

**WORKING IN
PARTNERSHIP
WITH**

EFFECTIVE SHARED CARE AGREEMENT (ESCA)
DRUG NAME: AZATHIOPRINE
INDICATION/S COVERED: FOR RHEUMATOLOGY AND DERMATOLOGY

Coastal West Sussex Traffic Light system classification: Amber

N.B. The eligibility criteria included here apply to new patients commencing treatment under this agreement & not to existing patients whose treatment was initiated under the previous version. However, monitoring and discontinuation criteria apply to all patients.

NOTES to the primary care prescriber

Amber drugs: Prescribing to be initiated by a consultant / specialist but with the potential to transfer to primary care. The expectation is that this agreement should provide sufficient information to enable primary care prescribers to be confident to take clinical and legal responsibility for prescribing these drugs.

The questions below will help you confirm this:

- Is the patient's condition predictable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this effective shared care agreement?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this ESCA), then it is appropriate for you to accept prescribing responsibility. Sign and return a copy of the final page to the requesting consultant / specialist. Until the requesting consultant / specialist has received a signed copy of the final page indicating that shared care has been agreed all care (including prescribing) remains with the consultant / specialist.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant / specialist within 14 days, outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, which will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your Medicines Management pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient's best interests are always paramount

The primary care prescriber has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant

Information

This information sheet does not replace the Summary of Product Characteristics (SPC), which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

1. **Link to the relevant SPC website:**

2.

<http://www.medicines.org.uk/emc/medicine/2881/SPC>

<http://www.medicines.org.uk/emc/medicine/2882/SPC>

1. **Background to use for the indication/s, including licence status**

2.

Licensed: Severe active rheumatoid arthritis, systemic lupus erythematosus, pemphigus vulgaris, polymyositis and dermatomyositis.

Unlicensed: Severe atopic eczema, bullous pemphigoid, chronic actinic dermatitis, pyoderma, gangrenosum, pityriasis rubra pilaris, psoriasis, Wegener's granulomatosis, cutaneous vasculitis.

1. **Dose & administration**

2.

Dose: Initially 1mg/kg/day increasing after 4-6 weeks to 2-3mg/kg/day, adjusted within these limits, depending on clinical response and haematological tolerance. Dermatology: normal or high TPMT activity 1-3 mg/kg daily; low TPMT activity 0.5-1mg/kg daily

Maintenance: < 1mg to 3mg/kg/day depending upon clinical response, including haematological tolerance, keeping doses to the minimum necessary to maintain a therapeutic response. Typical maintenance doses range from 100-150mg daily. Dermatology: < 1mg to 3mg/kg/day depending upon clinical response.

If no improvement occurs in the patient's condition within 3 months, consideration should be given to withdrawing azathioprine.

In patients with renal and/or hepatic insufficiency and the elderly, dosages should be given at the lower end of the normal range.

Route: Oral. Tablets swallowed whole with or after food.

1. **Cautions**

2.

- Pregnancy
- TPMT deficiency (heterozygous)
- Lesch-Nyhan syndrome
- Renal and/or hepatic insufficiency
-

5. **Contraindications**

6.

- Known hypersensitivity to 6-mercaptopurine (6-MP) or azathioprine
- Immunisation with live vaccines
- Breast feeding
- TPMT deficiency (homozygous)
- Lesch-Nyhan syndrome
-

6. **Side effects**

- 7.
8. **Infection and infestations:** Viral, fungal and bacterial infections
9. **Skin:** Rash, alopecia, photosensitivity and increased risk of skin cancer-high factor sunscreen and protective clothing recommended.
10. **Haematopoietic:** Bone marrow suppression is most frequently manifested by leucopenia, thrombocytopenia (which are usually reversible) and anaemia, or any combination may occur.
11. **Gastrointestinal:** Nausea, vomiting and diarrhoea. Rarely pancreatitis. Colitis reported in patients receiving corticosteroids.
12. **Hepatic:** Liver impairment. Cholestatic jaundice. Rarely hepatic veno-occlusive disease.
13. **Urogenital System:** Hypotension and interstitial nephritis.
14. **Respiratory System:** Infrequently interstitial pneumonitis.
15. **Central Nervous System:** Hypersensitivity reaction including malaise, dizziness, nausea, vomiting, diarrhoea, fever, rigors, exanthema, vasculitis, myalgia, arthralgia, rash, hypotension, hepatic dysfunction, renal dysfunction and interstitial nephritis—calling for immediate withdrawal
16. **Immunological:** Reduced resistance to infection. Live vaccines should not be administered whilst taking azathioprine. Pneumovax II and annual influenza vaccine should be given. Passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG) in non-immune patients exposed to chicken pox or shingles.
17. Increased risk of developing malignancies and mutagenicity.
- 18.
19. Also see SPC or BNF for further details of side effects.
- 20.

1. **Interactions**

- 2.
- Allopurinol - if given concomitantly and use is essential, azathioprine dose should be reduced to one quarter of the original dose, but ideally should be avoided
- Febuxostat – like allopurinol, this xanthine oxidase inhibitor should be avoided
- Antibacterials – increased risk of haematological toxicity with co-trimoxazole and trimethoprim
- Warfarin - anticoagulant effect possibly reduced.
- Aminosalicylates – possible increased risk of leucopenia (e.g. olsalazine, mesalazine, sulfasalazine)
- ACE Inhibitors – increased risk of leucopenia and anaemia
- Neuromuscular blocking drugs – action potentiated
- Penicillamine, Cimetidine and Indomethacin – myelosuppressive effects maybe enhanced
- Vaccines – there may be diminished response. Use of live vaccines is contraindicated.
- Phenytoin, sodium valproate, carbamazepine – absorption reduced by azathioprine
- Clozapine – increased risk of agranulocytosis
- Digoxin – absorption reduced by azathioprine
- Ribavirin – myelosuppressive effects of azathioprine possibly enhanced
-

8. **Criteria for use**

- 9.
10. As given under licensed and unlicensed indications. Should only be initiated by clinicians experienced in the treatment of chronic inflammatory rheumatic and dermatological diseases and prescribing transferred to primary care once patient's dose is stabilised.
- 11.

1. **Any further information (e.g. supporting therapies)**

- 2.
3. Reduce dose in hepatic and renal impairment.
- 4.
5. Advise patient that sunscreen and protective covering should be encouraged to decrease sunlight exposure due to photosensitivity risk.
- 6.

1. **References**

- 2.
 1. Summary of Product Characteristics –Imuran 25mg; Aspen (last updated January 2012) Available to access at: <http://www.medicines.org.uk/emc/medicine/2881/SPC>
 - 2.
 3. Summary of Product Characteristics –Imuran 50mg; Aspen (last updated January 2012) Available to access at: <http://www.medicines.org.uk/emc/medicine/2882/SPC>
 - 4.
 5. Chakravarty K *et al.* BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatology. *Rheumatology* 2008; 47: 924-5
 - 6.
- [British Association of Dermatologists' guidelines for the safe and effective prescribing of azathioprine 2011](#) SJ Meggitt, AV Anstey, MF Mohd Mustapa, NJ Reynolds and S Wakelin, *BJD* Vol. 165, No. 4, October 2011 (p711-734) <http://www.bad.org.uk/Portals/Bad/Guidelines/Clinical%20Guidelines/Azathioprine%20guidelines%202011.pdf>

RESPONSIBILITIES and ROLES

Consultant / Specialist responsibilities
1. Confirmation of diagnosis and identification of suitable patients
1. Request agreement of shared care with primary care prescriber
1. Initiation of appropriate therapy
1. Discussion of risks and benefits with patients, outline possible side effects
<p>1. Monitoring requirements and appropriate dose adjustments (if relevant to specific drug)</p> <p>Before Treatment: Exclude pregnancy Liver Function Tests (LFTs) (including AST/ALT) Full Blood Count (FBC) (including differential white blood cell count and platelets) U&E's (including creatinine) TPMT assay</p> <p>During treatment (first three months): Every week: FBC and LFTs for six weeks, then continue every two weeks until dose stable for 6 weeks, then monthly</p> <p>During treatment (after three months): Every THREE months FBC and LFTs if stable on maintenance dose for 6 months. After dose change do FBC and LFT two weeks later then monthly. In heterozygous TPMT, monitor at a minimum of monthly intervals. U&E/Creatinine 6 monthly</p> <p>The consultant will stop, or advise to stop, treatment if any of the following occur:</p> <ul style="list-style-type: none"> White blood cell count < 3.5x 10⁹/l Neutrophils < 2.0 x 10⁹/l Platelets < 150 x 10⁹/l AST / ALT > twice the upper limit of normal Rash or oral ulceration Unusual bruising, bleeding or sore throat - withhold until FBC result available MCV >105fl check B₁₂, serum folate and TSH levels and treat any underlying abnormality. <p>Hypersensitivity reactions (including malaise, dizziness, vomiting, diarrhoea, fever, rigors, myalgia, arthralgia, rash, hypotension and interstitial nephritis)</p> <p>Blood tests will be monitored by the Rheumatology/Dermatology Team and results fed back to primary care prescribers, together with advised action to continue as before or to adjust or stop prescribing as necessary.</p> <p>The Rheumatology/Dermatology Team will provide patients with blood forms to present to their primary care prescriber/Phlebotomist for all monitoring blood tests. The Rheumatology/Dermatology Team will ensure that the consultants name is on the form and that a copy of the result is sent to the patient's primary care prescriber.</p>
6. Issuing initial prescription(s) until the patient is stabilised (minimum of one month) and until ESCA is in place.
1. Ensure that all newly treated patients (and/or their carers) receive appropriate education and advice regarding their drug therapy and shared care arrangements. This should include written information where appropriate.
1. Providing primary care prescriber with clinic letter stating planned introduction and reviews.
1. Provide outpatient reviews, monitor effectiveness/side effects.
1. Give a copy of the information sheet to the patient/carers and explain their roles.
1. Notify the primary care prescriber of the patient's failure to attend for clinical review or drug monitoring.

Primary care prescriber responsibilities
1. Initial referral to secondary care.
1. To inform the consultant if unwilling to enter into shared-care arrangements.
1. To provide repeat prescriptions once ESCA is agreed and in place and the patient is stabilised (not before initial one month stabilisation period). A demonstrable system should be in place to ensure that prescribing is reviewed by the primary care prescriber if there is no record of the fact that monitoring has taken place within the agreed time scales.
1. To record any changes in therapy in the prescribing record on receipt of such communication from secondary care.
1. To monitor patients overall health and well-being and to report any adverse drug reactions or interactions to secondary care.
1. Liaise with Rheumatology/Dermatology Team if any cause for concern or drug discontinued.
1. To provide a copy of this ESCA to the patient to ensure that they are familiar with all roles and responsibilities.

Patient's / Carer's role
1. Ask the Rheumatology/Dermatology Team or primary care prescriber for information, if he or she does not have a clear understanding of the treatment.
1. Share any concerns in relation to treatment with azathioprine.
1. Tell the Rheumatology/Dermatology Team or primary care prescriber of any other medication being taken, including over-the-counter products.
1. Read the patient information leaflet included with the medication and report any side effects or concerns to the Rheumatology/Dermatology Team or primary care prescriber.
1. Arrange blood tests as per Rheumatology/Dermatology Team's request
1. Report to their primary care prescriber/specialist any side effects from the medicine.

BACK-UP ADVICE AND SUPPORT

	Name / position	Telephone	Email
Rheumatology Consultants:	Dr A Hepburn/Dr M Chard	01903 205 111, ext 5614 or 349101243 788 122, ext 3531	FAX 01903 252152
Dermatology Consultants:	Dr Woollons/Dr Atkinson Dr Hextall/Dr Coburn	01903 205111, ext 3701 or 3431 01903 205111, ext 4287 or 5783	
Alternative specialist (e.g. departmental contact):	Rheumatology Nurse Specialists Dermatology Nurse Specialists	01903 205 111, ext 5828 01903 205 111, ext 3212/3607	
Hospital Pharmacy:	Worthing Hospital St Richards Hospital	01903 205 111, ext 5698 01243 788 122, ext 3347	pharmacy@wsht.nhs.uk
Out of hours (e.g. medical team on call):	On call physicians On call	Bleep 118 or 119 01903 205 111	

Version History			
Document Name:	AZATHIOPRINE		
Document Type:	Effective Shared Care Agreement		
Relevant to:	All primary care prescribers working within Coastal West Sussex and all relevant clinicians at Western Sussex Hospitals NHS Trust.		
Version No.	Date	Author of original development or review	Details of document development
1	June 2008	Julie Sadler - Prescribing Support Pharmacist	Original development
2	05/10/12	Sarah Clarke - Prescribing Support Pharmacist	Full review and re-draft
3	30/11/12	Julie Sadler – Prescribing Support Pharmacist	Re-draft to include dermatological indications
Approval for organisational use			
ESCA authorised for use in Coastal West Sussex by	Rheumatology consultant: Dr Alastair Hepburn (Consultant Rheumatologist), 22/10/12 Dermatology consultant: Dr Atkinson (Consultant Dermatologist), 11/2/13		
	Coastal West Sussex Area Prescribing Committee (APC): Rheumatology - 22/10/12 (Chairman's action) Dermatology – 28/11/12		

EFFECTIVE SHARED CARE AGREEMENT (ESCA)

DRUG NAME: AZATHIOPRINE

Agreement for transfer of prescribing to PRIMARY CARE PRESCRIBER

Patient details:

Name:
Address:
DoB:
NHS No:
Hospital No:

Drug name and dose:

The following tests and investigations have been carried out:

Details of tests:

Date treatment initiated:

At the last patient review the drug appeared to be effectively controlling symptoms / providing benefit:

Yes/No

The patients has now been stabilised on a dose of:

I will arrange to review this patient regularly. Date of next clinic appointment:

Title of specialist: Name: Department: Hospital Address: Contact Number:
Primary care prescriber: Address: Contact Number:
Main Carer: Contact Number:
Key worker if appropriate: Contact Number:

Agreement to shared care, to be signed by primary care prescriber and consultant/specialist.
Consultant/specialist signature:
Date:
Primary care prescriber signature:
Date:
If shared care is agreed and the primary care prescriber has signed above please return a copy of this page to the requesting consultant or alternatively fax to: