Prescribing Framework for Azathioprine for Immunosuppression

Patients Name:…… Unit Number: ……

Patients Address:……(Use addressograph sticker)

G.P's Name:……..

Communication

We agree to treat this patient within this Prescribing Framework

Specialist Prescriber's Name…… Prof Reg. No. ……

Specialist Prescriber's Signature…… Date:……..

Where prescriber is <u>not</u> a consultant:

Consultant's Name: …… GMC No ……..

Consultant's Signature ……... ……. Date:……

GP's Signature:…… Date:……..

GP's Name (if different from listed above)……..

The front page of this form should be completed by the specialist and the form sent to the patient's general practitioner.
The patient's GP should sign and **<u>send back to specialist</u>**, to confirm agreement to enter into shared care arrangement. If the General Practitioner is **<u>unwilling</u>** to accept prescribing responsibility for the above patient the specialist should be informed within two weeks of receipt of this framework and specialist's letter.

Full copy of framework can also be found at : http://www.hey.nhs.uk/amber.htm

1. Background

These guidelines aim to provide a framework for the prescribing of azathioprine by GPs and to set out the associated responsibilities of GPs and hospital specialists who enter into the shared care arrangements.

For use in Inflammatory bowel disease please see specific Shared Care Frameworks

http://www.hey.nhs.uk/userfiles/file/prescribingCommittee/RedAmber/Azathioprine6Mercapturine.pdf

This document should be read in conjunction with the guidance "Responsibility for prescribing between Primary & Secondary/Tertiary Care" https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

2. Indication

Immune mediated disorders including moderate to severe rheumatoid arthritis, systemic lupus erythematosus; severe refractory eczema; dermatomyositis and polymyositis; auto-immune hepatitis; polyarteritis nodosa; refractory warm auto-immune haemolytic anaemia;chronic refractory idiopathic thrombocytopenic purpura; renal transplantation; immune mediated neurological disorders including myasthenia gravis, neuromyelitis optica, cranial vasculitis and immune medicated neuropathies.

Specific information will be provided by the specialist on the indication for immunosuppression with azathioprine.

3. Dose

Blood sample to screen for TPMT deficiency will be taken by the specialist, prior to commencing treatment.

Usual starting dose is 50mg daily for 1 month, then 100mg daily for second month.
Usual maintenance dose is 1.5 to 2.5 mg/kg daily, doses may vary according to condition being treated and specific information will be provided where appropriate.

NB In patients with renal and/or hepatic insufficiency, dosages should be given at the lower end of the normal range.

Doses may vary for individual patients and this will be documented in specialist letter.

Prednisolone may be used in combination with azathioprine as part of the immunosuppression regimen. If this is required specific information will be provided by the specialist.

Azathioprine should be taken with or after food, and the dose can be divided if preferred.

4. Duration of treatment

Advice will be given to the GP on duration of treatment and dose changes for each individual patient.

5. Contraindications and cautions

Azathioprine is contraindicated in patients with severe hepatic impairment; severely impaired bone marrow function; severe infections; pancreatitis

Use with caution in mild to moderate hepatic and / or renal impairment and in the elderly (see also Section 7).Avoid in porphyria

Pregnancy and breast feeding
Treatment with azathioprine should not generally be initiated during pregnancy, but it may be reasonable to continue during pregnancy.

All patients wanting to become pregnant who are taking either azathioprine or mercaptopurine should discuss this with their specialist.

Azathioprine has been reported to interfere with the effectiveness of intrauterine contraceptive devices. Therefore it is recommended to use other or additional contraceptive measures.

Breast feeding: present in milk in low concentration; no evidence of harm in small studies. BNF recommends use if potential benefit outweighs risk – this should be discussed with the patient.

Further information on use in pregnancy and breastfeeding can be found at www.bnf.org.uk or www.medicines.org.uk.

6. Adverse effects

Patients with thiopurine methyl transferase (TPMT) deficiency may be more susceptible to delayed haematotoxicity including bone marrow toxicity.

Hypersensitivity reactions: general malaise, dizziness, nausea, vomiting, diarrhoea, fever, rigors, exanthema, rash, myalgia, arthralgia, renal dysfunction and hypotension.
Haematological reactions: Dose dependant, general reversible bone marrow suppression, usually seen as leucopenia, anaemia, thrombocytopenia, increases in MCV and haemoglobin content of red blood cells, megaloblastic anaemia, euthyroid hypoplasia.
Gastrointestinal: Nausea (often relieved by administering after food), diarrhoea, pancreatitis.
Hepatic: Cholestasis and deterioration in liver function.
Infections: increased susceptibility to viral, fungal and bacterial infections.
Neoplasms: Rare - include non-Hodgkin's lymphomas, skin cancers (melanoma and non-melanoma), sarcomas (Kaposi's and non-Kaposi's) and uterine cervical cancer in situ, acute myeloid leukaemia and myelodysplasia.
Other: Reversible pneumonitis, alopecia

7. Interactions

Patients receiving azathioprine should be advised against immunization with live vaccines. (Influenza vaccines may be given in this group of patients)

Interactions include
Allopurinol – dose reduction required discuss with specialist
Febuxostat – avoid concomitant use
Trimethoprim, co-trimoxazole - increased risk of toxicity – avoid
Warfarin – may reduce anticoagulant effect

Increased risk of side effects with ACE inhibitors, aminosalicylate derivatives, cimetidine, indomethacin and other drugs with myelosuppressant properties – use with caution and monitor closely

8. Monitoring

Disease monitoring:
Clinical response to therapy

Drug monitoring:

Baseline – FBC, BCP (for renal function & LFTs) and TPMT assay

On-going

FBC & LFT should be checked once weekly for at least 4 weeks; if stable the monitoring may be reduced to fortnightly - monthly. Once the dose, disease and blood monitoring is stable the frequency of monitoring may be reduced to 3 monthly on advice of specialist.
If doses are changed then monitoring should done as if the drug has been started.

Monitoring parameter	Recommended response
WBC < 4.0 x 10^9 /1	withhold **until discussed** with specialist team
Neutrophils <2.0 x 10^9 /l	withhold **until discussed** with specialist team
Platelets <150 x 10^9 /l	withhold **until discussed** with specialist team
>2 fold rise in AST, ALT (from upper limit reference range)	withhold **until discussed** with specialist team
MCV> 105 fl	Check **serum folate and B12 & TSH**. Withhold until results are available and **discuss** with specialist team
Rash or oral ulceration	withhold **until discussed** with specialist team
Abnormal bruising or **severe sore** throat or rash	withhold **until FBC results** available & discuss with the specialist team

Details of contraindications, cautions, drug interactions and adverse effects listed above are not exhaustive. For further information always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).

9. Information to patient

Patients should be informed about benefits and risks of treatment and need for monitoring.

Patients should be told to go to their GP immediately if they experience any fever, rash, bruising, bleeding, sore throat, oral ulceration, jaundice or infection.

Responsibilities of clinicians involved

Stage of Treatment	Hospital Specialist	General Practitioner
Initiation	• Assess the patient following referral by GP • Carry out baseline full blood count, differential WCC, platelets, U&Es, LFTs and TPMT assay. • Recommend appropriate treatment to the GP by approved DMARDs clinic letter	Prescribe on FP10
Maintenance	• Assess clinical response to treatment • Provide adequate advice and support for the GP • Provide information to GP on frequency of monitoring if doses are changed	• FBC & LFT should be checked every week for at least 4 weeks and after each dose increase, if stable the monitoring may be reduced to fortnightly to monthly. • Once the dose, disease and blood monitoring is stable the monitoring may be reduced to 3 monthly, as advised by specialist.

DMARDs clinic letter box

DMARD COMMENCEMENT	Tick box
Bloods checked and satisfactory	
X-Ray checked and satisfactory	
Information given to patient	
Counselling given to patient	
Shared Care Protocol attached	

Contact Details:

During office hours

Contact the relevant consultant's secretary via HEY switchboard (01482 875875)

Specialist pharmacists

Interface Pharmacist – Antonio Ramirez	(01482) 674306
Neurology - Jane Morgan	(01482) 674411
Renal Medicine – Aaron Acqueye	(01482) 675207
Cancer Services & Immunology – Sarah Scargill	(01482) 461274
Rheumatology – Emily Hardaker	(01482) 675207

Out of hours – Contact on-call Registrar for specialty via HEY switchboard.

APPROVAL PROCESS

Written by:	**Marie Miller, Interface Pharmacist**
Consultation process:	**Specialists teams in Neurology, Immunology, Renal Medicine, Haematology, Rheumatology, Dermatology, Gastroenterology**
Approved by:	***Medicines Management Interface Group,***
Ratified by:	***HERPC March 2014 Updated June 2018***
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