Central Manchester University Hospitals NHS
NHS Foundation Trust

NHS

Greater Manchester Interface Prescribing Group Shared Care Template

Shared Care Guideline for **Azathioprine in Rheumatological Conditions**		**Reference Number** **CMFT-SCG-001**
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Date approved by Commissioners: **January 2013**	**Review Date:** **January 2015**	

Please complete all sections

1. Licensed Indications	*Licensed for use in rheumatoid arthritis, used as an immunosuppressant antimetabolite either alone or in combination with other agents and can include a steroid sparing effect.*
2. Therapeutic use & background	*Azathoprine tablets are used as an immunosuppressant anti-metabolite either alone or, more commonly, in combination with other agents (usually corticosteroids) and procedures which influence the immune response. Therapeutic effect may be evident only after weeks or months and can include a steroid-sparing effect, thereby reducing the toxicity associated with high dosage and prolonged usage of corticosteroids.*
3. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).	*Contraindications: Live vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster) should be avoided in patients taking azathioprine. Azathioprine is contra-indicated in patients known to be hypersensitive to azathioprine. Hypersensitivity to 6-mercaptopurine (6-MP) should alert the prescriber to probable hypersensitivity to azathioprine. TPMT (thiopurine methyl transferase) deficiency (homozygous state)- avoid can be fatal.* *Cautions: TPMT deficiency (heterozygous state), may be associated with delayed haematotoxicity including bone marrow toxicity. Localised or systemic infection including hepatitis B or C and history of tuberculosis.*
4. Prescribing in pregnancy and lactation	*Prescribing during pregnancy and lactation should be agreed with the Specialist.* *Azathioprine therapy should not be initiated in patients who may be pregnant, or who are likely to become pregnant without careful assessment of risk versus benefit by Rheumatology Team.* *Women treated with azathioprine should not breastfeed.*

<table>
<tr><td rowspan="9">5. Dosage regimen for continuing care</td><td>Route of administration</td><td colspan="2">oral</td></tr>
<tr><td colspan="3">Preparations available (include in this section any necessary information relating to availability of special preparations for children or those with swallowing difficulties

Azathioprine tablets disperse within 5 minutes in water. A “specials” suspension is available.</td></tr>
<tr><td colspan="3">Dose to be prescribed including units, frequency and duration of treatment.
Please prescribe: 1mg/kg/day increasing after 4-6 weeks to 2-3mg/kg/day</td></tr>
<tr><td>Is titration required</td><td>Yes (complete the following section) Yes</td><td></td></tr>
<tr><td colspan="3">Titrate dosage according to response.
Maintenance dosage up to a maximum 2-3mg/kg/day</td></tr>
<tr><td colspan="3">Adjunctive treatment regime

No adjunctive treatment</td></tr>
<tr><td colspan="3">Conditions requiring dose reduction

Lower doses if there is significant renal or hepatic impairment and in elderly patients.</td></tr>
<tr><td colspan="3">Usual response time

6 weeks to 3 months</td></tr>
<tr><td colspan="3">Duration of treatment ongoing</td></tr>
<tr><td colspan="3">Treatment to be terminated by healthcare professional in consultation with Rheumatology Team.</td></tr>
<tr><td colspan="3">NB. All dose adjustments will be the responsibility of the initiating specialist care unless directions have been specified in the medical letter to the GP.</td></tr>
<tr><td>6.Drug Interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics</td><td colspan="3">The following drugs must <u>not</u> be prescribed without consultation with the specialist:
Increased risk of haematological toxicity when azathioprine given with trimethoprim and co-trimoxazole.
Avoid use with clozapine, increased risk of agranulocytosis.
Enhanced effect and increased toxicity when given with allopurinol, dose of azathioprine should be reduced by 75%.
Azathioprine inhibits anticoagulant effect of warfarin.</td></tr>
<tr><td colspan="3">The following drugs may be prescribed with caution:
ACE inhibitors, increased risk of anaemia or leucopenia especially in renal impairment
Aminosalicylates may contribute to bone marrow toxicity.
Azathioprine reduces absorption of phenytoin, sodium valproate, carbamazepine.
Cytotoxics reduce absorption of digoxin.

Alcohol intake maximum 6 units weekly</td></tr>
</table>

7. Adverse drug reactions

For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of Product Characteristics or BNF

Specialist to detail below the action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

Adverse event System – symptom/sign	**Action to be taken** Include whether drug should be stopped prior to contacting secondary care specialist	**By whom**
WBC<3.5 x 10^9/l Neutrophils <2.0 x 10^9/l Platelets <150 x 10^9/l AST,ALT>twice upper limit of normal	*Withhold until discussion with Rheumatology Team*	*GP*
Rash or oral ulceration	*Withhold until discussion with Rheumatology Team*	*GP*
MCV>105 fl	*Check serum folate, B12 and TSH. Treat any underlying abnormality. If results normal discuss with Rheumatology Team*	*GP*
Abnormal bruising or severe sore throat	*Withhold until urgent FBC results available and discuss with Rheumatology Team as can cause bone marrow suppression.*	*GP*

The patient should be advised to report any of the following signs or symptoms to their GP without delay:

Malaise, dizziness, vomiting, diarrhoea, fever, rigors, myalgia, arthralgia, rash, hypotension and interstitial nephritis could be a sign of hypersensitivity reactions and treatment should be withdrawn immediately.

Other important co morbidities (e.g. Chickenpox exposure). Include advice on management and prevention and who will be responsible for this in each case:
Annual 'flu vaccine should be given. Passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles.
Sunscreens should be encouraged to reduce sunlight exposure.

Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the "Yellow Card" scheme.

8.Baseline investigations

List of investigations / monitoring undertaken by secondary care
FBC
U&Es
LFTs
TPMT assay (normal reference range > 68mu/L)
<20mu/l do not give Azathioprine
20-68mu/l Discuss with Consultant

<table>
<tr><td>9. Ongoing monitoring requirements to be undertaken by GP</td><td colspan="2">Is monitoring required?</td><td colspan="3">Yes or No (if yes complete following section) Yes</td></tr>
<tr><td></td><td>Monitoring</td><td>Frequency</td><td>Results</td><td>Action</td><td>By whom</td></tr>
<tr><td></td><td>FBC, U&E, LFT, (ESR desirable but not essential)</td><td>During dose titration: Every week until achieve maintenance dose

Maintenance dose: then weekly for 6 weeks then monthly thereafter.</td><td colspan="2">See Section 7: Adverse drug reactions above</td><td>GP</td></tr>
<tr><td>10. Pharmaceutical aspects</td><td colspan="5">e.g. special storage requirements, washout periods Or where there are “no special considerations”
no special considerations</td></tr>
<tr><td>11. Secondary care contact information</td><td colspan="5">If stopping medication or needing advice please contact:</td></tr>
<tr><td></td><td colspan="5">To contact The Kellgren Centre Rheumatology Manchester Royal Infirmary:
Enquiries regarding blood monitoring and results please contact the specialist nurses below:
Specialist Nurse Jane Hawthorne 0161 276 4688
Specialist Nurse Melissa Aris 0161 701 1454
Specialist Nurse Carole Hill 0161 701 1454
Fax number for GP blood results 0161 276 8690
Consultant contact details below:
Professor Ian Bruce 0161 276 4626
Professor Ann Barton 0161 276 4626
Dr Kimme Hyrich 0161 276 4627
Dr Pauline Ho 0161 276 4397
Dr Rachel Gorodkin 0161 276 4628

To contact Rheumatology Department Trafford General Hospital:
Trafford Rheumatology helpline number 0161 746 2162
Consultant contact details below:
Dr Frank McKenna 0161 746 2395
Dr Preeti Shah 0161 746 2395</td></tr>
<tr><td>12. Criteria for shared care</td><td colspan="5">Prescribing responsibility will only be transferred when
▪ Treatment is for a specified indication and duration.
▪ Treatment has been initiated and established by the secondary care specialist.
▪ The patient’s initial reaction to and progress on the drug is satisfactory.
▪ The GP has no objection in each individual case that shared care is appropriate.
▪ The patient’s general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements</td></tr>
</table>

13. Responsibilities of initiating specialist	Initiate treatment and prescribe for the 1st 3 months of treatment. Undertake baseline monitoring. Advise GP of any dose adjustments. Monitor patient's initial reaction to and progress on the drug. Ensure that the patient has an adequate supply of medication until GP supply can be arranged. Supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP. Provide GP with diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient *or* inform GP if the patient repeatedly does not attend appointments. Provide GP with advice on when to stop this drug. Provide patient with relevant drug information to enable informed consent to therapy. Provide patient with relevant drug information to enable understanding of potential side effects and appropriate action. Provide patient with relevant drug information to enable understanding of the role of monitoring. Provide patient with monitoring booklet. Provide patient with rheumatology nurse helpline contact number. ----------
14. Responsibilities of the GP	Continue treatment as directed by the specialist. Ensure no drug interactions with concomitant medicines (see section 6). To monitor and prescribe in collaboration with the specialist according to this protocol. To ensure blood monitoring is carried out once dose stable and responsibility transferred from secondary care. To inform Rheumatology Team if patient repeatedly does not attend routine blood monitoring. To ensure that the monitoring and dosage record is kept up to date in the shared care booklet. To undertake vaccination as directed by the initiating consultant, the BNF or Green Book Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary. ----------
15. Responsibilities of the patient	To take medication as directed by the prescriber, or to contact the GP if not taking medication

	To attend hospital and GP clinic appointments, bring monitoring booklet. Failure to attend will result in medication being stopped (on specialist advice). To report adverse effects to their Specialist or GP.
17. Supporting documentation	The SCG must be accompanied by a patient information leaflet. Patient Information Leaflet EMC medicine Azathioprine Arthritis Research UK Patient Information Leaflet Azathioprine
18. Patient monitoring booklet	The patient must receive a monitoring booklet from the specialist upon initiation of treatment. The patient must bring this booklet to all specialist and GP appointments where it will be updated by the health professional conducting the appointment. The patient must also produce the booklet to any health professional involved in other aspects of their care e.g. pharmacists and dentists.