SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR AZATHIOPRINE TABLETS (RENAL ADULT)

N.B. This document should be read in conjunction with the current Summary of Product Characteristics (SmPC).

Patient safety is paramount. The prescriber who prescribes the medicine legally assumes clinical responsibility for the drug and the consequences of its use.

GENERIC AND BRAND NAME (formulations and strength)

Name: Azathioprine

Formulation: Tablets

Strength: 25mg, 50mg

STATUS OF MEDICINE

Licence status: Licensed (indicated in combination with other immunosuppressive agents for the prophylaxis of transplant rejection in patients receiving allogenic kidney/pancreas transplants).

Formulary status: Formulary

Black triangle medicine: NO

Risk minimisation materials: NO

CONDITION(S) TO BE TREATED

Immunosuppressive regimens as an adjunct to immunosuppressive agents that form the mainstay of treatment (basic immunosuppression).

In combination with other immunosuppressive agents for the prophylaxis of transplant rejection in patients receiving allogenic kidney or pancreas transplants.

Systemic Lupus Erythematous (SLE).

Anti-neutrophil cytoplasmic antibodies (ANCA) – associated vasculitis.

Sarcoidosis.

TYPICAL DOSAGE REGIME	
Licensed dose	See Renal Specialist for advice
Route of administration	Oral
Recommended starting dose	See Renal Specialist for advice
Titration dose/increment	See Renal Specialist for advice
Maximum dose	See Renal Specialist for advice
Situations requiring dose adjustment	See Renal Specialist for advice
Duration of treatment	See Renal Specialist for advice

RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

1. **Baseline:**
   Full Blood Count (FBC)
   Liver Function Tests (LFT), U&Es and creatinine.
2. Copy of results to be sent to GP.
3. Initiation of therapy and recommendations for dose increments. This will be controlled by the Renal Unit.
4. The Renal Unit has primary responsibility for monitoring clinical response to treatment according to the schedule below:
   - FBC and LFTs (including ALT and Alk Phos) weekly for six weeks and then fortnightly until dose stable for six weeks. Thereafter, monthly.
   - U&Es and creatinine every six months.
   - Patients should be asked about the presence of sore throat, abnormal bruising or bleeding at each visit.

RESPONSIBILITY OF PRIMARY CARE

To preserve vital venous access, monitoring will be done by the renal service at ARI unless otherwise notified or the patient develops an intercurrent illness which would require bloods to be taken in primary care.

A Practice agreeing to prescribe Azathioprine should:

1. Prescribe medication under the guidance of the Renal Consultant.
2. Ensure the GP is aware that the drug can cause:
   - Bone marrow suppression
   - Leucopenia
   - Increased risk of malignancy
   - Lymphomas and skin cancer
   - Patients should be asked about the presence of sore throat, abnormal bruising or bleeding at each visit.

3. Ensure that the relevant monitoring requirements have been undertaken at the correct frequency.
4. Ensure when the patient has an intercurrent illness FBC, U+E and LFTs are done and make sure abnormal results are acted upon promptly.
5. Only continue to prescribe medication if it is being satisfactorily monitored.
6. Contact the consultant in the event of a drug reaction, monitoring abnormality, or if you are concerned in any way regarding the current treatment regime.
7. Be alert for any of the known adverse reactions.

CARE WHICH IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN

1. Prescribe medication under guidance of consultant.
2. Check before prescribing each instalment of medication that the monitoring is up to date and that results are within the normal range.
3. Ensure no interacting medications are prescribed in primary care.
4. Monitor for concordance with therapy.
5. Report any adverse events to consultant and the MHRA using the Yellow Card System.
6. If an intercurrent illness occurs, when writing laboratory request forms always include details of the patient' medication.
7. If bloods are taken due to intercurrent illness, ensure they are monitored and contact hospital consultant to advise if results are out with range.
8. A single dose of pneumococcal polysaccharide vaccine and annual influenza vaccine should be given.
9. Varicella Zoster Immunoglobulin should be given to non-immune individuals if exposed to shingles or chickenpox.

N.B. In addition to absolute values for haematological or biochemical indices a rapid change or a consistent upward/downward trend in any value should prompt caution and extra vigilance.

N.B. If something unexpected occurs contact Renal Unit, On Call Registrar or Consultant. Notify the consultant if the drug is stopped.

RESPONSIBILITY OF OTHER HEALTHCARE PROFESSIONALS

N/A

RESPONSIBILITY OF THE PATIENT

- Take medication regularly as directed by the specialist/doctor.
- Attend hospital and GP clinic appointments as requested by specialist/GP practice. Failure to attend appointments may result in medication being reviewed/stopped.
- Report any adverse effects/illness to the specialist/GP and present rapidly to specialist/GP should their condition significantly worsen.
- To minimise the risk of skin cancer, exposure to sunlight and Ultra Violet light should be limited by wearing protective clothing and using sunscreen with a high protection factor.

PRESCRIBING INFORMATION

For specific product information consult the current summary of product characteristics (http://emc.medicines.org.uk/), the BNF/BNF for Children (https://www.medicinescomplete.com/mc/index.htm)

CONTRAINDICATIONS

- Hypersensitivity to azathioprine, 6-mercaptopurine (metabolite of azathioprine) or to any excipients listed in the SmPC.
- Severe infections.
- Seriously impaired hepatic or bone marrow.
- Pancreatitis.
- Any live vaccine, especially BCG, smallpox, yellow fever.

PREGNANCY

Discuss with consultant. Azathioprine should not be given to patients who are pregnant or likely to become pregnant without careful assessment of risk versus benefit. Transplant patients and those with SLE should not stop azathioprine on becoming pregnant.

BREAST-FEEDING

Not recommended. Discuss with Aberdeen Maternity Hospital.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

- Nausea
- Diarrhoea
- Vomiting
- Anorexia
- Abdominal discomfort
- Headaches
- Mutagenicity and carcinogenicity increased risk of developing lymphoproliferative disorders and other malignancies, notably skin cancers (melanoma and non-melanoma) sarcomas (Kaposi's and non-Kaposi's) and uterine cervical cancer in situ
- Macrophage activation syndrome
- Patients with NUDT15 variant gene are at increased risk for severe 6-mercaptopurine toxicity such as early leucopenia and alopecia, from conventional doses of thiopurine therapy.

Abnormal Monitoring Results	Action To Be Taken
• **WBC** <4 X 10^9/L	Discuss with Renal Unit/Registrar on call or Consultant
• **Platelets** <150x10^9/L	Discuss with Renal Unit/Registrar on call or Consultant
• **>2-fold rise in ALT or Alk Phos.** (from upper limit of reference range) • Other significantly deranged LFT results	Discuss with Renal Unit/Registrar on call or Consultant
• MCV>105fl	Discuss with Renal Unit/Registrar on call or Consultant
• Abnormal bruising, sore throat, rash, oral ulceration	Check FBC. Discuss with Renal Unit/Registrar on call or Consultant
• Unexplained fever	Discuss with Renal Unit/Registrar on call or Consultant
• Suspicion of or newly diagnosed malignancies	Discuss with Renal Unit/Registrar on call or Consultant

COMMON DRUG INTERACTIONS (for a full list see SmPC)

- Live vaccines should be avoided in patients taking azathioprine.
- Do not prescribe with **allopurinol** (unless discussed/advised by a Renal Consultant).
- Inhibition of the anticoagulant effect of warfarin, when administered with azathioprine has been reported. Monitor concurrent use.
- Special care with neuromuscular acting agents like tubocurarine or succinylcholine has to be taken inform anaesthetist before surgery as can enhance the neuromuscular block.
- Increased risk of haematological toxicity with co-trimoxazole and trimethoprim.

ADVERSE DRUG REPORTING

If an adverse reaction should occur, inform relevant medical practitioner as soon as possible.

Report to the MHRA using the Yellow Card System https://yellowcard.mhra.gov.uk/

REFERENCES

https://www.medicines.org.uk/emc/product/9945/smpc

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

In the event of concern being raised, the primary care practitioner should contact the referring consultant via the hospital switchboard, via their secretary, by e-mail or letter, whichever is more appropriate. If the concern is urgent, and out of hours advice is required, the on call Renal Registrar may be contacted via switchboard.

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