Shared Care Guideline

Azathioprine for dermatology conditions (Adults)

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs).
This guideline reinforces the basic premise that:
When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the "sharing of information with the individual GP and their mutual agreement to the transfer of care."
These are not rigid guidelines. On occasions, Consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Indications:	**Dosage and administration:**
Azathioprine is used in the management of psoriatic arthritis, atopic eczema (unlicensed), chronic contact dermatitis (unlicensed), immunobullous diseases (unlicensed), cutaneous lupus and other dermatological conditions.	The usual starting dose is 50mg – 100mg daily orally (if TPMT normal). This can be slowly increased, depending on tolerance, response and haematological tolerance, to a typical maintenance dose of 2–3mg/kg/day. When the therapeutic response is evident, this dose can maintained, although consideration can be given to reducing the maintenance dose to the lowest level that maintains the response. Patients with renal or hepatic insufficiency should be given the lowest effective dose. Azathioprine is taken as a single dose after food or with at least 200mls of liquid.

Additional Information

- Mercaptopurine is the active metabolite of azathioprine.
- Pneumovax® and annual flu vaccine is recommended
- Passive immunisation should be carried out in non-immune patients exposed to chickenpox or shingles, using Varicella Zoster Immunoglobulin.
- Patients should inform GP immediately about ulcerations of throat, fever, infections, bruising, bleeding or other signs of myelosuppression.

Monitoring requirements:

Before treatment:

- Full blood count (FBC) including platelets, urea and electrolyes (U&Es), creatinine and liver function tests (LFTs)
- Test for thiopurine methyl transferase (TPMT). If TPMT deficiency then other agents should be considered or therapy initiated with great caution.

During treatment:

- FBC, LFTs, U/Es and creatinine weekly for the first eight weeks, then monthly thereafter if stable
- If dose is increased, repeat FBC and LFTs after 2 weeks, and then return to monthly.
- Annual fasting lipids (HDL, Cholesterol, HDL/Cholesterol ratio)

Responsibility for monitoring rests with the GP once the patient is stabilised

Action to be taken if abnormal results/adverse effects:

- WBC< 3.5 x 10^9/l Check neutrophil count
- Neutrophils < 2.0 x 10^9/l Monitor weekly. If it falls below 1.5 x 10^9/l **STOP azathioprine** and

contact prescribing consultant.

- Platelets < 150 x 10^9/l Monitor weekly. If it drops below 100 x 10^9/l contact prescribing consultant
- 3 fold rise in ALT/AST Monitor weekly. If ALT continues to rise, contact prescribing consultant.
- If LFTs show a rapid and significant rise during the first weeks of treatment, **STOP AZATHIOPRINE** and contact the prescribing consultant urgently
- Rash Mild: drug can be continued at reduced dose if necessary.
  Severe: **STOP** azathioprine and contact prescribing consultant
- Oral ulceration Repeat FBC and act on results as above
  Mild: salt water mouth wash
  Moderate: Hydrocortisone Buccal Tablets (1 applied to affected area four times a day)
  Severe: Hydrocortisone Buccal Tablets and contact prescribing consultant
- MCV > 100fl Check B12, Folate and TSH and, if low, start appropriate supplements
- Abnormal bruising Repeat FBC and act on results as above
- Sore throat Repeat FBC and act on results as above

Please note that in addition to absolute values for haematological indices, a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Contraindications:

- TPMT deficiency (homozygous state). Avoid, can be fatal.
- Seriously impaired hepatic or bone marrow function
- Pancreatitis
- Severe infections
- Azathioprine should not be given to women who are pregnant, or likely to become pregnant without a careful assessment of risk versus benefit.
- Breastfeeding
- Hypersensitivity to azathioprine, mercaptopurine or any of the excipients in the SPC
- Live vaccines are contra-indicated in patients receiving azathioprine due to impaired immune response.

Drug interactions – see current BNF/SPC for the full list:

- Azathioprine activity is inhibited by allopurinol -avoid co-prescription where possible. If essential, contact consultant's team (via secretary)for advice on azathioprine dose reduction
- Azathioprine can inhibit the anticoagulant effect of warfarin.
- Avoid co-prescription of co-trimoxazole (sulfamethoxazole + trimethoprim) as increased risk of haematological toxicity. There is a possibility of haematological abnormalities with concomitant administration of captopril.
- Azathioprine should be administered with caution in patients receiving aminosalicylate derivatives eg olsalazine, mesalazine or sulfasalazine as these drugs can also inhibit TPMT.
- A diminished response to killed vaccines is likely.
- Penicillamine should be avoided where possible due to its myelosuppressive action
- Theoretical increased risk of myelosuppression with cimetidine and indometacin

Cautions:

- TPMT deficiency (heterozygous state). May be associated with delayed haematotoxicity including bone marrow toxicity. Lower doses of azathioprine can be used (max 1mg/kg/day)
- Renal or hepatic insufficiency may enhance the toxicity of azathioprine. The haematological response should be carefully monitored and doses at the lower end of the range should be used.
- Increased risk of skin cancers; avoid exposure to sunlight and UV light by using sunscreen and protective clothing.

Adverse Effects – see current BNF/SPC for full details:

Hypersensitivity reactions (incl. malaise, dizziness, vomiting, diarrhoea, fever, myalgia, arthralgia, rash, hypotension & interstitial nephritis) - requires immediate withdrawal

Depression of bone marrow function, leucopenia, thrombocytopenia, anaemia and other blood disorders.

Alopecia and increased risk of infections and colitis for patients also receiving corticosteroids.

Neoplasms, including non-Hodgkin's Lymphomas, skin cancers, sarcomas and uterine cervical cancer.

Nausea, hepatic impairment

Specialist responsibilities:

1. Confirm the diagnosis of a dermatological condition and discuss with the patient the benefits and side effects of treatment with azathioprine.
2. Ensure baseline monitoring of full blood count, biochemical profile and TPMT, also subsequent monitoring until dose is stabilised.
3. Check for interactions with any concomitant medication prior to initiating azathioprine.
4. Review the patient after six weeks and if the patient is tolerating and benefiting from azathioprine at this first visit, a written request should be made to the GP to continue prescribing the medication and to continue the monitoring.
5. Prescribe the initial 3 months of azathioprine during the trial period and discontinue if no response or significant adverse effect.
6. Regularly review the patient to monitor efficacy of the treatment and the ability to tolerate it, and consider whether continuation of treatment is appropriate.
7. Communicate promptly with the GP when treatment is changed and each time the patient is seen.
8. Undertake any necessary monitoring at review appointments.
9. Ensure clear backup arrangements exist for GPs for advice and support.
10. Report serious adverse events via the yellow card scheme at https://yellowcard.mhra.gov.uk/

GP's responsibilities:

1. Provide the patient with monthly repeat prescriptions of medication once the specialist has recommended continuation therapy.
2. Continue monitoring as outlined on the first page and document in patient record
3. Ensure any newly prescribed medications do not interact with azathioprine or other concomitant medication.
4. Report any adverse effects to the consultant and via yellow card scheme at https://yellowcard.mhra.gov.uk/
5. Refer back to the consultant if the patient's condition deteriorates or if there is a change in the patient's status.
6. Contact the consultant if they do not agree with the treatment recommendation, or if there is a perceived problem with compliance or concordance, or if they have any questions about the management plan.

Patient responsibilities:

- Read the written information provided about the drug and have a clear understanding of the risks / benefits of oral azathioprine treatment.
- Attend for blood tests.
- Allow at least 48 hours for a prescription from the GP to be generated (once the GP has agreed to take on prescribing)
- Report any adverse effects to their GP and/or specialist whilst treated with azathioprine
- Limit alcohol to national safe weekly limits

Secondary care review: Patients will be reviewed six weeks after starting azathioprine and thereafter at a frequency determined according to clinical need by the consultant, or if requested to review by the GP.

Availability: 25mg tablet: 28 = £2.63 50mg tablet: 56 = £2.79 *Prices from March 2016 Drug Tariff*		
Back up advice and support: Dr Farrar Dr Hashim Dr BB Tan		**Telephone:** 0151 482 7782 0151 482 7778 0151 482 7778
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