Introduction:

Indication:
Disease modifying drug for rheumatoid arthritis, connective tissue disease, vasculitis, Crohn’s disease and ulcerative colitis, autoimmune conditions, ophthalmic inflammatory disease, eczema

Licensing Information:
See SPC for full list of licensed indications

Formulations:
Tablets of 25mg or 50mg

Dosage & administration:
Treatment is usually started at one 50mg tablet daily with or after breakfast for the first week. Subsequently, if no problems occur, the dose is usually increased weekly to 100mg daily and then 150mg daily, taken at the same time or in divided doses with meals. The dose is usually increased up to 2.5mg/kg per day and occasionally more if needed. Typical maintenance doses vary and should be in line with specialist advice.

In the elderly it is recommended that the dosages used should be at the lower end of the dosage range

Contraindications & Cautions:

Contraindications:
- Hypersensitivity to 6-mercaptopurine
- Hypersensitivity to azathioprine
- Azathioprine therapy should not be initiated in patients known to be
pregnant or in those who are likely to become pregnant in the near future without careful assessment of risk versus benefit. Normal recommendation however is to advise on appropriate contraception in men and women of child bearing potential and discuss any planned/unplanned pregnancy with the specialist. Azathioprine may be continued during pregnancy if the benefit outweighs the risk and may sometimes be the only available treatment option. Women who are considering pregnancy or become pregnant should be referred to the specialist and treatment continued.

Caution:
- Known TPMT (thiopurine methyltransferase) deficiency
- Renal or hepatic dysfunction – consider need for dose reduction to avoid haematological toxicity.
- Patients should be instructed to report immediately any evidence of infection, unexpected bruising or bleeding or other manifestations of bone marrow depression
- Breast feeding - use if potential benefit outweighs risk
- Increased risk for skin cancer – monitoring of skin for any new lesions and/or changes. Provide advice on sunscreen and protective clothing
- Live vaccines should not be administered + avoid for 6 months after stopping. Zoster vaccine may be considered when dosage is low.
- Consider check Varicella Zoster Virus status

For full list see SPC at [www.medicines.org.uk/EMC](http://www.medicines.org.uk/EMC) and BNF

<table>
<thead>
<tr>
<th>Interactions:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopurinol, oxypurinol and thiopurinol – reduced elimination of azathioprine and 6-mercaptopurine, reduce dose by one quarter or original dose.</td>
</tr>
<tr>
<td>Warfarin – reduced anticoagulant effect.</td>
</tr>
<tr>
<td>Captopril and possibly other ACE inhibitors – increased risk of myelosuppression.</td>
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<tr>
<td>Co-trimoxazole and trimethoprim - increased risk of myelosuppression</td>
</tr>
<tr>
<td>Clozapine – increased risk of agranulocytosis.</td>
</tr>
<tr>
<td>Sulfasalazine, mesalazine and olsalazine – possible increased risk of leucopenia due to inhibition of TPMT enzyme.</td>
</tr>
<tr>
<td>Live vaccines – avoid</td>
</tr>
</tbody>
</table>

For full list see SPC at [www.medicines.org.uk/EMC](http://www.medicines.org.uk/EMC) and BNF

<table>
<thead>
<tr>
<th>Adverse Effects:</th>
</tr>
</thead>
<tbody>
<tr>
<td>In general side effects are considered to be dose related and most will resolve on reduction of azathioprine dose or on cessation of treatment.</td>
</tr>
</tbody>
</table>

**Common**
- Leucopenia, Depression of bone marrow function, thrombocytopenia, increased susceptibility to infection

**Uncommon**
- Hypersensitivity, cholestatic jaundice, alopecia, pancreatitis, raised transaminases, hepatotoxicity – see GP responsibilities section.
- Nausea (may be relieved by taking tablets after meals)
Rare
Agranulocytosis, pancytopenia, aplastic anaemia, megaloblastic anaemia, erythroid hypoplasia, Life-threatening hepatic damage.
For full list see SPC at www.medicines.org.uk/EMC and BNF

Responsibilities of the specialist initiating treatment:

General:
- To assess the suitability of the patient for treatment
- As per national, regional and local guidelines, to ensure that the patient/carer has received counselling and understands the therapy, its benefits, limitations, continued monitoring (where applicable), adverse effects, and is aware of actions to take if adverse effects are suspected.
- Go through patient information leaflet with patient.
- Inform patients of the long term monitoring requirements and provide a monitoring booklet.
- Inform the GP of the information provided to the patient.
- To review the patient as agreed intervals and copy all relevant results to the GP.
- Carry out disease and initial drug monitoring as listed below. Formally hand over to GP by letter and patient informed - send a copy (either electronically or paper copy) of the Shared Care Guideline to the GP and ask whether they are willing to participate in shared care.

Prescribing:
- Issue all prescriptions for 8 weeks minimum until patient is safely established on azathioprine and specialist team are satisfied that it is appropriate to share care.

Disease & drug monitoring:
- Monitor bloods according to schedule:

<table>
<thead>
<tr>
<th>Test</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC LFTs U&amp;Es</td>
<td>Every 2 weeks for the first 8 weeks at clinical discretion whilst under secondary care and then as advised by specialist team (see responsibilities of GPs- monitoring).</td>
</tr>
<tr>
<td>TMPT</td>
<td>Consider testing</td>
</tr>
<tr>
<td>Hepatitis B and C status</td>
<td>Consider testing</td>
</tr>
</tbody>
</table>

- Discuss shared care arrangement with patient.
- Support and advise GPs as required.
- Assess response to treatment and initiate any dose changes as clinically appropriate including discontinuation of treatment.

General and Prescribing:
- To reply to the request for shared care within 2 weeks of receipt of the Consultant letter.
- Monitor and prescribe as recommended by the specialist - ensure continued prescribing of azathioprine remains clinically appropriate at dose advised by initiating team. The GP will be typically asked to take up the monitoring and prescribing no earlier than 8 weeks after

Responsibilities of other prescribers (GP):

- To reply to the request for shared care within 2 weeks of receipt of the Consultant letter.
- Monitor and prescribe as recommended by the specialist - ensure continued prescribing of azathioprine remains clinically appropriate at dose advised by initiating team. The GP will be typically asked to take up the monitoring and prescribing no earlier than 8 weeks after
treatment has been initiated.
- Notify Consultant if treatment with azathioprine is discontinued
- Ensure there are no drug interactions with any other medications initiated in primary care.
- **Live vaccines – avoid.** Polio and typhoid are available in killed inactivated form but may not be as effective. Zoster vaccine may be considered when dosage is low (seek advice from Specialist).
- **Other vaccinations**-
  - Annual influenza vaccine should be offered unless otherwise advised by the initiating specialist.
  - Individuals who have not been vaccinated or pre-existing immunity cannot be verified, the need for
    - Varicella immunoglobulin (VZIG) should be considered if there has been significant exposure to chicken pox or shingles.
    - Normal Human Immunoglobulin (HNIG)) should be considered if there has been significant exposure to measles.

### Disease & drug monitoring:
- Carry out drug monitoring as listed – and communicate abnormal results to the Specialist.
- Urgent drug discontinuation/ referral to specialist as clinically appropriate.
- To stop treatment on the advice of the specialist.
- To refer back to the Specialist if the patient’s condition deteriorates.
- Identify adverse effects to azathioprine and report these to the Specialist and where appropriate to the Commission on Human Medicines/MHRA (Yellow card scheme).

#### Unless otherwise stated by the secondary care Specialist, apply the following monitoring frequencies following handover from secondary care:

<table>
<thead>
<tr>
<th>FBC</th>
<th>LFTs</th>
<th>U&amp;Es</th>
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<tbody>
<tr>
<td>Monthly for 4 months (2-6 months) then 3 monthly (assuming dose stable).</td>
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<tr>
<td>On dose increase by hospital – at weeks 2, 4 and 8 and then resume 3 monthly regimen unless informed otherwise by the specialist.</td>
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<table>
<thead>
<tr>
<th>At consultations</th>
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<tbody>
<tr>
<td>Ask about oral ulceration, unexplained bruising/bleeding, rash, sore throat</td>
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</tbody>
</table>

Discontinue azathioprine and seek advice from initiating team if:

<table>
<thead>
<tr>
<th>Test</th>
<th>Abnormal Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WCC:</td>
<td>&lt;3.5 x10⁹/L</td>
</tr>
<tr>
<td>Neutrophils:</td>
<td>&lt;2.0 x10⁹/L</td>
</tr>
<tr>
<td>Platelets:</td>
<td>&lt;150 x10⁹/L</td>
</tr>
<tr>
<td>AST or ALT:</td>
<td>&gt;3 times the normal range</td>
</tr>
<tr>
<td>Mouth or throat ulceration</td>
<td></td>
</tr>
<tr>
<td>---------------------------</td>
<td></td>
</tr>
<tr>
<td>Unexplained bruising or bleeding</td>
<td></td>
</tr>
<tr>
<td>Fever, nausea, vomiting or diarrhoea</td>
<td></td>
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<tr>
<td>Diffuse alopecia</td>
<td></td>
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</tbody>
</table>

### Responsibilities of the Patient / Carer:

**General:**
- Report any possible side effects to their GP, in particular potential signs and symptoms of bone marrow suppression (e.g. unexplained bruising, bleeding, sore throat, infection etc).
- Practice safe exposure to the sun.
- Ensure they have adequate supply of medication.
- Attend appointments and take along monitoring book.
- Discuss with specialist before breastfeeding.
- Inform GP if unexpected pregnancy is suspected. They should then be referred to the specialist and treatment continued.

### Disease & drug monitoring:

As above – contact GP or initiating team if side effects develop (see adverse effects) and attend appointments including those for routine blood tests/investigations.

### Communication:

**Specialist to Primary Care Prescriber:**
- The specialist will inform the GP when they have initiated azathioprine and when there are any subsequent changes in treatment – standard clinic letter.
- Send a copy (either electronically or paper copy) of the Shared Care Guideline to the GP and ask whether they are willing to participate in shared care.
- Inform the GP of the information provided to the patient.

**Primary Care Prescriber to Specialist:**
- To reply to the request for shared care within 2 weeks of receipt of the Consultant letter.
- Irrespective of whether you accept prescribing responsibility or not, you should inform the consultant of relevant medical information regarding the patient and changes to the patient’s medication regime irrespective of the indication.
- Notify Consultant if treatment with azathioprine is discontinued.

### Contact names & details:
If you have any concerns regarding individual patients, see clinic letter for details of consultant and contact via switchboard.

- York: 01904 631313
- Scarborough: 01723 368111

Alternatively contact one of the following:

<table>
<thead>
<tr>
<th>Name</th>
<th>Telephone / Email</th>
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<tbody>
<tr>
<td>Rheumatology advice line (York)</td>
<td>01904 721854</td>
</tr>
</tbody>
</table>
### Rheumatology advice line (Scarborough)
- 01723 385058

### York inflammatory bowel disease nurse specialists
- 01904 726154

### Dermatology Specialist Nurse (York)
- 01904 726048

### Ophthalmology
- Consultant/Secretary via switchboard

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### Drug Tariff October 2018:

<table>
<thead>
<tr>
<th>Strength</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>25mg x 28</td>
<td>£1.58</td>
</tr>
<tr>
<td>50mg x 56</td>
<td>£2.25</td>
</tr>
</tbody>
</table>

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### References

1. Medicines complete BNF accessed 21st February 2018
3. Imuran SPC via www.medicines.org.uk accessed 21st February 2018

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This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the SPC (data sheet) or BNF for further prescribing information.

The original Microsoft Word file of this document is located on:
York Teaching Hospital NHS Foundation Trust Pharmacy Department X:\MEDICINES INFORMATION\Shared Care Guidelines\Approved Shared Care Guidelines\Shared Care Guidelines are also available electronically via [http://www.yorkandscarboroughformulary.nhs.uk/](http://www.yorkandscarboroughformulary.nhs.uk/)

Prepared by: Faisal Majothi / Jane Crewe

Checked by: Sally Kingscott, Rheumatology Specialist Nurse

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Approved by: York and Scarborough Medicines Commissioning Meeting