Azathioprine for management of auto-immune conditions (inflammatory arthritis, connective tissue disease and vasculitis)

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE
This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of Azathioprine can be shared between the specialist and general practitioner or non-medical prescriber in primary care (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In that case, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe drugs for this treatment, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with auto-immune conditions, who are under regular specialist follow-up. This provides an opportunity to discuss and to monitor drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

<table>
<thead>
<tr>
<th>Specialist responsibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Ensure FBC, liver and renal function are within normal parameters to allow Azathioprine to commence.</td>
</tr>
<tr>
<td>- If abnormalities found at baseline inform GP as soon as possible.</td>
</tr>
<tr>
<td>- Initiate treatment with Azathioprine or advise GP on initiating treatment.</td>
</tr>
<tr>
<td>- Discuss the benefits and side effects of treatment with the patient and then inform GP this has occurred.</td>
</tr>
<tr>
<td>- Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care arrangement with the patient.</td>
</tr>
<tr>
<td>- Review the patient’s condition and monitor response to treatment regularly where indicated.</td>
</tr>
<tr>
<td>- Advise GP if monitoring is needed, and the frequency.</td>
</tr>
<tr>
<td>- Monitor any other parameters considered necessary, or advise GP on which to monitor.</td>
</tr>
<tr>
<td>- Communicate promptly with the GP when treatment is changed or needs to be changed by the GP, any results of the monitoring undertaken, and assessment of adverse events.</td>
</tr>
<tr>
<td>- Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.</td>
</tr>
<tr>
<td>- Advise GPs on when to stop treatment (if appropriate).</td>
</tr>
<tr>
<td>- Report adverse events to the MHRA via Yellow Card Scheme.</td>
</tr>
<tr>
<td>- Ensure that clear backup arrangements exist for GPs to obtain advice and support.</td>
</tr>
</tbody>
</table>
General Practitioner responsibilities

- Reply to the request for shared care as soon as practicable.
- Prescribe Azathioprine at the dose recommended.
- Adjust the dose as advised by the specialist.
- Monitor any parameters considered necessary, if agreed with the specialist to do so.
- Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
- Refer patient to specialist if his or her condition deteriorates.
- Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- Report adverse events to the specialist and to the MHRA via the Yellow Card Scheme.

Patient’s role

1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
3. Report any adverse effects to the specialist or GP.

BACK-UP ADVICE AND SUPPORT

<table>
<thead>
<tr>
<th>Contact details</th>
<th>Telephone No.</th>
<th>Email address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialist:</td>
<td>01592 648193</td>
<td><a href="mailto:janegibson@nhs.net">janegibson@nhs.net</a></td>
</tr>
<tr>
<td>Rheumatology Dept</td>
<td>01592 265967 (fax)</td>
<td><a href="mailto:helenharris@nhs.net">helenharris@nhs.net</a>, <a href="mailto:johnmclaren@nhs.net">johnmclaren@nhs.net</a>, <a href="mailto:sharontcullinane@nhs.net">sharontcullinane@nhs.net</a></td>
</tr>
</tbody>
</table>

Other:
ADTC website - FRDU adverse drug reaction document

SUPPORTING INFORMATION (taken from the SPC)

Licensed indications
Auto-immune conditions - Inflammatory arthritis, connective tissue disease and vasculitis diagnosed by a rheumatologist, usually supported by indices of inflammation.

Dosage and Administration
The usual dose of azathioprine is between 1-3mg/kg/day. The maximum dose differs between individuals.
Azathioprine - 25mg and 50mg tablets.

Contraindications and precautions for use
- The use of live vaccines with Azathioprine is contra-indicated.
- Women of childbearing potential should be advised to use effective contraceptive precautions. Evidence of mutagenicity is equivocal in men. In most cases, azathioprine should not be prescribed if there is a possibility of pregnancy, although there may be some circumstances where the benefit of continuing treatment outweighs the possible risks related to the unborn child. A careful assessment of risk vs. benefit is advised.
- Women treated with azathioprine should not breast feed
- TPMT deficiency (homozygous state): Avoid, can be fatal

Any queries relating to this Shared Care Protocol contact the Clinical Effectiveness Pharmacist (01592) 226915
Document approved by NHS Fife Area Drugs & Therapeutics Committee on behalf of NHS Fife. Date: February 2013
Ishtiaq Mohammed, Clinical Effectiveness Pharmacist
- Individuals with Lesch-Nyhan Syndrome - due to congenital hypoxanthine-guanine phosphoribosyl transferase (HGPRT) deficiency.
- Patients taking allopurinol (see interactions)

**Side Effects (also state any specific side-effects which require the consultant to be notified)**
- The most common side effects (affecting approximately 20% of patients) are flu-like symptoms (myalgia, headache, diarrhoea) which characteristically occur 2-3 weeks after initiating treatment and usually subside if treatment is continued.
- Rash, excessive bruising and recurrent infections are less common side effects.
- The most important complication is bone marrow suppression causing leucopenia or thrombocytopenia (both more likely to develop in those with a low TPMT activity) and is most likely to occur in the first few weeks of treatment. An urgent FBC must be performed on any patient who becomes unwell as profound myelosuppression can develop between routine tests. In this instance Azathioprine must be stopped immediately.
- Rare: Interstitial nephritis – treatment must be withdrawn immediately and the rheumatology Department contacted.
- Please note that lymphopenia should be expected (lymphocyte count <1.0 x10^9/l suggests compliance with treatment).

For a complete list of side effects see BNF/ Summary of product Characteristics.

**Treatment should be withheld and the Rheumatology Department contacted if:**
- **NEUTROPHILS** < 1.5 x10^9
- **PLATELETS** < 100 x 10^9
- >2 fold increase in **ALT** (from upper limit of reference range)
- **RASH, EXCESS BRUISING OR ORAL ULCERATION**

**Monitoring (State specific monitoring to be undertaken by the GP / Consultant) see FRDU blood monitoring forms (ADTC website)**

**Rheumatologist responsibilities:**
FBC, liver and renal function are within normal parameters to allow Azathioprine to commence.
TPMT assay prior to commencing.

**General Practitioner responsibilities:**
- While taking Azathioprine patients will require WEEKLY F.B.C. for 6 weeks, and 2 weekly after any dose increase, then monthly if Azathioprine dose remains stable.
- Liver function should be checked monthly until dose is stable.
- If monitoring remains stable for at least 3 months, then FBC and Liver function can be reduced to three monthly.

**Drug Interactions**
- Allopurinol and Febuxostat: Discuss with a Rheumatologist if urate lowering drugs are required
- Warfarin: Azathioprine inhibits the anticoagulant effects of warfarin. Monitor INR and alter the dose of warfarin accordingly
- Phenytoin, sodium valproate, carbamazepine: Azathioprine reduces the absorption of these drugs
- Angiotensin-converting enzyme (ACE) inhibitors: Co-prescription of azathioprine may cause anaemia (if significant, consider alternative to ACE inhibitor or different DMARD)
- Aminosalicylates i.e. mesalazine, olsalazine, balsalazide or sulfasalazine, may contribute to bone marrow toxicity
- Co-trimoxazole and trimethoprim can cause life threatening haematoxicity and should not be used in patients taking azathioprine
- Avoid concomitant use of live vaccines.

For a complete list of drug interactions please see the BNF / Summary of Product Characteristics.

**Cost** (July 2012)

- 28 X 25mg tabs = £5.08
- 56 X 50mg tabs = £4.16