Azathioprine in various conditions

Licensed Indication and key points

This guideline covers its use in the following areas:

Organ transplantation **Severe 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** **Ulcerative colitis and Crohn's disease (unlicensed)** **Inflammatory bowel disease**

- **Azathioprine is converted in the body to mercaptopurine**.
- **This is an anti-metabolite interfering with nucleic acid synthesis. It metabolised by the enzyme thiopurine methyltransferase (TPMT). Patients with intermediate or low TPMT activity and are at greater risk of adverse drug reactions on standard doses and are at risk of suffering life-threatening complications even when treated with low doses of azathioprine. TPMT activity is usually measured before a patient is prescribed azathioprine.**
- **Patients on azathioprine should be advised to wear protective clothing and use sunscreen with a high protection factor.**
- **Live vaccines should be AVOIDED**

Initiation and maintenance

Oral:

Azathioprine is administered orally and is available as 25mg and 50mg tablets taken with or after food and the dose can be divided if preferred

Dose:

- **Starting dose usually 0.5 to 1.5 mg/kg/day increased (after 4 to 6 weeks) to 2 to 3mg/kg.**
- **Organ Transplant: starting and maintenance dosage in adult renal transplant recipients 1.5 mg/kg daily taken orally and rounded to nearest 25 mg.**
- **Inflammatory bowel disease: The usual dose is between 2 to 2.5 mg/kg/day. The maximum dose differs between individuals**
- **Inflammatory arthritis, connective tissue disease and vasculitis: 1.5 to 2.5 mg/kg daily in divided doses**

Monitoring

MONITORING	RESPONSIBILITY	CONDITIONS	TESTS
Pre-treatment	Hospital team	All	• FBC, U&Es, LFTs, TPMT phenotype • Varicella Zoster **Results to be known before drug is commenced Patients to be counselled to report symptoms of infection promptly- written information should be provided. Patients should have baseline thiopurine methyltransferase (TPMT) status assessed**
Initiation to stabilisation	Hospital team/GP	All	• FBC, LFT **At initiation and after any increase in dose - Every week for 2 weeks until stabilised for 6 weeks**
Ongoing	GP	All	• FBC, LFT, U&Es **3 monthly**

Criteria for managing events & symptoms occurring during Azathioprine therapy in primary care

LABORATORY EVENTS	VALUES	ACTION
MCV	Increased > 105 fL	**Seek specialist advice**. Check TFT, B12 and folate, Monitor LFTs as could be dose-related.
WBC	< 3.5 x 109/L	**Seek specialist advice**, repeat FBC in 1 or 2 weeks.
Neutrophils	< 1.6 x 10^9/l – consider stopping drug 1.6-2 x 10^9/l – check trend	
Platelets	< 140x 10^9/l - consider stopping drug	
Haemoglobin	<80g/dL - consider stopping drug 80-100g/dL – check trend	
Significant deterioration in renal function	Creatinine increase >30% over 12 months or calculated GFR <60ml/min	**Seek specialist advice.** Caution dose reduction advised in renal impairment
Elevation in liver enzymes (AST, ALT) or falling albumin	>2x upper limit of normal (ULN) - consider dose adjustment; >3x ULN - consider stopping drug Albumin <30 g/l - please review patient for other medical problems	**Seek specialist advice.**

SYMPTOMS	MANAGEMENT
Rash , oral ulceration, stomatitis	**Stop azathioprine** , repeat FBC immediately and discuss with specialist
Cough, dyspnoea infection, fever, rigors	
Abnormal bruising or bleeding or severe or persistent sore throat	
Abdominal pain suggestive of pancreatitis, jaundice,	
Nausea, vomiting and diarrhoea	Withdrawal of drug may be necessary if persistent
Hair loss, pneumonitis	Rare but stop and discuss with specialist

Drug interactions, contraindications and precautions

See BNF and manufacturer's SPC Home - electronic Medicines Compendium (eMC) for up-to-date advice

Prescribing Responsibilities

- Refer to principles of shared care document

Contact details

Department / Specialist	Contact Telephone Number
Hospital switchboard – ask for specialist or On-Call specialist (rheumatologist/dermatologist/gastroenterologist) out-of-hours	01268 524900
Rheumatology	01268 598461
Email contact for shared care queries ONLY: RheumatologyOsteoporosisPOD@btuh.nhs.uk (48 hours response)	
Dermatology	01268 524900 ext 8250 or 3729
Gastroenterology	01268 524900 ext 3970 or 3987

Local Enhanced Services for Shared Care Monitoring

Level 1: The prescribing of this medication only.
Level 2: The prescribing and monitoring of this medication and disease

Document Control	
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Shared Care Guidelines are also available electronically via: https://basildonandbrentwoodccg.nhs.uk/your-health/medicines-management	
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