

ADULT SHARED CARE GUIDELINES

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 the hospital to the 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.

Drug Name: **AZATHIOPRINE TABLETS – Idiopathic pulmonary fibrosis**

Indications:

Azathioprine has immunosuppressive and steroid-sparing properties. It is used locally for idiopathic pulmonary fibrosis (IPF), however due to the interim results of the PANTHER-IPF trial, patients newly diagnosed with IPF should **NOT** be started on azathioprine. For patients currently taking azathioprine for IPF, consideration should be given to stopping treatment if there are any signs of clinical deterioration.

Dosage and administration:

The usual starting dose is 50mg daily for 2 weeks. This should be gradually increased by 25mg increments every 7-14 days, to a typical maintenance dose of 2-3mg/kg/day (maximum of 150mg/day), depending on response and haematological tolerance, When the therapeutic response is evident, this dose can be 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.

Additional Information

- Mercaptopurine is the active metabolite of azathioprine.
- Pneumovac and annual flu vaccine are recommended
- Passive immunisation should be carried out in non-immune patients exposed to chickenpox or shingles, using Varicella Zoster vaccination

Monitoring requirements:

Before treatment:

- Full blood count (FBC) including platelets, urea and electrolytes (U&Es) and liver function tests (LFTs) (hospital)
- Test for thiopurine methyl transferase (TPMT), as a deficiency increases the risk of myelosuppression

During treatment:

- FBC weekly for the first four weeks, then monthly for 3 months thereafter if stable. Once fully stabilised, monitoring can be every 3 months
- LFTs and U&Es weekly for the first four weeks, then monthly thereafter if stable.
- If dose is increased, repeat FBC and LFTs after 2 weeks and 4 weeks, and then return to monthly.

Responsibility for monitoring, once stable, rests with the GP

Action to be taken if abnormal results/adverse effects:

- WBC < 4 x 10⁹/l Check neutrophil count
- Neutrophils < 2.0 x 10⁹/l Monitor weekly. If it falls below 1.5 x 10⁹/l STOP DRUG and contact respiratory consultant.
- Platelets < 150 x 10⁹/l Monitor weekly. If drop below 100 contact hospital
- 3 fold rise in ALT/AST Monitor weekly. If ALT continues to rise, contact hospital
- Rash Mild, drug can be continued at reduced dose if necessary. Severe – STOP DRUG and contact hospital
- Oral ulceration Mild –salt water mouth wash Moderate – Corlan pellets (1 applied to affected area qds) and STOP DRUG for at least one week and if resolved, restart. Consider reduced dose. Severe – STOP DRUG, Corlan pellets and contact hospital
- MCV > 105fl Check B12 and Folate 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
- Drug-related acute shortness of breath STOP DRUG, contact hospital and if severe, refer to AMAU
- Sudden cough If persistent, organise CXR and if abnormal, contact help line

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:

- Azathioprine should not be given to women who are pregnant, or likely to become pregnant without a careful assessment of risk versus benefit.
- Live vaccines are contra-indicated in patients receiving azathioprine on theoretical grounds.

Drug interactions:

- Azathioprine activity is inhibited by allopurinol. Avoid co-prescription. If this is not possible, only give one quarter of the usual dose of azathioprine
- Azathioprine can inhibit the anticoagulant effect of warfarin.
- Avoid co-prescription of drugs that may have a myelosuppressive effect, such as penicillamine, co-trimoxazole, captopril, cimetidine or indometacin as serious haematological abnormalities may result.
- For patients with an inherited deficiency of the TPMT enzyme, lower doses of azathioprine should be used and it should also be administered with caution in patients receiving aminosalicylate derivatives e.g. olsalazine, mesalazine or sulfasalazine as these drugs inhibit TPMT.
- A diminished response to killed vaccines is likely.

Cautions:

- 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:

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

Viral, fungal and bacterial infections.

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

Nausea, pancreatitis, altered liver function, alopecia, hypersensitivity reactions, SJS, toxic epidermal necrolysis

Specialist responsibilities:

1. Do not commence azathioprine in patients newly diagnosed with IPF
2. For patients already prescribed azathioprine consider stopping azathioprine if there are any signs of clinical deterioration. For patients that are stable on triple therapy (azathioprine, prednisolone, acetylcysteine) the decision to withdraw azathioprine should be made on a case-by-case basis – the threshold for withdrawing in elderly patients should be low.
3. Ensure existing patients have a shared care booklet and enter the blood results into the booklet when these are checked during a clinic visit.
4. Regularly review the patient to monitor efficacy of the treatment and the ability to tolerate it, and consider whether continuation of treatment is appropriate.
5. Communicate promptly with the GP when treatment is changed and each time the patient is seen.
6. Undertake any necessary monitoring at review appointments.
7. Ensure clear backup arrangements exist for GPs for advice and support.
8. Report serious adverse events to the Committee on Human Medicines (CHM).

GP responsibilities:

1. Provide the patient with monthly repeat prescriptions of medication once the specialist has recommended continuation therapy. The patient should allow at least 48 hours for the prescription from the GP to be generated once they have agreed to take on prescribing.
2. Continue monitoring as outlined on the first page and document the results in the shared care booklet.
3. Report any adverse effects to the consultant.
4. Refer back to the consultant if the patient's condition deteriorates or if there is a change in the patient's status.
5. 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:

Report any adverse effects, concerns or lack of understanding of the treatment to the GP or specialist.

Attend for blood tests and take the monitoring booklet to all appointments.

Secondary care review: Patients will be reviewed one month after starting azathioprine and thereafter at a frequency determined by the clinical need in the consultant clinic.

Back up advice and support:	Specialist	Telephone/Fax	Email address:
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