SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR AZATHIOPRINE TABLETS (ADULTS ONLY – NON-RENAL PATIENTS)

NHS Grampian

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 AND BRAND 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). Used within rheumatology, gastroenterology and dermatology (possible licensed and off-label indications) specialist services.

Formulary status: Formulary – available for restricted use under specialist supervision.

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):

- To enhance the survival of organ transplants, e.g. liver transplant
- Moderate to severe inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis)
- Severe active rheumatoid arthritis
- Systemic lupus erythematosus
- Dermatomyositis and polymyositis
- Auto-immune chronic active hepatitis
- Pemphigus vulgaris
- Polyarteritis nodosa
- Auto-immune haemolytic anaemia
- Chronic refractory idiopathic thrombocytopenic purpura.

TYPICAL DOSAGE REGIME	
Licensed dose	See Specialist service/SmPC for advice – variable according to condition being treated
Route of administration	Oral
Recommended starting dose	See Specialist service for advice – variable according to condition being treated
Titration dose/increment	See Specialist service for advice
Maximum dose	See Specialist service for advice
Situations requiring dose adjustment	See Specialist service for advice and Monitoring Schedule for DMARDs
Duration of treatment	See Specialist service for advice

RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

- Baseline:
  - Full Blood Count (FBC)
  - Liver Function Tests (LFTs), U&Es, creatinine thiopurine S-methyltransferase (TPMT) and additional tests, e.g. Hep B core antibody, Hepatitis C, HIV and EBV as indicated, dependant on condition being treated.
- Copy of baseline results to be shared with primary care.
- Initiation of therapy and recommendations for dose increments. This should remain under the control of the specialist service.
- A single dose of pneumococcal polysaccharide vaccine and annual influenza vaccine should be given, patients should be referred to receive these vaccines in accordance with local protocol.

RESPONSIBILITY OF PRIMARY CARE

A Practice agreeing to prescribe Azathioprine should:

- Prescribe medication under the guidance of the Consultant from the relevant specialist service.
- The General Practitioner (GP) has primary responsibility for monitoring according to the Monitoring Schedule for DMARDs
- 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.
- Ensure that the relevant monitoring requirements have been undertaken at the correct frequency.

- Ensure when the patient has an inter-current illness FBC, U+Es and LFTs are done and abnormal results are acted upon promptly.
- Only continue to prescribe medication if it is being satisfactorily monitored.
- 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.
- Be alert for any of the known adverse reactions.
- 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 annual vaccinations in order to ensure patients receiving DMARDs are called yearly by the HSCP teams for required vaccinations.

CARE WHICH IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN

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

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.

Note: If something unexpected occurs contact on call registrar or Consultant for the appropriate speciality. Notify the consultant if the drug is stopped.

MONITORING

Refer to the NHSG Guidelines For The Monitoring of Disease Modifying Anti-Rheumatic Drugs (DMARDs) For Healthcare Professionals. Results should be reviewed and action taken as per monitoring guidance.

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.
- The patient should ensure all blood tests are undertaken at the correct intervals.

PRESCRIBING INFORMATION

For specific product information consult the current summary of product characteristics (http://emc.medicines.org.uk/), the BNF/BNF for Children Digital Medicines Information Suite | MedicinesComplete

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 vaccines; especially BCG, smallpox, yellow fever.

PREGNANCY

Azathioprine should not be given to patients who are pregnant or likely to become pregnant without careful assessment of risk versus benefit. Should pregnancy occur during treatment this should be discussed with this with the relevant specialist service as soon as possible.

BREAST-FEEDING

Further discussion is required with the specialist service.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

- Nausea
- Diarrhoea
- Vomiting
- Anorexia
- Abdominal discomfort
- Headaches
- Pancreatitis
- 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.

  Action abnormal monitoring results are per NHSG Disease Modifying Anti-Rheumatic Drugs (DMARDs) Monitoring Guidance.

  The specialist service should be contacted if there are any patient specific issues or concerns regarding side effects or abnormal results.

COMMON DRUG INTERACTIONS (for a full list see SmPC)

- Live vaccines should be avoided in patients taking azathioprine.
- Inhibition of the anticoagulant effect of warfarin, when administered with azathioprine has been reported. Monitor concurrent use.
- Increased risk of haematological toxicity with co-trimoxazole and trimethoprim.
- Allopurinol should not be co-prescribed with azathioprine unless under the specific direction of specialist service.

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 referring consultant for the appropriate specialist service via the hospital switchboard, via their secretary, by email or letter, whichever is more appropriate. If the concern is urgent, and out of hours advice is required, the on call Registrar for the speciality may be contacted via the switchboard.

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