

DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE
SHARED CARE AGREEMENT

Azathioprine/6-mercaptopurine for patients 16+ years

1. REFERRAL CRITERIA

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring
- When transfer agreed the patient will be given a supply of Azathioprine/6-mercaptopurine sufficient for 4 weeks maintenance therapy.

2. AREAS OF RESPONSIBILITY

GP responsibilities	Consultant responsibilities
<ol style="list-style-type: none"> 1. If NOT participating in shared care reply to the request from the consultant/specialist as soon as practicable (see appendix 1) 2. Ensure compatibility with other concomitant medication. 3. Prescribe the dose and formulation recommended. 4. Perform monitoring tests as specified in section vii. 5. Adjust the dose as advised by the specialist. 6. Stop treatment on the advice of the specialist or immediately if any urgent need to stop treatment arises. 7. Ensure the patient is offered an annual flu vaccination and a one off pneumococcal vaccination. Live vaccinations can be used with caution in patients taking Azathioprine up to 3.0 mg/kg/day or 6-mercaptopurin up to 1.5mg/kg/day, as per green book chapter 6, see section 4 iv 8. Report any adverse effects to the referring specialist and the MHRA yellow card scheme 	<ol style="list-style-type: none"> 1. Discuss the possible benefits and side effects of treatment with the patient. 2. Perform baseline tests (as recommended in section vii) 3. Provide results of baseline tests 4. Prescribe Azathioprine/6-mercaptopurine for the first three months or until medication monitoring is stable. 5. To contact patient's GP to request prescribing under shared care and send a link to or copy of the shared care protocol. 6. Recommend dose of the drug and frequency of monitoring as per section 4vii. 7. Annually review the patient and advise the GP promptly on when to adjust the dose, stop treatment or consult with the specialist. 8. Ensure that clear backup arrangements exist for GPs to obtain advice and support. 9. Report any adverse effects to the MHRA yellow card scheme and GP 10. Advise on the suitability for e.g. herpes zoster vaccination in accordance with national screening programme 11. Communicate any dose increase to the GP and transfer monitoring to GP when the patient's condition is stable or predictable following 6 weeks period of titration. .
<p>Patient responsibilities</p> <ul style="list-style-type: none"> • Report to the specialist or GP if there is not a clear understanding of the treatment and share any concerns in relation to treatment. • Inform specialist or GP of any other medication being taken including over-the-counter products. • Report any adverse effects or warning symptoms to the specialist or GP whilst taking the drug. 	

3. COMMUNICATION AND SUPPORT

<p>i. Hospital contacts: <u>Chesterfield Royal Hospital NHS Foundation Trust</u> Contact the referring consultant/nurse via switchboard: 01246 277271 Nurse advice line: 01246 513097 Available Monday-Thursday 9am-4:30pm, Friday 9am- 12:30pm <u>University Hospital of Derby and Burton NHS Foundation Trust</u> <u>Derby sites</u> <u>Rheumatology</u> Rheumatology helpline: 01332 787710 <u>Gastroenterology</u> IBD helpline: 01332 785504 Consultant/specialist nurse via switchboard: 01332 340131 <u>Renal</u> Specialist Pharmacist: 07500 976569 If unable to contact the specialist renal pharmacist, consultants secretaries can be contacted: 01332 789344 <u>Dermatology</u> Consultant/specialist nurse via switchboard: 01332 265500 <u>Respiratory</u> Consultant via switchboard: 01332 340131 <u>Neurology</u> Consultant via neurology secretaries 01332 786478/783548 or email:dhft.neurologysecretaries@nhs.net <u>Burton sites</u> Switchboard: 01283 511511/566333 <u>Rheumatology</u> Consultants; Dr R Laximinarayan ext. 3167 Dr S Das/ Dr D Ray ext. 3211/3247 Clinical Rheumatology Nurse Specialist ext. 4112 bhft.rheumatologynurses@nhs.net <u>Gastroenterology</u> Consultants: Drs Palejwala/Dor ext 3004; Dr Watmough/Guerra ext 3002. IBD nurse helpline: ext 5854 (voicemail service only) Bleep:590 dhft.ibdcns@nhs.net</p>	<p>ii. Out of hours contacts and procedures: <u>Chesterfield</u> Contact the on-call Medic for the relevant speciality via switchboard: 01246 277271 <u>Derby</u> Pharmacy, UHDB, ask for on-call pharmacist via switchboard: 01332 340131 Messages can be left on the Derby Rheumatology nurse advice line: 01332 787710 The aim is to address these next working day <u>Burton</u> 01283 511511 / 566333 ask for on-call pharmacist via switchboard Messages can be left on the nurse advice line out of hours. 01283 511511 ext 4112 (Rheum) / 5854 (Gastro) If the advice line is not staffed, messages may be left 24 hours a day. The team aim to respond at latest within two working days. The specialist nurses may also be bleeped via switchboard for urgent enquiries.</p>
<p>iii. Specialist support/resources available to GP including patient information: <u>Rheumatology</u> British Society of Rheumatology Specialist website: http://www.rheumatology.org.uk/ Arthritis Research Campaign Patient Information website: http://www.arthritisresearchuk.org/arthritis-information.aspx Versus Arthritis Patient Information website: https://www.versusarthritis.org/media/12943/azathioprine-information-booklet-2019.pdf</p>	

4. CLINICAL INFORMATION

i. Prescribed Indications	Licensed Rheumatoid Arthritis Inflammatory intestinal disease (Ulcerative colitis and Crohn's disease) Dermatomyositis Autoimmune hepatitis Systemic lupus erythematosus	Unlicensed Vasculitis Psoriatic arthritis Autoimmune bullous disorder Cutaneous lupus Asthma Severe eczema Pemphigus vulgaris Neuromuscular junction disorder (Myasthenia Gravis, Lambert-Eaton myasthenic syndrome) Chronic inflammatory demyelination polyneuropathy Neuromyelitis Optica Spectrum Disorder Sarcoidosis Autoimmune encephalitis
ii. Therapeutic summary	Azathioprine is a pro-drug and is rapidly broken down to 6-mercaptopurine (6-MP) <i>in vivo</i> . It is an immunosuppressive drug which is effective in controlling several inflammatory and autoimmune diseases. For rheumatoid diseases improvement may take 2 to 3 months to occur.	
iii. Dose & Route of administration	<u>Azathioprine</u> Initially up to 2.5 mg/kg daily in divided doses, adjusted according to response, rarely more than 3 mg/kg daily; maintenance 1–3 mg/kg daily, consider withdrawal if no improvement within 3 months.	

	<p><u>Mercaptopurine</u> 6-Mercaptopurine for azathioprine intolerance: Crohn's/Ulcerative colitis Adult 1–1.5 mg/kg daily, some patients may respond to lower doses. For other indication see BNF or as per specialist advice</p> <p>Doses outside the recommended range may be considered with prior agreement with the specialist team and GP involved.</p> <p>Lower doses should be considered for frail elderly and patients with renal impairment.</p>
iv. Duration of treatment	<p>Indefinite but may be withdrawn after a prolonged period of disease remission in selected cases. It is also used as a rotational treatment in eczema.</p>
v. Adverse effects	<p>Dose related Bone marrow suppression, increased susceptibility to infections</p> <p>Hypersensitivity reactions (including malaise, dizziness, vomiting, diarrhoea, fever, rigors, rash, hypotension) – requires immediate withdrawal</p> <p>Increased risk of skin cancer - Patients should be aware of the need for adequate sun protection measures. This risk is greater in patients who have a history of previous treatment with PUVA.</p> <p>Hepatic impairment, pancreatitis (rare) Nausea Neoplasms benign and malignant (including cysts and polyps) Increased risk of developing non-Hodgkin's lymphomas and other malignancies Viral, fungal and bacterial infections</p>
vi. Immunisation	<ul style="list-style-type: none"> • Live vaccinations can be used with caution in azathioprine usage when less than 3.0 mg/kg/day or in mercaptopurin less than 1.5mg/kg/day as per Green book chapter 6. • In patients receiving azathioprine exposed to chickenpox or shingles, passive immunisation should be carried out using VZIG • Annual flu vaccination is recommended • One off Pneumococcal vaccination recommended
vii. Monitoring Requirements	<p><u>Before commencing immunosuppressant therapy</u></p> <ul style="list-style-type: none"> • Record patient's blood pressure, weight and height if clinically indicated. • Screening for lung disease should be undertaken at clinician discretion on a case-by-case basis. The extent of screening should be influenced more by a patient's clinical features and risk factors for lung disease (e.g. underlying autoimmune disease or smoking history) rather than subsequent immunomodulating choice. Pre-existing lung disease should not be considered an absolute contraindication to any immunomodulating medication. • Consultant to consider ECG where appropriate <i>especially when commencing medications associated with hypertension</i> • Screen for viral hepatitis B&C and HIV in all patients • Investigate patient medical history including co-morbidities and previous immunomodulating medication use. <p>For patients with inflammatory arthritis CRP/ESR may be done every 3 months (this is not done for dermatology patients). These tests are part of the assessment of the underlying rheumatic disease rather than a requirement for monitoring of immunomodulation therapy. The monitoring CRP/ESR may be coordinated between secondary and primary care on an individual basis.</p> <p>Individuals with severely reduced TPMT activity (<u>homozygous</u>) should not be prescribed AZATHIOPRINE as serious and fatal toxicity may occur within 6 weeks of starting the drug.</p> <p>For mild/moderate (heterozygous) deficiency serious adverse events may occur anytime and as late as 6 months after treatment commences. Serious Adverse Events can be exacerbated by minor infections or drug interactions (See Drug Interactions & contra-indications).</p> <p><u>Heterozygous</u> individuals should be prescribed Azathioprine/6-Mercaptopurine with caution and reduced drug dosage.</p> <p>Consultant/specialist monitoring schedule Baseline and 2 weekly until on a stable dose for at least 6 weeks</p> <ul style="list-style-type: none"> • FBC • ALT and/or AST and albumin • U&E including creatinine/calculated GFR

Annually review the patient and advise the GP promptly on when to adjust the dose, stop treatment or consult with the specialist

GP responsibility monitoring schedule*

In patients following the 6 weeks of dose stability conduct monthly monitoring as above for three months followed by three monthly monitoring thereafter of:

- FBC
- ALT and/or AST and albumin
- U&E including creatinine/ calculated GFR

Dosage increase

For dose **increase**, monitor 2 weekly until stable for 6 weeks. Dose and monitoring to be agreed with consultant

- FBC
 - ALT and/or AST and albumin
 - U&E including creatinine/ calculated GFR
- Monitoring to then continue at 3 monthly intervals

***The Neurology team may advise more frequent monitoring for patients heterozygote for TPMT (increased risk of toxicity).**

Restarting treatment after an abnormality has been detected:

If felt to be appropriate to restart azathioprine after an abnormality has settled, consider a lower dose (with discussion with specialist) and monitor as follows: repeat bloods in 2 weeks and then monthly for 3 months. Following this resume monitoring frequency to what it was prior to the abnormality.

Actions to be taken

<ol style="list-style-type: none"> 1. Immunosuppressants prescribed to prevent transplant rejection should not be stopped without discussion with a member of the specialist team. 2. In addition to responding to absolute values in laboratory tests, it is also relevant to observe trends in results (e.g gradual decreases in white blood cells (WBC) or albumin, or increasing liver enzymes) 3. Parameters below are to be used as a guide for clinicians rather than absolute values, where monitoring should be based on individualized basis. It is important to consider alternative explanations other than the immunomodulation agents, especially in patients who have been stable for prolonged periods 	
WBC <3.5 x10 ⁹ /l	Contact Specialist urgently and consider interruption
Neutrophils <1.6 x 10 ⁹ /l	Contact Specialist urgently and consider interruption
Platelets <140 x 10 ⁹ /l	Contact Specialist urgently and consider interruption
ALT and/or AST >100 U/l	Contact Specialist urgently and consider interruption
Unexplained fall in albumin <30g/l	Contact Specialist urgently and consider interruption
Mean cell volume >105 f/l	Withhold and check serum B12, folate & TFT and discuss with specialist team.
Creatinine increase for example >30% over 12 months and/or calculated GFR <60ml/min/1.73m ²	Contact Specialist urgently and consider interruption
Drug specific	
Abnormal bruising or severe sore throat	Withhold until FBC results available and discuss with the specialist team.
Rash or oral ulceration	Contact Specialist urgently and consider interruption
IgG	Contact Specialist urgently and consider interruption
CRP/ESR	Contact Specialist urgently and consider interruption

Note: specific monitoring of eosinophil counts has been removed, as historically eosinophilia was an important marker for identifying toxicity from only gold therapy. This has been agreed with local specialists.

NB – a rapidly increasing or decreasing trend in any value should prompt caution irrespective of actual value.

viii. Clinically relevant drug interactions

For a full list of

- ACE inhibitors
- Allopurinol
- Aminosalicylates
- Antiepileptic medications (Azathioprine may reduce the absorption of: Phenytoin,

interactions please refer to the BNF	Sodium Valproate and Carbamazepine.) <ul style="list-style-type: none"> • Febuxostat • Clozapine • Trimethoprim and Co-trimoxazole • Warfarin and other anticoagulants • See section vi for live vaccines.
ix. Contraindications and cautions	<p>Contraindications</p> <ul style="list-style-type: none"> • Suspected serious infection (requiring IV antibiotics or hospitalization) treatment should be discontinued. • Seriously impaired hepatic or bone marrow function • Pancreatitis TPMT see advice above. <p>*Pregnancy Azathioprine must not be used during pregnancy without careful assessment of risks and benefit. Patients will be assessed for suitability by the specialist on an individual basis. Follow specialist advice.</p> <p>*Breast Feeding 6-Mercaptopurine, the active metabolite of azathioprine, has been identified in the colostrum and breast-milk of women receiving azathioprine treatment. See SPS and follow specialist advice.</p> <p>*JAPC recognises difference between the contraindications from SPC advice and that given above. This follows consultant advice and literature (BSR guidance/ SPS advice)</p> <p>Cautions:</p> <ul style="list-style-type: none"> • 6-mercaptopurine should not be taken with milk or dairy products. Mercaptopurine should be taken at least 1 hour before or 2 hours after milk or dairy products. • TPMT deficiency: may be associated with delayed haematotoxicity including bone marrow toxicity (see above) • Patients with clinically significant renal impairment from any cause • Localised or systemic infection including hepatitis B or C and a history of TB. Appropriate to continue with therapy in patients with minor infections (EG. Uncomplicated urinary tract infections treated with a short course of antibiotics) seek advice from specialist • Unexplained anaemia and/or cytopenia associated with marrow failure. • Patients with deranged liver biochemistry or synthetic function • Sunscreens and protective covering should be encouraged (self-care) to reduce sunlight exposure.
x. Supply of ancillary equipment	N/A
xi. Supply, storage and reconstitution instructions	N/A
<p>Prepared by</p> <p>In consultation with</p> <p>Reviewed by (2020)</p>	<p>The Shared Care Guidelines Group, University Hospitals of Derby and Burton, Chesterfield Royal Hospital</p> <p>Dr Austin, Consultant Hepatologist Dr Bleiker, Consultant Dermatologist Dr Badcock, Consultant Rheumatologist Dr Ferguson, Consultant Dermatologist Dr Goddard, Consultant Gastroenterologist and Hepatologist Dr O'Reilly, Consulant Rheumatologist Dr Raj, Consultant Rheumatologist Dr Shum, Consultant Dermatologist Dr Vaithianathar, Consultant Neurologist</p> <p>The Derbyshire Medicines Management Shared Care and Guidelines Group</p> <p>Dr L Badcock – ACD Consultant Rheumatology UHDB Dr R Laxminaryan Deputy ACD Rheumatology UHDB In conjunction with fellow consultant rheumatologist Dr. Kid wan Shum Consultant Dermatologist UHDB Dr. K Fairburn, Consultant rheumatologist CRH Angela Lawrence, Rheumatology Lead Clinical Nurse Specialist CRH</p>

This does not replace the SPC, which should be read in conjunction with it

Date Prepared: October 2011 **Reviewed:** September 2019 **Review Date:** August 2022 (Extended to February 2023)

References

1. EMC Summary of Product Characteristics for Azathioprine and Mercaptopurine accessed online 08/03/2017, 1/8/2019
2. British National Formulary accessed online 1/8/2019
3. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, The British Society for Rheumatology, February 2017
4. The Green book, Immunisation against infection disease, September 2014, accessed online 1/8/2019
5. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding. Rheumatology Vol 55(9) 1693-1697 September 2016. Accessed online August 2019

Document control	Date
New indications for neurological condition added	November 2020
UHDB renal contact numbers added	October 2021

Sample Transfer Letter

Hospital No: «HOSPITAL_NUMBER»

NHS No: «NHS_NUMBER»

{Insert date}

PRIVATE & CONFIDENTIAL

«GP_TITLE» «GP_INITIALS» «GP_SURNAME»

«GP_ADDRESS_1»

«GP_ADDRESS_2»

«GP_ADDRESS_3»

«GP_ADDRESS_4»

«GP_POSTCODE»

DERBYSHIRE JAPC SHARED CARE AGREEMENT LETTER

Dear «GP_TITLE» «GP_SURNAME»

«FORENAME_1» «SURNAME» «DATE_OF_BIRTH»

«CURRENT_ADDRESS_1» «CURRENT_ADDRESS_2» «CURRENT_ADDRESS_3»

«CURRENT_ADDRESS_4» «CURRENT_POSTCODE»

Your patient was seen on *{Insert date}* with a diagnosis of *{Insert diagnosis}*. I have initiated the following medication *{Insert drug name}* and am writing to ask you to participate in the shared care for this patient.

This medication has been accepted as suitable for shared care by the Derbyshire Joint Area Prescribing Committee (JAPC). I agree to the secondary care responsibilities set out in the shared care agreement for this medication (available from www.derbyshiremedicinesmanagement.nhs.uk/clinical_guidelines/shared_care_guidelines). I am therefore requesting your agreement to share the care of this patient. Where preliminary tests are set out in the agreement I have carried these out and results are below.

Dose Regimen	Date <i>{Insert medicine name}</i> started	Date for GP to start prescribing <i>{Insert medicine name}</i> from
The baseline test results are (if applicable): See overleaf for initiation criteria.		

I can confirm that the following has happened with regard to 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>	

If you do **NOT** wish to participate in shared care for this patient, usually under clinical grounds, please complete the attached form.

Yours sincerely

{Consultant name}

GP RESPONSE TO SHARED CARE (only complete & send if **NOT** participating in shared care*)

* For completeness please record medication on GP clinical system as per guidance- [Recording medicines prescribed and issued by other Healthcare Providers](#)

Shared care is produced by GPs and specialists knowledgeable in the field of that drug usage. The shared care has been approved by the JAPC. This allows a more convenient service to the patient and cost effective use of NHS resources.

Patient:	NHS No:
Consultant:	Medicine requested for shared care:

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care guideline. My clinical reasons for declining shared care for this patient are listed in the box below:

		Tick which apply
1.	<p>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</p> <p>As the patients 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>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.</p>	
2.	<p>The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement</p> <p>As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC 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>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</p>	
3.	<p>A minimum duration of supply by the initiating clinician</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 in order to provide them with the medication that you have recommended.</p> <p>Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.</p>	
4.	<p>Initiation and optimisation by the initiating specialist</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 in order to provide them with the medication that you have recommended.</p> <p>Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.</p>	
5.	<p>Shared Care Protocol not received</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 in order to provide them with the medication that you have recommended.</p> <p>Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.</p>	
6.	<p>Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)</p>	

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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

{GP name}
{Surgery}

Please send a copy of this response to the specialist/consultant requesting shared care