discuss potential benefits and side effects of treatment with patient
3. Carry out baseline monitoring requirements and initiate therapy. The GP will receive copies of the baseline blood test results.
4. The specialist will advise the GP of any dose adjustments required. The GP will then take over prescribing and blood test monitoring responsibilities.
5. An initial prescription will be provided by the specialist for 1 month.
6. Secondary care will advise on the appropriate monitoring blood tests as well as frequency.
7. Monitor the patient's response to therapy.
8. Decide when to stop therapy on safety grounds and inform the GP.
9. Secondary care will direct the GP to a copy of the concise drug information sheet and the shared care guidelines via the BNSSG Joint Formulary website.
10. Secondary care will supply the patient with a 'patient help record' and explain its role.
11. The dosage regimen should be clearly explained to the patient.
12. The patient should be asked to report side-effects (see individual drug fact sheet for specific information) and the GP should be informed if any side effects are reported to secondary care. Serious side effects should be reported to the MHRA via the yellow card scheme.

Other specific to drug

Nil

Section 9: Responsibilities for Primary Care

Core responsibilities

1. Take on shared care proposal from the specialist after the first month of treatment (including prescription and blood monitoring)
2. If shared prescribing is declined, an arrangement should be made with the initiating department to ensure patients are adequately supported. The GP practice and initiating department should also inform the interface pharmacists at the CCG, see contact details section below.
3. To ensure that all relevant staff and patients are aware of the shared care arrangements. Blood test results, dosage adjustments, should be recorded in the patient held record and GP medical record. Any dosage adjustments should also be recorded in computer-based prescribing systems.
4. The dosage regimen should be clearly explained to the patient.
5. Contact the specialist to discuss any significant changes in the blood test results or patient's condition e.g.; the medication becomes less effective.

6. Respond to dosage changes advised and prescribe appropriately. Receive copies of any blood test results carried out in secondary care for information and record in patient's record appropriately. 7. Monitor the patient for any side-effects to therapy and refer back to the Specialist should any serious side-effect occur. Side-effects / discontinuation of medication should be documented in the patient held record.
Other specific to drug
Nil

Section 10: Contact Details

Organisation	Contact	Contact details	Availability
University Hospitals Bristol and Weston	UHBW – Bristol Rheumatology Telephone Advice Line	Tel: 0117 3424881 Registrar bleep: 7021	**Mon – Thu 9am to 5pm** **Fri 9am to 1pm**
	UHBW – Weston Rheumatology Telephone Advice Line	Tel:01934 881075 Fax: 01934 647025 On Call registrar bleep: 279	**Mon – Fri 9am to 5pm**
	UHBW – Bristol Eye Hospital Ocular inflammation specialist nurses	Nurse Tel: 0117 342 1421 Secretary Tel: 0117 342 1400 0117 342 1401	Mon- Fri 9am to 5pm
	UHBW – Interstitial lung disease (ILD) team Specialist nurse	Nurse Tel: 0117 342 4101	Mon- Fri 9am to 5pm
North Bristol Trust, Southmead Hospital	Consultant secretary as per clinic letter OR Rheumatology Telephone Advice Line	Tel: 0117 4140600 Fax: 0117 4140570 Tel: 07894800989 On Call Tel: 07894800989 Sat/Sun 9am-noon (GP service for existing NBT rheum patients only)	**Mon – Fri 9am to 5pm**
	NBT ILD telephone advice line	Tel: 0117 414 7762	Mon-Fri 9am to 5pm
BNSSG CCG	Interface Pharmacists)	bnssg.formulary@nhs.net	**Mon-Fri 9am to 5pm**

Section 11: Document Details

Date prepared	August 2017 (updated to include ocular inflammation 26/10/2021 and ILD 11/11/21)
Prepared by	Collated and updated from previous guidelines by Dr Randa Alshakh on behalf of Bristol and Weston Rheumatology consultants. Dr Roy, Dr Webber (updated to include ocular inflammation 26/10/2021 completed by BNSSG Formulary Team) ILD indication added by ILD team 1/11/21. Change to information about PEP for varicella/shingles February 2023 added by BNSSG Formulary Team.
Date approved by JFG	November 2021
Date of review	April 2020
Document Identification: Version	V3.2

Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

This document has been sent to rheumatology consultants across Bristol and Weston for comment and approval. ILD indications and content approved by ILD teams at NBT and UHBW.

Section 13: References

Please list references

1. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, February 2017
2. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids, January 2016
3. BNF 73 (March –September 2017)