

## SHARED CARE PROTOCOL - AZATHIOPRINE AND MERCAPTOPURINE FOR PATIENTS WITHIN ADULT SERVICES (NON-TRANSPLANT INDICATIONS)

As well this protocol, please ensure that [summaries of product characteristics](#) (SPCs), [British national formulary](#) (BNF) or the [Medicines and Healthcare products Regulatory Agency](#) (MHRA) or [NICE](#) websites are reviewed for up-to-date information on any medicine.

### Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol ([section 2](#)) and communicated to primary care.
- Use a shared decision-making approach; discuss the benefits and risks of the treatment with the patient and provide the appropriate counselling (see [section 11](#)) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Explain where drugs are used outside their license.
- Assess for contraindications and cautions (see [section 4](#)) and interactions (see [section 7](#)).
- Conduct required baseline investigations, arrange, and review the results of any blood tests for the first 12 weeks of treatment (see [section 8](#)).
- Initiate, assess response and optimise treatment as outlined in [section 5](#). Transfer to primary care is normally after the patient has been treated for 3 months and with satisfactory investigation results for at least 4 weeks.
- Explain the intention to share care for drug prescribing and monitoring to the patient. Explain the process and the potential timescales for this.
- Prescribe sufficient medication considering any delays in communication to general practice to enable transfer to primary care, including where there are unforeseen delays to transfer of care
- Once treatment is established and stabilised, request shared care from the primary care provider either using the documentation in Appendix 1 or by clinic letter detailing the diagnosis, current and ongoing dose, baseline, and most recent test results, confirm the

monitoring schedule and when the next monitoring is required. Include contact information ([section 13](#)).

- Conduct the required monitoring in [section 8](#) and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in [section 9](#) remains appropriate.
- Ensure there is a mechanism to receive rapid referral of a patient from primary care in the event of deteriorating clinical condition, non-adherence to monitoring requirements or need for further advice and support.
- Give advice to primary care on continuing treatment if a woman becomes or wishes to become pregnant or breastfeed. (See [section 12](#))
- Provide advice to primary care on the management of adverse effects if required.
- Patients should be regularly reviewed, and the risk benefit re-assessed as patients get significantly older and frail with increasing co-morbidities and polypharmacy. Dose optimisation and/or dose tapering should be considered if clinically appropriate aiming for the lowest effective dose.
- Advise primary care if treatment should be discontinued.

### Primary care responsibilities

- Respond to the request from the specialist for shared care if further clarification or a refusal is intended. Acceptance of shared care is implied by nil response. It is asked that this be undertaken within 14 days of the request being received where possible.
- If accepted, prescribe ongoing treatment as detailed in the specialists' request and as per [section 5](#) taking into any account potential drug interactions in [section 7](#).
- Assess for interactions with azathioprine or mercaptopurine when starting new medicines (see [section 7](#)). It is recommended to add allopurinol as an allergy warning to the patient's record to alert for any co-prescribing.
- Adjust the dose of azathioprine or mercaptopurine prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in [section 9](#). Communicate any abnormal results to the specialist.
- Manage any adverse effects as detailed in [section 10](#) and discuss with specialist team when required.
- Stop azathioprine or mercaptopurine and discuss urgently with the specialist if bone marrow suppression is suspected.
- Contact the specialist team for advice if the patient becomes or plans to become pregnant.

- Stop treatment as advised by the specialist. If the decision to stop treatment is made in primary care e.g. due to increased frailty index, to let the specialist team know so they can arrange a review as needed.

### **Patient and/or carer responsibilities**

- Take azathioprine or mercaptopurine as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
- Maintain engagement with specialist and primary care; attending regularly for monitoring and review appointments as requested; keeping their contact details up to date with both teams. Be aware that medicines may be stopped if they do not attend for the blood monitoring or review appointments.
- Advised to take part in all national screening programmes e.g., for breast, bowel, and cervical cancers.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in [section 11](#).
- Report the use of any over the counter medications to their prescriber and be aware they should discuss the use of azathioprine or mercaptopurine with their pharmacist before purchasing any OTC medicines.
- Tell anyone who prescribes them a medicine that they are taking azathioprine or mercaptopurine.
- Inform the specialist or primary care prescriber as soon as possible if they become pregnant or wish to become pregnant.

## 1. Background

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This shared care guideline has been prepared to support the transfer of responsibility for prescribing from secondary to primary care. Shared Care is only appropriate if it provides the optimum solution for the patient.

Azathioprine and mercaptopurine are disease modifying anti-rheumatic drugs (DMARDs). They are used as immunosuppressant anti-metabolites either alone or, more commonly, in combination with other agents (usually corticosteroids) to 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.

Azathioprine and mercaptopurine are not licensed for all the conditions they are used to treat, as noted below. However, their use for the indications below are established and supported by various sources and bodies including the BNF, NICE, British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR), British Association of Dermatologists (BAD), British Thoracic Society (BTS), Association of British Neurologists (ABN) and British Society of Gastroenterology (BSG).

This shared care protocol does not cover for transplant or oncology indications, or treatment of people less than 18 years old.

## 2. Indications

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### **Azathioprine**

The licensed indications for azathioprine include:

- Auto-immune chronic active hepatitis
- Auto-immune haemolytic anaemia
- Chronic refractory idiopathic thrombocytopenic purpura
- Dermatomyositis
- Inflammatory bowel disease (IBD)
- Pemphigus vulgaris
- Polyarteritis nodosa
- Polymyositis
- Pyoderma gangrenosum
- Rheumatoid arthritis

- Systemic lupus erythematosus (SLE)

Licensed indications vary with brand. See relevant summary of product characteristics ([see SPC](#)) for full details.

This shared care protocol also includes treatment of chronic inflammatory conditions where off-label use of azathioprine is appropriate, including, but not limited to the following specialities and conditions. The initiating specialist must specify the indication for each patient when initiating shared care and clearly state when use is off label.

- Dermatology (e.g. severe eczema)
- Neurology (e.g. myasthenia gravis, demyelinating conditions)
- Ophthalmology (e.g. uveitis, scleritis)
- Oral medicine (e.g. Behçet's disease, refractory inflammatory oral disease)
- Renal medicine (e.g. immune-mediated nephritis)
- Respiratory disease (e.g. interstitial lung disease)
- Rheumatology (e.g. inflammatory arthritis, connective tissue disease, vasculitis, giant cell arteritis)
- Gastroenterology (e.g. refractory coeliac disease)

### **Mercaptopurine**

This shared care protocol includes treatment of chronic inflammatory conditions where off-label use of mercaptopurine is appropriate, including, but not limited to the following conditions. The specialist must specify the indication for each patient when initiating shared care and clearly state when use is off label:

- Inflammatory bowel disease
- Autoimmune encephalitides
- Autoimmune hepatitis

This shared care protocol applies to adults aged 18 and over. It does not include use of azathioprine or mercaptopurine for transplant or oncology indications.

### 3. **Locally agreed off-label use**

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Nil further identified- see above

## 4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see [BNF](#) & [SPC](#) for comprehensive information.

### Contraindications:

- Known hypersensitivity to the active substance or any excipients. Hypersensitivity to 6-mercaptopurine (6-MP) should alert the prescriber to probable hypersensitivity to azathioprine.
- Absent or very low thiopurine methyltransferase (TPMT) activity – risk of life-threatening pancytopenia.

### Cautions:

- Live vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever): should be avoided in patients taking azathioprine at a dose greater than 3 mg/kg/day, or mercaptopurine greater than 1.5 mg/kg/day. Please refer to the [Green Book Chapter 6](#) for current advice regarding the use of live vaccines in patients taking immune modulators. Contact the specialist if further guidance is required.
- Patients with active/history of pancreatitis.
- Concomitant prescribing of allopurinol: A 75% dose reduction of azathioprine/mercaptopurine is required, see [section 7](#). It is recommended to add allopurinol as an allergy warning to the patient's record to alert for any co-prescribing.
- Patients receiving azathioprine or mercaptopurine are at an increased risk of developing lymphoproliferative disorders and other malignancies, notably skin cancers, sarcomas, and uterine cervical cancer in situ. Exposure to sunlight and UV light should be limited and patients should wear protective clothing and use a sunscreen with a high protection factor to minimize the risk of skin cancer and photosensitivity
- Patients with low thiopurine methyltransferase (TPMT) activity are at increased risk of myelosuppression. Substantial dose reduction is required.
- Severe infection.
- Severely impaired hepatic or bone marrow function.
- Pregnancy and breastfeeding (see [section 12](#)).

Treatment may need to be monitored more frequently in the following:

- Frail or elderly – consider reduced/ minimum effective dose.
- Impaired renal function
- Mild/moderately impaired hepatic function
- Mild/moderately impaired bone marrow function

## 5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after at least 12 weeks, and when the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

There is a wide dose range depending on the indication. The selected dose will be tailored to the individual patient and decided by the specialist.

**The initial stabilisation period must be prescribed by the initiating specialist.**

Transfer of monitoring and prescribing to primary care is usually after 3 months. The duration of treatment will be determined by the specialist based on clinical response and tolerability.

### **Maintenance dose (following initial stabilisation):**

Usual dose range:

- **Azathioprine: 0.5–3 mg/kg daily**, adjusted according to response.
- **Mercaptopurine: 1-1.5mg/kg daily**, adjusted according to response.

Some patients may respond to lower doses. Please note patients may be initiated on more than one DMARD.

**The initial maintenance dose must be prescribed by the initiating specialist.**

### **Conditions requiring dose adjustment:**

Lower doses may be required if there is significant renal or hepatic impairment, in elderly patients, and in patients with mild/moderately impaired bone marrow function, TPMT deficiency or NUDT15 mutation ([see SPC](#)).

**6. Pharmaceutical aspects**[Back to top](#)

Route of administration:	Oral
Formulation:	<p>Azathioprine 25mg and 50mg tablets</p> <p>Azathioprine 10 mg/mL oral suspension (Jayempi®)- this is significantly more expensive than the tablets</p> <p>Mercaptopurine 50mg tablets</p> <p>Mercaptopurine 20mg/ml oral suspension (Xaluprine®) this is significantly more expensive than the tablets</p>
Administration details:	<p>The tablets should be swallowed whole and not split / crushed.</p> <p>Can be taken either with or without food, but patients should standardise which method is chosen. Tablets should be taken at least 1 hour before or 2 hours after milk or dairy products.</p> <p>Taking with or after food may relieve nausea, however the oral absorption of azathioprine or mercaptopurine may be reduced. Consideration should be given to monitoring therapeutic efficacy more closely if patient is taking azathioprine or mercaptopurine consistently with food.</p> <p>For azathioprine or mercaptopurine oral suspension, the bottle should be shaken vigorously for at least 30 seconds to ensure the suspension is well mixed. For both products two dosing syringes are provided for accurate measurement of the prescribed dose of the oral suspension. It is recommended that the healthcare professional advises the patient or carer which syringe to use to ensure that the correct volume is administered. To assist accurate and consistent dose delivery to the stomach water should be taken after each dose</p> <p>Mercaptopurine displays diurnal variation in pharmacokinetics and efficacy. Administration in the evening compared to morning administration may lower the risk of relapse. Therefore, the daily dose of mercaptopurine should be taken in the evening</p>

Other important information:	<p>Providing the film coating of azathioprine tablets remains intact, there is no risk or additional precautions required when handling tablets.</p> <p>Azathioprine and mercaptopurine are cytotoxic. It is recommended that they are handled following local recommendations for the handling and disposal of cytotoxic agents. Anyone handling the tablets should wash their hands immediately afterwards.</p> <p>Mercaptopurine tablets and oral suspension are not bioequivalent with respect to peak plasma concentration; increased haematological monitoring is advised if switching between formulations.</p> <p>When prescribing mercaptopurine, remain vigilant with regards to the similarity in name with mercaptamine.</p>
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## 7. Significant medicine interactions

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The following list is not exhaustive. Please see [BNF](#) or [SPC](#) for comprehensive information and recommended management.

### The following drugs must not be prescribed without consultation with the specialist:

- **Allopurinol** has the potential to cause thiopurine toxicity and should be avoided, except with specialist input. Allopurinol may be recommended in combination with thiopurines by the specialist for IBD patients, particularly in those who are unable to tolerate to or do not respond to treatment with a thiopurine alone. The dose of azathioprine or mercaptopurine should be reduced by 75% if used concurrently with allopurinol. If considering prescribing allopurinol, discuss with the specialist for advice and a dose adjustment. It is recommended to add allopurinol as an allergy warning to the patient's record to alert for any co-prescribing.
- **Febuxostat** has the potential to cause thiopurine toxicity; avoid in combination with azathioprine or mercaptopurine.
- **Live vaccines** (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever) can be given to patients on stable long term low dose corticosteroid therapy (defined as  $\leq 20\text{mg}$  prednisolone per day for  $>14$  days) alone or in combination with low dose non-biological oral immune modulating drugs (e.g. azathioprine up to  $3\text{mg/kg/day}$  or mercaptopurine up to  $1.5\text{mg/kg/day}$ ). Clinician discretion is advised. Please refer to the [Green Book Chapter 6](#) for current advice, and advice for patients taking higher doses.
- **Warfarin** – thiopurines may reduce anticoagulant effects of warfarin.
- **Co-trimoxazole / trimethoprim** – possible increased risk of haematological toxicity, however evidence is conflicting, and this combination is often used in practice.

- **Clozapine** - avoid due to increased risk of agranulocytosis.
- **Ribavirin** - increased risk of haematological toxicity when azathioprine given concurrently and this combination should be avoided.
- **Aminosalicylates** (sulfasalazine, mesalazine or olsalazine) - increased risk of haematological toxicity with concomitant thiopurine due to TPMT inhibition. Dose adjustment of azathioprine or mercaptopurine and additional monitoring of FBC may be required.

**The following drugs may be prescribed with caution:**

- **ACE inhibitors** - increase the risk of anaemia and or leukopenia.
- **Cimetidine and indomethacin** - concomitant administration of thiopurines may increase the risk of myelosuppression.

## 8. Baseline investigations, initial monitoring, and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

### Baseline investigations:

- Height and weight
- Blood pressure
- Full blood count (FBC)
- Urea and electrolytes (U&Es) & creatinine clearance (CrCl)
- Alanine aminotransferase (ALT) and albumin
- Baseline thiopurine methyl transferase (TPMT) status
- Screening for viral infections as per local policy, e.g. HIV, hepatitis B and C, varicella zoster, Epstein Barr virus, cytomegalovirus
- Screening for lung disease, including tuberculosis, should be undertaken at clinician discretion on a case-by-case basis
- Confirm cervical screening is up to date. Provide or request appropriate vaccination prior to treatment initiation, according to local arrangements (e.g. pneumococcal, shingles, influenza, COVID-19)

### Initial monitoring and at dose change:

To be repeated every 2 weeks until the dose has been stable for 6 weeks, then monthly for 3 months. After which, the transfer of prescribing to primary care should normally only take place when the patient has received a stable dose for at least 4 weeks and their blood and physical tests results have been satisfactory:

- FBC
- U&Es, including creatinine and CrCl
- ALT and albumin (LFTs)
- Rheumatology patients: C-reactive protein (CRP) &/or erythrocyte sedimentation rate (ESR) (for monitoring disease activity/outcomes rather than for safety- this may continue to be monitored by the rheumatology team but will not be part of the primary care safety monitoring parameters)

Following a dose increase repeat every 2 weeks until the dose has been stable for 6 weeks, then revert to previous schedule. More frequent monitoring is appropriate in patients at higher risk of toxicity.

#### **Ongoing monitoring:**

The specialist will retain the responsibility for monitoring the patient's ongoing response to treatment and advise if a dose change or treatment cessation is appropriate. This should usually be undertaken annually unless the patient has been stabilised on treatment for a long time and considered suitable for patient initiated follow up (PIFU). Access to the specialist team for advice and guidance should still be available if the patient is enrolled with PIFU.

After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in [section 9](#) remains appropriate.

## 9. Ongoing safety monitoring requirements to be undertaken by primary care

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See [section 10](#) for further guidance on management of adverse effects/responding to monitoring results.

Monitoring and actions	Frequency
<ul style="list-style-type: none"> <li>FBC</li> <li>U&amp;Es including creatinine and CrCl</li> <li>LFTs/ Albumin</li> </ul>	<p>Every 12 weeks. Where necessary seek advice on increased frequency of monitoring on a case-by-case basis.</p> <p><b>The exact frequency of monitoring to be communicated by the specialist in all cases.</b></p>
<ul style="list-style-type: none"> <li>Shingles vaccination- immunocompromised patients aged 50 years and over are eligible for the shingles vaccine (Shingrix®)</li> <li>The eligible age for Immunocompetent patients will change in a phased implementation over a 10-year period</li> </ul> <p>Specialist input may be required. If patient is taking additional DMARDs, check advice for all drugs. Please refer to <a href="#">Green Book Chapter 6</a> and <a href="#">Chapter 28a (Shingles)</a> for further details.</p> <p><b>Annual</b> influenza (<a href="#">The Green Book, Chapter 19</a>) vaccinations are recommended</p> <p>COVID-19 vaccination is safe and recommended (see <a href="#">The Green Book, Chapter 14a</a>).</p> <p>Repeat pneumococcal vaccine may be indicated. See <a href="#">Green Book Chapter 25</a> for advice.</p>	<ul style="list-style-type: none"> <li>Shingles vaccination: one-off.</li> <li>Influenza vaccination: annual. It is advisable to add the patient to the influenza vaccine list.</li> <li>COVID-19 vaccination as per national schedule.</li> </ul>
<p><b>(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.</b></p>	

## 10. Adverse effects and other management

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**Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard)**

For information on incidence of ADRs see relevant summaries of product characteristics

Result	Action for primary care
<b>As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance</b>	
<b>Full blood count:</b> <ul style="list-style-type: none"> <li>White blood cells less than <math>3.5 \times 10^9/L</math></li> <li>Lymphocytes less than <math>0.5 \times 10^9/L</math></li> <li>Neutrophils less than <math>1.6 \times 10^9/L</math></li> <li>Platelets less than <math>140 \times 10^9/L</math></li> <li>Eosinophilia greater than <math>0.5 \times 10^9/L</math></li> </ul>	<b>Discuss urgently with specialist team and consider interruption.</b> NB: Isolated lymphopenia or eosinophilia is often a feature of the underlying autoimmune indication and is rarely an indication to discontinue azathioprine.
Mean cell volume $>105$ fl NB: Reversible, dose-related increases in mean corpuscular volume are a known effect of thiopurines.	Consider interruption in treatment if there is a significant increase from baseline. Check serum folate, B12, alcohol history and TSH and treat any underlying abnormality. If results of these additional investigations are normal discuss with specialist team urgently.
Signs or symptoms of bone marrow suppression, e.g. unexplained bleeding or bruising with or without sore throat, mouth ulcers	Check FBC immediately, withhold treatment while awaiting results, and discuss with the specialist team. See haematological monitoring above.
<b>Infections:</b> Systemic infection requiring antibiotics	Temporarily withhold thiopurine until the patient has recovered. Consider additional investigations (e.g. FBC), if clinically appropriate. Contact specialist for advice as needed

<b>Liver function tests:</b> ALT >100 units/L, or any sudden increases (e.g. double of baseline), OR unexplained fall in serum albumin <30g/L Jaundice	Withhold and discuss with specialist team. When used for hepatology indications, continue treatment, and discuss with specialist urgently. Check any other reason for risk of hepatic dysfunction such as alcohol history and drug interactions, including OTC or complementary medication.
<b>Renal function:</b> Creatinine increases of greater than 30% from baseline in the last 12 months, or CrCl reduces to <60ml/min	Use clinical judgement and repeat in 1 week. Rule out other causes. If still more than 30% from baseline withhold and discuss with specialist team
<b>Gastrointestinal disorders:</b> Nausea	Review for reversible causes and treat as appropriate. Advise patient to take with food. If no improvement contact specialist team.
Suspected pancreatitis	Withhold and discuss with specialist team.

## 11. Advice to patients and carers

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The specialist will counsel the patient regarding the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

### **The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:**

Signs or symptoms indicating haematological toxicity, e.g. sore throat, infection, unexplained or abnormal bruising or bleeding.

Signs or symptoms of pancreatitis, e.g. abdominal pain, nausea, or vomiting

Signs of symptoms of hepatic toxicity, e.g. Jaundice (yellowing of the skin or whites of the eyes)

### **The patient should be advised to:**

- What shared care means for their treatment, what to expect, and their responsibilities under shared care.

- During a serious systemic infection azathioprine or mercaptopurine should be temporarily discontinued until the patient has recovered from the infection.
- That vaccination in line with current national advice (e.g. for COVID-19, influenza) is safe and recommended.
- Tell anyone who prescribes them a medicine that they are taking azathioprine or mercaptopurine. Always ask a pharmacist before purchasing any medicines over the counter, including herbal remedies, and ask if they are safe.
- To inform their specialist or primary care prescriber promptly if pregnancy occurs or is planned.
- All women aged 25-64 years old should be encouraged to participate in national cervical cancer screening programmes. There is no need to attend more frequently than recommended.
- Patients have a small increased risk of skin cancers so should be advised to wear high factor sunscreen and to wear a hat and protective clothing when in strong sunshine. Sun beds should be avoided. Patients should be advised to carry out regular self-examination of the skin and report if there are any new lesions and/or changes to skin.
- Patients taking azathioprine at a dose of 3 mg/kg or more, or mercaptopurine at a dose of 1.5 mg/kg/day or more should be advised to avoid contact with people with chicken pox or shingles and report any such contact urgently to their primary care prescriber. If the patient is exposed, contact the specialist for advice. For detailed advice on risk assessment and post exposure prophylaxis following exposure to chicken pox and shingles, see:

the [Green Book \(Chapter 34\)](#) [Guidelines on post exposure prophylaxis \(PEP\) for varicella or shingles \(October 2024\)](#) - GOV.UK

#### Patient information:

- General information: <https://www.nhs.uk/medicines/azathioprine/>
- General information: <https://patient.info/medicine/azathioprine-azapress-imuran>
- Rheumatology: <https://www.versusarthritis.org/about-arthritis/treatments/drugs/azathioprine/>
- Dermatology: [British Association of Dermatologists](#) Azathioprine patient information leaflet Patient information leaflets are also available from <https://www.medicines.org.uk/emc/search?q=azathioprine>

#### Gastroenterology:

- <https://www.crohnsandcolitis.org.uk/about-crohns-and-colitis/publications/azathioprine-mercaptopurine>
- <https://gutscharity.org.uk/advice-and-information/conditions/crohns-disease/>

- <https://gutscharity.org.uk/advice-and-information/conditions/ulcerative-colitis/>

## 12. Pregnancy, paternal exposure, and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

**All patients should be informed of the risks and benefits of taking this medicine during pregnancy and breastfeeding. The specialist team should be contacted if a patient becomes pregnant or is planning to become pregnant or breastfeed.**

### **Pregnancy:**

The [British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding](#) 2022 advises that azathioprine is compatible throughout pregnancy

Current available data do not suggest that mercaptopurine exposure during pregnancy increases the risk of miscarriage, congenital malformation, intrauterine death, foetal growth restriction, or preterm delivery but the data are limited for some outcomes. A careful assessment of risk versus benefit should be made before mercaptopurine is prescribed to patients who are pregnant.

The [British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease](#) advises that both maintenance and flares can be treated as normal with thiopurines (azathioprine and mercaptopurine) during pregnancy.

Prescribers should be aware of the recent MHRA warning about the risk of intrahepatic cholestasis during pregnancy and advise patients to report symptoms of cholestasis of pregnancy which include intense itching without a rash, nausea, and loss of appetite.

[Thiopurines and intrahepatic cholestasis of pregnancy - GOV.UK](#)

### **Information for healthcare professionals:**

<https://www.medicinesinpregnancy.org/bumps/monographs/USE-OF-AZATHIOPRINE-OR-MERCAPTOPURINE-IN-PREGNANCY/>

**Information for patients and carers:** [Azathioprine / Mercaptopurine in Pregnancy](#)

### **Breastfeeding:**

Azathioprine is compatible with breastfeeding, although the active metabolite mercaptopurine is present in breast milk. A risk versus benefit assessment is advised. If used during breastfeeding, monitor for signs of infection or immunosuppression. If high doses of azathioprine are used, monitor infant blood counts. If mercaptopurine is used, monitor infant's blood count and liver function.

The [British Society for Rheumatology updated guideline on prescribing drugs in pregnancy and breastfeeding 2022](#) advises azathioprine is compatible with breastmilk exposure

Information for healthcare professionals:

- <https://www.sps.nhs.uk/medicines/azathioprine/>
- <https://www.sps.nhs.uk/medicines/mercaptopurine/>

### **Paternal exposure:**

Azathioprine and mercaptopurine are compatible with paternal exposure. There is currently no evidence of adverse foetal effects relating to paternal use.

The [British Society for Rheumatology updated guideline 2022](#) advises based on limited evidence that paternal exposure to azathioprine is compatible with pregnancy

- Information for healthcare professionals:  
<https://www.medicinesinpregnancy.org/bumps/monographs/PATERNAL-USE-OF-AZATHIOPRINE-OR-MERCAPTOPURINE/>

## **13. Specialist contact information**

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Please approach the patient's named secondary care clinician via the usual method of communication, this may be via letter or if more urgent via advice and guidance

Renal medicine (e.g. immune-mediated nephritis)

Respiratory disease (e.g. interstitial lung disease)

### **Rheumatology**

- Advice and Guidance.
- Consultant Connect - during office hours
- UHD switchboard – on-call rheumatologist during office hours
- Rheumatology advice line: This is not a direct connection (answerphone service) and is not for emergency calls. It requires patients/clinicians to leave a message via the

answerphone service. The messages will be logged, triaged and answered in order of need.

### **Gastroenterology (UHD and DCH)**

- Advice and Guidance
- Consultant Connect- during office hours
- IBD advice line: This is not a direct connection (answerphone service) and is not for emergency calls. It requires patients/clinicians to leave a message via the answerphone service. The messages will be logged, triaged and answered in order of need.

### **Neurology**

- Advice and Guidance
- Consultant Connect- during office hours
- UHD Switchboard- on-call neurologist during office hours

### **Dermatology (UHD and DCH)**

- Advice and Guidance (please mark as urgent)
- Via switchboard to the on-call dermatology doctor

### **Respiratory (UHD and DCH)**

- Advice and Guidance

## **14. Additional information**

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Where patient care is transferred from one specialist service or GP practice to another the GP is responsible for letting the specialist team know if they are unhappy with continuing the shared care. All involved healthcare professionals should ensure a prompt transfer of care that includes effective information sharing and continued access to the medicines by the patient during the transition.

## **15. References**

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- eBNF accessed via [Azathioprine | Drugs | BNF | NICE](#) and [Mercaptopurine | Drugs | BNF | NICE](#)
- Azathioprine 50mg tablets (Imuran®). Aspen. Last updated 12<sup>th</sup> August 2024. Accessed via <https://www.medicines.org.uk/emc/product/3823>
- Mercaptopurine 50mg tablets. Aspen. Last updated 20<sup>th</sup> December 2024. Accessed via <https://www.medicines.org.uk/emc/product/4655/smpc>

- Mercaptopurine 20mg/ml oral suspension (Xaluprine®). Nova Laboratories Ltd. Last updated 1<sup>st</sup> August 2024. Accessed via <https://www.medicines.org.uk/emc/product/2949/smpc>.
- British Society of Rheumatology and British Health Professionals in Rheumatology. 2017. [Guidelines for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs](#).
- [British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids | Rheumatology | Oxford Academic 2022](#)
- British Association of Dermatologists. 2011. [British Association of Dermatologists' guidelines for the safe and effective prescribing of azathioprine 2011 | British Journal of Dermatology | Oxford Academic](#) .
- [British Association of Dermatologists](#) Azathioprine patient information leaflet
- British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. 2008. [Interstitial lung disease guideline](#) (archived).
- British Society of Gastroenterology. 2019. [Consensus guidelines on the management of inflammatory bowel disease in adults](#).
- British Society of Gastroenterology. 2011. [Autoimmune Hepatitis Care Guidelines | BSG](#).
- Public Health England. [Immunisation against infectious disease: The Green Book](#). Accessed 01/10/2020.
- Specialist Pharmacy Service. Lactation Safety Information: azathioprine. Reviewed 2<sup>nd</sup> July 2024. Accessed via <https://www.sps.nhs.uk/medicines/>
- Specialist Pharmacy Service. Lactation Safety Information: mercaptopurine. Reviewed 20<sup>th</sup> September 2023. Accessed via <https://www.sps.nhs.uk/medicines/mercaptopurine/>
- UK Teratology Information Service. Toxbase monograph: Azathioprine or mercaptopurine in pregnancy. December 2019. Accessed via [www.toxbase.org](http://www.toxbase.org) on 06/10/2021.
- UK Teratology Information Service. Toxbase monograph: Paternal use of azathioprine or mercaptopurine. December 2019. Accessed via [www.toxbase.org](http://www.toxbase.org) on 06/10/2021.
- The Renal Drug Database. Mercaptopurine monograph. Accessed via <https://renaldrugdatabase.com/monographs/mercaptopurine> on 09/12/21
- NICE Guidance: Crohn's disease: management (NG129) May 2019. Accessed via: <https://www.nice.org.uk/guidance/ng129>
- NICE Guidance: Ulcerative colitis: management (NG130) May 2019. Accessed via <https://www.nice.org.uk/guidance/ng130> on 09/12/21

## 16. Other relevant national guidance

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- Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from <https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/>
- NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from <https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/>
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from <https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care>
- NICE NG197: Shared decision making. Last updated June 2021. <https://www.nice.org.uk/guidance/ng197/>.

## 17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

**Via the usual methods**

## Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear [insert Primary Care Prescriber's name]

Patient name: [insert patient's name]

Date of birth: [insert date of birth]

NHS Number: [insert NHS Number]

Diagnosis: [insert diagnosis]

As per the agreed [insert APC name] shared care protocol for [insert medicine name] the treatment of [insert indication], this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care, and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened regarding this treatment:

	Specialist to complete
<i>The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:</i>	
<i>Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory</i>	Yes / No
<i>The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care</i>	Yes / No
<i>The risks and benefits of treatment have been explained to the patient</i>	Yes / No
<i>The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed</i>	Yes / No
<i>The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments</i>	Yes / No
<i>I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)</i>	Yes / No
<i>I have included with the letter copies of the information the patient has received</i>	Yes / No
<i>I have provided the patient with sufficient medication to last until</i>	
<i>I have arranged a follow up with this patient in the following timescale</i>	

Treatment was started on, [insert date started] and the current dose is [insert dose and frequency].

If you agree, please undertake monitoring and treatment from [insert date] NB: date must be at least 1 month from initiation of treatment.

The next blood monitoring is due on [insert date] and should be continued in line with the shared care guideline.

Please respond to this request for shared care, in writing, within 14 days of the request being made where possible.

**Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist) Not routinely used in the Dorset system; acceptance of shared care is implied by a nil return.**

**Primary Care Prescriber Response**

Dear *[insert Doctor's name]*  
Patient *[insert Patient's name]*  
NHS Number *[insert NHS Number]*  
Identifier *[insert patient's date of birth and/or address]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: \_\_\_\_\_ Date:  
\_\_\_\_\_

Primary Care Prescriber address/practice stamp

## Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

**Re:**

Patient *[insert Patient's name]*  
 NHS Number *[insert NHS Number]*  
 Identifier *[insert patient's date of birth and/or address]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety NHS *[insert CCG name]*, in conjunction with local acute trusts have classified *[insert medicine name]* as a Shared Care drug and requires a number of conditions to be met before transfer can be made to primary care.

**I regret to inform you that in this instance I am unable to take on responsibility due to the following:**

		Tick which applies
1.	<p><b>The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care</b></p> <p>As the patient's primary care prescriber, I do not feel clinically confident to manage this patient's condition because <i>[insert reason]</i>. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice.</p> <p><b>I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.</b></p>	
2.	<p><b>The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement</b></p> <p>As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMO or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time.</p> <p><b>Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you</b></p>	

3.	<p><b>A minimum duration of supply by the initiating clinician</b></p> <p>As the patient has not had the minimum supply of medication to be provided by the initiating specialist, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible to provide them with the medication that you have recommended.</p> <p><b><i>Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.</i></b></p>	
4.	<p><b>Initiation and optimisation by the initiating specialist</b></p> <p>As the patient has not been optimised on this medication, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible to provide them with the medication that you have recommended.</p> <p><b><i>Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.</i></b></p>	
5.	<p><b>Shared Care Protocol not received</b></p> <p>As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed.</p> <p>For this reason, I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible to provide them with the medication that you have recommended.</p> <p><b><i>Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.</i></b></p>	
6.	<p><b>Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)</b></p>	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs

would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs.” In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible

Yours sincerely

**Primary Care Prescriber signature:** \_\_\_\_\_

**Date:** \_\_\_\_\_

**Primary Care Prescriber address/practice stamp**