**SHARED CARE Guideline – Amber Traffic Light Classification**

<table>
<thead>
<tr>
<th>Name of medicine</th>
<th>Azathioprine (oral)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>Licensed: Rheumatoid Arthritis, Systemic Lupus Erythematosus and other chronic inflammatory conditions in Adults (excluding IBD)</td>
</tr>
<tr>
<td>(including whether for adults and/or children)</td>
<td></td>
</tr>
</tbody>
</table>

**PCN policy statement reference**

Not applicable

**Author(s):** Georgina Randall, Senior Commissioning Technician, 22nd September 2016

**Organisation(s):** Medicines Management (Hosted Service), Surrey Downs CCG

**Version:** 1  
**PCN recommendation date:** 05-Apr-2017  
**Review date:** April 2020

The Shared Care Guideline (SCG) is intended to facilitate the accessibility and safe prescribing of complex treatments across the secondary/primary care interface. This AMBER information sheet sets out the patient pathway relating to this medicine and any information not available in the British National Formulary and manufacturer's Summary of Product Characteristics. Prescribing must be carried out with reference to those publications. The SCG must be used in conjunction with the PCN agreed core roles and responsibilities stated in annex A.

An agreement notification form is included in annex B for communication of request for shared care from provider and agreement to taken on prescribing by primary care.

**Roles and Responsibilities**

Listed below are specific medicine/indication related responsibilities that are additional to those core roles and responsibilities that apply to all SCGs listed in annex A.

**Consultant or Specialist responsibilities**

**Pre-treatment checks:**

1. Confirm diagnosis and indication for treatment with oral azathioprine.
2. Prior to treatment ask Primary Care Prescriber whether patient has had pneumococcal vaccination and flu vaccination and, if not, immunise (unless contra-indicated). Inform patient not to start medication until after immunisation.
3. Exclude existing pregnancy in women with child bearing potential.
4. Record varicella status.

**Patient education:**

5. To discuss fully the aims, benefits, risks and side effects of treatment and the intended treatment plan with the patient and/or carer and for written information to be supplied to the patient and/or carer.
6. Inform patients to report immediately any exposure to Varicella Zoster Virus.
7. To discuss the potential implications of pregnancy and breastfeeding in women of child bearing potential and agree a risk minimisation strategy where appropriate.
8. Discuss the possibility of shared care with the patient and/or carer and ensure that they understand the plan for their subsequent treatment.

**Starting of treatment:**

9. To initiate treatment by prescribing and monitoring (as per monitoring section below) usually for a minimum of 3 months.

**Subsequently:**

10. Monitor and prescribe according to guidelines until handover is appropriate (including when
Shared care agreement for:
Azathioprine
for
Rheumatoid Arthritis, SLE and other chronic inflammatory conditions (excl. IBD)
in Adults

Shared care:-

11. Supply Primary Care Prescriber with a summary of the patient’s review (including anticipated length of treatment) and a link to, or a copy of, the shared care guideline when requesting transfer of prescribing to GP or primary care prescribers.

12. Ensure that the patient has been given a copy of this guideline, and if not, supply a copy to them.

GP or Primary Care Prescriber responsibilities

1. Add information about the medicine to patient record, initially as “hospital prescribed”, and highlight the importance that this medicine is only to be prescribed under a shared care guideline in primary care.

2. Ensure that the patient has been given a copy of this guideline, and if not, supply a copy to them

3. Provide patient with pneumococcal vaccination and flu vaccination unless contra-indicated or already give pre-treatment

4. Inform patients to report immediately any unexplained bleeding, bruising, purpura, sore throat, fever, pallor, jaundice or malaise and take the actions outlined in this shared care guideline.

5. Inform patients to report immediately any exposure to Varicella Zoster Virus.

6. Continue prescribing azathioprine at the dose recommended and undertake monitoring requirements.

7. Prescribe any change in dose as advised by the specialist team and monitor (as per monitoring section below)

Patient’s or Carer’s role

Please ensure that you read and understand your responsibilities with regards to your treatment, as listed in Annex A of this document

In addition to these it is important to be aware of the following:–

1. Report immediately to your doctor, if you come into contact with someone with Varicella Zoster Virus (e.g. chicken pox or shingles).

2. Report immediately to your doctor, the start of any feature of:
   - blood disorders (e.g. sore throat, bruising, and mouth ulcers)
   - liver toxicity (e.g. nausea, vomiting, abdominal discomfort, and dark urine)
   - respiratory effects (e.g. shortness of breath)
   - fever

3. Keep all appointments with your healthcare providers (i.e. GP, consultant, specialist, nurse, pharmacist). Appointments will include those required for testing that azathioprine is being effective and that it is not causing any side effects.

Key information on the medicine


Background to use for the indications, including licence status:

Azathioprine tablets are used as an immunosuppressant antimetabolite either alone or in combination with other agents which influence the immune response.

It has a marketing authorisation for the treatment of rheumatoid arthritis and systemic lupus erythematosus.

Indication

Rheumatoid Arthritis, Systemic Lupus Erythematosus and other chronic inflammatory conditions in Adults (excluding IBD).

Dosage and Administration

1mg to 3mg per kg bodyweight per day. Dose to be set by consultant or specialist during initiation period.

When a therapeutic response is evident, consideration should be given to reducing the maintenance dose. A therapeutic response may not be evident for 6 to 12 weeks. Consider withdrawal of treatment if no response after 3 months.
Monitoring
Blood samples may be taken at the patient’s Primary Care Prescriber practice whenever this avoids a patient attendance in secondary care. Where the specialist is responsible for monitoring, they need to have the appropriate systems to capture the testing.

<table>
<thead>
<tr>
<th>Monitoring requirements and appropriate dose adjustments</th>
<th>Responsible clinician</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-treatment:</strong> FBC, U&amp;Es, creatinine, LFTs, ESR and / or CRP and TPMT assay.</td>
<td>Specialist</td>
</tr>
<tr>
<td><strong>Initiation:</strong> Weeks 2, 4, 6, 8, 10, 12: FBC, U&amp;Es, LFTs, ESR and / or CRP.</td>
<td>Specialist</td>
</tr>
<tr>
<td><strong>weeks 18 and 24:</strong> FBC, U&amp;Es, LFTs, ESR and / or CRP.</td>
<td>Specialist</td>
</tr>
<tr>
<td><strong>Maintenance:</strong> Every three months thereafter: FBC, U&amp;Es, creatinine, LFTs, ESR and / or CRP.</td>
<td>Specialist until primary care prescriber has accepted transfer of care</td>
</tr>
<tr>
<td>Dose increase when on maintenance: Recheck FBC, LFTs, ESR and / or CRP 2 weeks after dose change.</td>
<td>Specialist until primary care prescriber has accepted transfer of care</td>
</tr>
</tbody>
</table>

- Check for medicine interactions on initiating new treatments.
- Elderly – doses should be at the lower end of the dosage range.
- Hepatic &/or Renal impairment – doses should be at the lower end of the dosage range.
- Pregnancy – dose reduction at 32 weeks of gestation may prevent neonatal leucopenia.

<table>
<thead>
<tr>
<th>Test</th>
<th>Abnormal Result</th>
<th>Action if Abnormal Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>&lt;3.5 X 10^9/l</td>
<td>Discuss with specialist (note frequently used in connective tissue disease where values may be low).</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>&lt;1.5 X 10^9/l</td>
<td>Discuss with specialist (note frequently used in connective tissue disease where values may be low).</td>
</tr>
<tr>
<td>Platelets</td>
<td>&lt;150 X10^9/l</td>
<td>Discuss with specialist (note frequently used in connective tissue disease where values may be low).</td>
</tr>
<tr>
<td>Liver function</td>
<td>AST/ALT &gt;twice upper limit of reference range</td>
<td>Withhold and discuss with specialist.</td>
</tr>
<tr>
<td>MCV</td>
<td>&gt;105 fl</td>
<td>Check serum B12, Folate and TFT and treat if appropriate. If normal results, continue treatment.</td>
</tr>
<tr>
<td>Rash</td>
<td></td>
<td>Withhold and seek urgent specialist (preferably dermatological) advice.</td>
</tr>
<tr>
<td>Oral ulceration</td>
<td></td>
<td>Withhold and discuss with specialist</td>
</tr>
<tr>
<td>Abnormal bruising, sore throat, unexplained bleeding</td>
<td></td>
<td>Withhold and check FBC urgently. Discuss with specialist.</td>
</tr>
</tbody>
</table>

Please note that in addition to absolute values, a rapid fall/rise or consistent downward/upward trend in haematological or biochemical index should prompt caution and extra vigilance.

Cautions (including pregnancy and lactation):
- Elderly – doses should be at the lower end of dosage range.
- Patients with impaired renal function – doses should be at the lower end of dosage range. Dosage should be further reduced if haematological toxicity occurs.
- Patients with impaired hepatic function – metabolism of azathioprine may be impaired, dosage should be reduced if hepatic or haematological toxicity occurs.
- Patients with thiopurine methyl transferase (TPMT) deficiency – may be associated with delayed haematotoxicity including bone marrow toxicity.
- Patients receiving multiple immunosuppressive agents – treatment should be maintained at lowest effective level.
- Varicella Zoster Virus Infection – in patients with severe exposure to chickenpox or shingles consider passive immunization with varicella zoster immunoglobulin (VZIG) – see Green Book Chapter 34 for further details.
- All patients contemplating becoming pregnant must be seen by a Consultant at the earliest opportunity to discuss the complex issues surrounding therapy with azathioprine.
- All patients contemplating breast feeding must be seen by a Consultant at the earliest opportunity to discuss the complex issues surrounding therapy with azathioprine.

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

Contraindications
- Patients with known hypersensitivity to azathioprine, its metabolites or any of the excipients.
- Patients with known hypersensitivity to mercaptopurine.
- Patients with hypoxanthine-guanine-phosphoribosyltransferase deficiency (Lesch-Nyhan syndrome).
- Patients with absent thiopurine S-methyltransferase (TPMT) activity.
- If the formulation contains lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.
- Severe infections.
- Seriously impaired hepatic or bone marrow function.
- Pancreatitis.
- Live vaccines (see medicine interactions section).

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

Adverse effects
The most common side effects are:
- Flu-like symptoms (myalgia, headache, diarrhoea) which characteristically occur 2-3 weeks after initiating treatment and usually subside if treatment is continued.
- Nausea – which can usually be relieved by taking the tablets after food.
- Bone Marrow suppression causing leucopenia or thrombocytopenia (both more likely to occur in those with low TPMT activity).

Other side effects include hypersensitivity reactions (including malaise, dizziness, vomiting, diarrhoea, fever, rigors, myalgia, arthralgia, rash, hypotension and interstitial nephritis—calling for immediate withdrawal); liver impairment, cholestatic jaundice, hair loss and increased susceptibility to infections and colitis in patients also receiving corticosteroids; nausea; rarely pancreatitis, pneumonitis, hepatic veno-occlusive disease, lymphoma, red cell aplasia.

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

Notable drug interactions:
- Allopurinol / xanthine oxidase inhibitors – avoid concomitant use if possible. If concomitant use, it is essential that only 25% of the usual dose of azathioprine is given since allopurinol decreases the rate of catabolism of azathioprine.
- Aminosalicylates & derivatives (i.e. mesalazine, olsalazine or sulfasalazine) - may increase risk of bone marrow toxicity when used concomitantly with azathioprine.
- Anticoagulants – azathioprine reduces the effect of warfarin.
- Angiotensin-converting enzyme (ACE) Inhibitors – concomitant use may cause anaemia.
- Co-trimoxazole & Trimethoprim – Increased risk of haematological toxicity. Avoid concomitant use.
- Cytostatic/myelosuppressive agents – where possible avoid concomitant administration of cytostatic drugs, or drugs which may have a myelosuppressive effect, such as penicillamine.
- Febuxostal – avoid concomitant use.
- Methotrexate – when azathioprine is administered concomitantly with high dose methotrexate, the dose should be adjusted to maintain a suitable white blood cell count.
- Phenytoin, sodium valproate, carbamazepine: Azathioprine reduces the absorption of these drugs.
• Ribavirin – avoid concomitant use.
• **Live Vaccines** – should **NOT** be administered to patients receiving treatment with azathioprine. Herpes zoster vaccine is not contraindicated in these patients. Please see [http://tinyurl.com/nvdeqp2](http://tinyurl.com/nvdeqp2).

*This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.*

**Any further information (e.g. supporting therapies):**
Prior to starting azathioprine, best practice recommends checking the TPMT (thiopurine methyltransferase) activity; this enzyme is involved in the metabolism of 6-mercaptopurine (a metabolite of azathioprine) and its activity is controlled by a genetic polymorphism. TPMT testing, initial dosing and subsequent adjustments will be the responsibility of the specialist team.

**Support and Advice for the Primary Care**

<table>
<thead>
<tr>
<th>Name</th>
<th>Speciality</th>
<th>Telephone No.</th>
<th>Email address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Charles Li</td>
<td>Rheumatology</td>
<td></td>
<td><a href="mailto:charles.li@nhs.net">charles.li@nhs.net</a></td>
</tr>
<tr>
<td>Dr Cai Neville</td>
<td></td>
<td>Secretary to Dr Li</td>
<td><a href="mailto:c.neville@nhs.net">c.neville@nhs.net</a></td>
</tr>
<tr>
<td>Dr Sumeet Chander</td>
<td></td>
<td>Tel 01483 464159</td>
<td><a href="mailto:sumeetchander@nhs.net">sumeetchander@nhs.net</a></td>
</tr>
<tr>
<td>Hospital Pharmacy</td>
<td>Medicines information</td>
<td>01483 464120</td>
<td><a href="mailto:rsc-tr.MedicinesInformation@nhs.net">rsc-tr.MedicinesInformation@nhs.net</a></td>
</tr>
<tr>
<td>Out of Hours</td>
<td>A&amp;E</td>
<td>01483 571122 and use interactive system to connect to A&amp;E</td>
<td></td>
</tr>
</tbody>
</table>

**References**
SMSKP SCG Azathioprine Version: 1, October 2015
### Patients

- Make sure that you understand all aspects of your treatment and ask for more information if needed, including raising any concerns you may have relating to your treatment with whoever is prescribing this medicine for you.
- Express your preferences and wishes for how your treatment should be provided.
- Follow the course of treatment which you have agreed, and talk to your healthcare providers if you find this difficult.
- Give permission to have aspects of your care, i.e. prescribing information, test results, communicated to the relevant healthcare providers.
- Be aware of your rights and responsibilities under the NHS Constitution for England (updated October 2015).
- Keep all appointments with your healthcare providers (i.e. GP, consultant, specialist, nurse, pharmacist). It may be necessary to have certain tests before, during, and after your treatment to check that it is working and not causing side effects.
- Keep all follow up appointments. Not attending clinic appointments may result in your doctor stopping treatment, as it might be unsafe for you to continue on treatment without the checks that occur during appointments.
- Ensure that you read and understand the Patient Information Leaflet included with your medication and know how to report any side effects or concerns you have with your healthcare providers.
- Keep a written list of all of the prescription and non-prescription (over-the-counter) medicines you are taking or using, as well as any products such as vitamins, minerals, or other dietary supplements. You should bring this list with you each time you visit a healthcare provider or if you are admitted to a hospital. It is also important information to carry with you in case of emergencies.
- Do not let anyone else take your medication. Ask your pharmacist any questions you have about your prescription.

### Relatives and Carers

- To support the patient in fulfilling their roles and responsibilities as outlined above.

### Consultant/ Specialist

**Good Prescribing Guidelines**

- Be aware that if you recommend that a colleague, for example a junior doctor or Primary Care Prescriber, prescribes a particular medicine for a patient, you must consider their competence to do so. You must satisfy yourself that they have sufficient knowledge of the patient and the medicine, experience (especially in the case of junior doctors) and information to prescribe. You should be willing to answer their questions and otherwise assist them in caring for the patient, as required (Ref GMC).
- Be aware that if you delegate assessment of a patients’ suitability for a medicine, you must be satisfied that the person to whom you delegate has the qualifications, experience, knowledge and skills to make the assessment. You must give them enough information about the patient to carry out the assessment required.
- Be aware that you are asking the Primary Care Prescriber to take full medico-legal responsibility for the prescription they sign (Ref GMC). For this reason the shared care guidelines (SCGs) are agreed at the PCN with input from specialists and Primary Care Prescribers, and, for individual patients, the patient’s Primary Care Prescriber must agree to take over responsibility before transfer of care, before the patient is discharged from specialist care.
- Be aware of the formulary status and the traffic light classification of the medicine you are prescribing within the patient's CCG.
- Assume clinical responsibility for the guidance given in the SCG, and where there is new information needed on the SCG to liaise with your Formulary Pharmacist who will facilitate an update via the PCN.

### Before initiating treatment

- Evaluate the suitability of the patient for treatment, including consideration of the patient’s current medication and any significant interactions.
- Discuss and provide the patient with information about the reason for choosing the medicine, the likelihood of both harm and benefits, consequences of treatment, and check that their treatment choice is consistent with their values and preferences.
- Advise patient of unlicensed status of treatment (including off-label use) if appropriate and what this may mean for their treatment.
- Undertake baseline monitoring and assessment.

### Initiating and continuing treatment in secondary care

- Prescribe initial treatment and provide any associated training and counselling required.
Inform the Primary Care Prescriber when initiating treatment so that the Primary Care Prescriber is aware what is being prescribed and can add to Primary Care Prescriber clinical record.

Continue to prescribe and supply treatment with appropriate monitoring until the patient’s condition is stable; the patient is demonstrably benefiting from the treatment and is free from any significant side effects.

At any stage of treatment, advising Primary Care Prescriber of concerns regarding monitoring or potential adverse effects of treatment.

**Transfer of care to Primary Care prescriber**

- Liaise with the primary care prescriber to agree to share the patient’s care and provide relevant accurate, timely information and advice.
- Only advise the patient that shared care will take place, and prescribing will be transferred, once the primary care prescriber has agreed to share responsibility of the patient care, and that this has been confirmed in writing.
- If the primary care prescriber feels unable to accept clinical responsibility for prescribing then the consultant must continue to prescribe the treatment to ensure consistency and continuity of care.
- Ensure that the patient (and carer/relatives) are aware of their roles and responsibilities under the SCG.
- Provide sufficient information and training for the patient to participate in the SCG.

**Post transfer of care**

- Follow up and monitor the patient at appropriate intervals.
- Advise Primary Care Prescriber if treatment dose changes or treatment is discontinued.
- Inform Primary Care Prescriber if patient does not attend planned follow-up.

**Primary Care Prescriber**

- Be aware of the formulary and traffic light status of the medicine you have been asked to prescribe.
- Be aware that Amber medicines have been assessed by the PCN as requiring careful transition between care settings but SCGs will be available to support safe transfer of care.
- It would be usual for Primary Care Prescribers to take on prescribing under a formal SCG. If you are uncertain about your competence to take responsibility for the patient’s continuing care, you should seek further information or advice from the clinician with whom the patient’s care is shared or from another experienced colleague. If you are still not satisfied, you should explain this to the other clinician and to the patient, and make appropriate arrangements for their continuing care.
- Be aware that if you prescribe at the recommendation of another doctor, nurse or other healthcare professional, you must satisfy yourself that the prescription is needed, appropriate for the patient and within the limits of your competence (Ref GMC).
- Be aware that if you prescribe, you will be responsible for any prescription you sign (Ref GMC).
- Keep yourself informed about all the medicines that are prescribed for the patient.
- Be able to recognise serious and/or frequently occurring adverse side effects, and what action should be taken if they occur.
- Make sure appropriate clinical monitoring arrangements are in place and that the patient and healthcare professionals involved understand them.
- Keep up to date with relevant guidance on the use of the medicines and on the management of the patient’s condition.
- Respond to requests to share care of patients in a timely manner, in writing (including use of form in annex B).
- Liaise with the consultant to agree to share the patient’s care in line with the SCG in a timely manner.
- Continue prescribing medicine at the dose recommended and undertake monitoring requirements.
- Undertake all relevant monitoring as outlined in the monitoring requirements section below, and take appropriate action as set out in this shared care guideline.
- Monitor for adverse effects throughout treatment and check for drug interactions on initiating new treatments.
- Inform the Consultant or specialist of any issues that may arise.
- Ensure that if care of the patient is transferred to another prescriber, that the new prescriber is made aware of the share care guideline (e.g. ensuring the patient record is correct in the event of a patient moving practice).

**All**

- Where it has been identified that a SCG requires update e.g. new information needed, liaise with the SCG author and/or your organisation PCN representative who will facilitate an update via the PCN.
Annex B: Shared care agreement notification form for medicines and indications approved as amber on the Surrey PAD or Crawley, Horsham and Mid-Sussex net formulary.

For the attention of the Practice Manager

FAX – Confirm you have the correct Safe Haven Fax Number before sending
E-mail – Confirm both sender and recipient e-mail addresses are nhs.net before sending

<table>
<thead>
<tr>
<th>To:</th>
<th>[Recipient Name]</th>
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<th>[fax number]</th>
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<tr>
<td>From:</td>
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[Notes]

<table>
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<th>Name of medicine</th>
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<tr>
<td>Indication</td>
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<table>
<thead>
<tr>
<th>Person removing form from fax machine</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Relevant patients Primary Care Prescriber available to action within 5 days (if not Trust needs to be informed on day of receipt of request)</td>
<td>Yes/ No</td>
</tr>
<tr>
<td>If Primary Care Prescriber is NOT available within 5 days, please communicate to the requesting specialist the date when the Primary Care Prescriber will be available</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hospital/ Patient information</th>
<th>Practice information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant Making Request</td>
<td>Primary Care Prescriber Name:</td>
</tr>
<tr>
<td>Consultant Speciality Details:</td>
<td>Practice:</td>
</tr>
<tr>
<td>Patient Name:</td>
<td>I agree to undertake shared care:</td>
</tr>
<tr>
<td>Patient NHS Number:</td>
<td>I do not agree to undertake shared care:</td>
</tr>
<tr>
<td>Patient Hospital Number:</td>
<td>If NOT please give reasons:</td>
</tr>
<tr>
<td>Patient DOB:</td>
<td>Signed:</td>
</tr>
<tr>
<td>Drug Name/ Dose:</td>
<td>Date:</td>
</tr>
<tr>
<td>Next Prescription Due:</td>
<td>Please return form to: Specialist safe haven fax number</td>
</tr>
<tr>
<td>Discharge letter written and sent:</td>
<td></td>
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</tbody>
</table>

Please refer to the Surrey PAD or Crawley, Horsham and Mid-Sussex net formulary for relevant shared care documents

Primary Care Prescriber should reply within 5 days of receipt of this form indicating participation (or not) in shared care of the patient

Shared care agreement for:
Azathioprine for Rheumatoid Arthritis, SLE and other chronic inflammatory conditions (excl. IBD) in Adults

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