RENAL TRANSPLANT PATIENTS ONLY

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

Clinicians must ensure they are referring to the correct SCA for specialty/situation.

This SCA is for RENAL TRANSPLANT PATIENTS ONLY. Some content and recommendations may differ from the SCA for patients receiving this treatment for conditions other than renal transplant. This is due to the specialist service clinical recommendations and monitoring requirements for managing renal transplant patients.

Note: 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 NAME (formulations and strength)

Name: Azathioprine

Formulation: Tablets

Strength: 25mg, 50mg

STATUS OF MEDICINE

Licence status: Licensed, indicated in combination with corticosteroids and/or other immunosuppressive agents and procedures, indicated to enhance the survival of organ transplants such as renal transplants.

Formulary status: Formulary

Black triangle medicine: No

Risk minimisation materials (RMM): No

CONDITION(S) TO BE TREATED UNDER THIS SCA

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

RENAL TRANSPLANT: In combination with corticosteroids and/or other immunosuppressive agents and procedures, is indicated to enhance the survival of organ transplants such as renal transplants. It also reduces the corticosteroid requirements of renal transplant recipients.

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

TYPICAL DOSAGE REGIME	
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

- Baseline blood tests:
  - Full Blood Count (FBC), Liver Function Tests (LFTs), and Urea and Electrolytes (U&Es)
  - Thiopurine S-methyltransferase (TPMT). Azathioprine induced myelosuppression is linked to thiopurine methyl-transferase (TPMT) deficiency therefore the consultant will test for this prior to initiation of treatment
- Copy of baseline results to be shared with Primary Care.
- Request for initiation of therapy and recommendations for dose increments to Primary Care.
- Monitoring clinical response to treatment and advising on final dose required for the patient.
- Ongoing Blood monitoring - the Renal service has the primary responsibility for **RENAL TRANSPLANT** patients blood monitoring and review of results.

  This will follow a normal schedule, at initiation post transplant of:
  - full blood counts, U+E, Creatinine and LFTs three times a week for first two weeks after discharge,
  - weekly until week 8,
  - alternate weeks until week 12 to 16 (depending on graft function),
  - monthly until end of first six months,
  - two to three monthly until end of first year;
  - then three to six monthly during year two and beyond if stable with satisfactory graft function.

    For individuals transferred from an alternative immunosuppressant monitoring would begin at alternate weeks for 4 weeks, then monthly following the schedule above from this point.

    If any individual monitoring is to be performed out with this schedule the renal service should advise primary care accordingly, this is necessary to ensure compliance with monitoring schedules prior to prescribing.

- Patients should be asked about the presence of sore throat, rash or abnormal bruising at each visit.
- Pneumococcal polysaccharide vaccine (PPV), COVID-19 vaccine and annual influenza vaccine should be given as per Joint Committee of Vaccination and Immunisation (JCVI)/The Green Book recommendations. Shingles vaccine should be given to those individuals who are severely immunocompromised, or anticipating immunosuppressive therapy, and eligible in line with JCVI/The Green Book recommendations and Scottish Government vaccination programme. Patients should be referred by specialist services to receive these vaccines in accordance with local protocol.
- Provide counselling, as appropriate, regarding pregnancy and breastfeeding.

RESPONSIBILITY OF PRIMARY CARE/PRESCRIBING CLINICIAN

To preserve vital venous access, blood monitoring for RENAL TRANSPLANT patients will be done by the renal specialist service 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 for **RENAL TRANSPLANT** should:

- Prescribe medication under the guidance of the Renal Consultant. Checking before prescribing each instalment of medication that the monitoring is up to date and that results are within a satisfactory range.
- Ensure that the relevant monitoring requirements have been undertaken at the correct frequency (see information under responsibility of Acute care /specialist service).
- Only continue to prescribe medication if it is being satisfactorily monitored. Noting medication should not be stopped without first discussing with Renal Consultant, specialist service.
- Ensure the GP/prescriber 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.
- Ensure when the patient has an inter-current illness FBC, U+Es and LFTs are done, results reviewed, and abnormal results are acted upon promptly. If an intercurrent illness occurs, when completing laboratory request always include details of the patient's medication.
- If bloods are taken due to intercurrent illness, ensure they are monitored and contact Renal Consultant to advise if results are unsatisfactory/out with range (see Abnormal Monitoring section).
- Contact the Renal Consultant in the event of a drug reaction, monitoring abnormality, or if you are concerned in any way regarding the current treatment regime.
- Be alert for any of the known adverse reactions.
- Ensure no interacting medications are prescribed in primary care.
- Monitor for concordance with therapy.
- The patient should be encouraged to ensure blood tests are undertaken at the correct intervals.
- It is responsibility of primary care to ensure that the medication is recorded on the patient's clinical medication record. This will facilitate central searches for vaccinations in order to ensure patients receiving immunosuppressants are called by the HSCP teams for required vaccinations, e.g. influenza and covid programmes.
- Report any adverse events to consultant and the MHRA using the Yellow Card System.
- Post exposure prophylaxis (PEP) should be considered in non-immune individuals if exposed to shingles or chickenpox as per The Green Book.
- If something unexpected occurs contact on call renal registrar or consultant.

MONITORING

To preserve vital venous access, blood monitoring for **RENAL TRANSPLANT** patients will be done by the renal specialist service unless otherwise notified OR the patient develops an intercurrent illness which would require bloods to be taken in primary care.

Results should be reviewed and action taken as per Abnormal Monitoring Section below.

For **RENAL TRANSPLANT** the renal specialist service will review results, for monitoring they have undertaken.

All results should also be reviewed by Primary Care routinely prior to prescribing, and if additional monitoring due to an intercurrent illness.

Note: 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.

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.
- The patient should ensure all blood tests are undertaken at the correct intervals.
- Report any adverse effects/illness to the specialist/GP and present rapidly to specialist/GP should their condition significantly worsen.
- To minimize 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 (minimum SPF30).

PRESCRIBING INFORMATION

For specific product information consult the current Summary of Product Characteristics (SmPC) (http://emc.medicines.org.uk/), the BNF/BNF for Children BNF (British National Formulary) | NICE

CONTRAINDICATIONS

For full details please refer to the current Summary of Product Characteristics (SPC) available at www.medicines.org.uk.

- Hypersensitivity to azathioprine, 6-mercaptopurine (metabolite of azathioprine) or to any excipients listed in the SmPC.
- Severe Infections – discuss with specialist service/see also common side effects.
- Seriously impaired hepatic or bone marrow function.
- Pancreatitis.
- It is recommended patients do not receive any live vaccines, especially BCG, smallpox, yellow fever until at least 3 months after the end of azathioprine treatment.

PREGNANCY RENAL TRANSPLANT

Azathioprine should not be given to patients who are pregnant or likely to become pregnant without careful assessment of risk versus benefit.

Transplant patients should not stop azathioprine on becoming pregnant.

Discuss with Renal Consultant.

BREAST-FEEDING RENAL TRANSPLANT

Not recommended, discuss with Renal Consultant.

COMMON SIDE EFFECTS

Infections and infestations	Viral, fungal, and bacterial infections in transplant patient receiving azathioprine in combination with other immunosuppressants. Increased sensitivity to infection in patients with inflammatory bowel disease. In the event of infection please do not discontinue immunosuppression without discussion with the renal consultant. It can be considered appropriate to continue these drugs in patients with minor viral and bacterial infections.
Neoplasms benign and malignant (including cysts and polyps)	In up to 2.8% of renal homograft patients (in order of falling frequency) squamous cell skin carcinoma, non-Hodgkin's lymphoma, cervical cancer, Kaposi's sarcoma, vulval cancer.
Blood and lymphatic disorders	Bone marrow depression, leucopenia, anaemia and thrombocytopenia.
Gastro-intestinal disorders	Nausea and anorexia with isolated reports of vomiting, pancreatitis.
Hepato-biliary disorders	Hepatic impairment, various pathologies including cholestasis, destructive cholangitis, peliosis hepatitis, perisinusoidal fibrosis and nodular regenerative hyperplasia in 3 to 10 % with renal homograft.
Macrophage activation syndrome	
Patients with NUDT 15 variant gene are 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 <150 x 10^9/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

- Live vaccines - should be avoided in patients taking azathioprine.
- Co-trimoxazole/trimethoprim - increased risk of haematological toxicity.
- Allopurinol - do not prescribe (unless discussed/advised by a Renal Consultant).
- Warfarin - monitor concurrent use. Inhibition of the anticoagulant effect of warfarin, when administered with azathioprine has been reported.
- Surgery - Special care with neuromuscular blocking agents (e.g. rocuronium) anaesthetist to consider prior surgery.

This information is not intended to be a complete list of interactions. For further information consider appropriate reference sources such as SmPC/Vision system.

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

Azathioprine 25mg Film-Coated Tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

In the event of a concern being raised, the primary care practitioner should contact the Renal 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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