

## Azathioprine/6 mercaptopurine in Inflammatory bowel disease Shared Care Agreement

<i>Alternatively, apply an addressograph label here</i> <b>Patient Name:</b>	<b>Consultant/Specialist Nurse:</b>
<b>Patient's Hospital number:</b>	<b>Date of initiation:</b>
<b>Date of Birth:</b>	<b>Intended duration of treatment:</b>
<b>NHS No:</b>	<b>Most recent eGFR and date of result:</b>
<b>GP name and Practice:</b>	<b>Allergy status and reaction if known:</b>

### Introduction

Inflammatory bowel disease (IBD), includes ulcerative colitis (UC) and Crohn's Disease (CD), it is a chronic condition that requires drug treatment for symptom control. Steroids are still the most effective drugs to induce remission. Unfortunately, steroids also have common and serious side effects, which limit their use in long-term management. Immunomodulatory agents are important steroid-sparing alternatives for those treatment resistant or frequently relapsing cases.

### Therapeutic Use

Azathioprine (AZA) and 6-Mercaptopurine (6-MP) are immunomodulatory agents. However, both drugs are not licensed for the treatment of inflammatory bowel disease although their use is acknowledged by the BNF. Azathioprine is metabolised into mercaptopurine. The treatment duration is usually 5 years after which patients are asked to take a drug holiday or stop the treatment completely if their disease is in remission. Should the patient not tolerate Azathioprine, 6-Mercaptopurine can be an effective alternative.

### Dosage and Administration

Azathioprine: Start dose 0.5-1.5mg/kg daily, maintenance dose 2-2.5mg/kg daily  
6-Mercaptopurine: start on 0.25-0.5mg/kg daily, maintenance dose 1-1.5mg/kg daily  
Some patients may respond to lower doses.

### Monitoring

- Initial Monitoring Under Hospital Specialists Care: (at least 4 months)  
First 2 months: Weekly FBC and LFT and Amylase  
Following 2 months: Fortnightly FBC and LFT  
Thiopurine metabolites monitoring is used to assess the therapeutic range of Aza /6-MP and is requested by the specialist team periodically to optimise therapy.
- Continue Monitoring by General Practitioners under Shared Care Agreement (after patient stabilised on treatment for at least 4 months):  
Full blood counts, renal function tests & liver function tests should be performed every three months or once the patient is stable.

### Side Effects (for a full list of side effects, please consult the BNF or data sheets)

- Azathioprine:** Bone marrow suppression (leucopenia, thrombocytopenia,

anaemia) which are reversible; nausea, pancreatitis, cholestasis and occasionally hepatic veno-occlusive disease, pneumonitis (very rarely); alopecia, skin rash.

- **6-Mercaptopurine:** Bone marrow suppression (leucopenia, thrombocytopenia, anaemia) which are reversible; anorexia, nausea, oral ulceration, hepatotoxicity, biliary stasis, pancreatitis; rarely, drug fever and skin rash.
- **Guidance for Male and Female of Reproductive Age:** If a patient wishes to start a family, specialist advice MUST be sought before conception, disease control is the paramount concern. **Pregnancy:** Thiopurine maintenance therapy should be continued throughout pregnancy due to the low risk of adverse outcomes.
- **Breast feeding:** is considered acceptable in women taking Azathioprine or 6-Mercaptopurine.

**Contraindications** ~ Absent or very low thiopurine methyltransferase activity ( TPMT ) increased risk of myelosuppression ( this is checked as part of the pre treatment screening which includes latent infections, i.e. hepatitis.B & C). Avoid live vaccinations 2-3 months prior to starting immunomodulator therapy, during and up to 6 months after stopping treatment. Likewise defer live vaccinations up to 6 months in newborns whose mothers are on a thiopurines when possible, to avoid disseminated infection.

**Caution** Consider reduced dose in elderly – reduced TPMT activity

**Drug Interactions** (For a full list of interactions, please consult data sheets/SPC)

- **Allopurinol** inhibits metabolism of Azathioprine and 6-Mercaptopurine and increases the risk of drug toxicity. Avoid concomitant use if possible, unless specialist's advice.

**NB** BEFORE initiating Allopurinol, as dose of Azathioprine or 6-Mercaptopurine will need to be reduced by 50% due to increased risk of drug toxicity.

- **Warfarin.** Azathioprine and 6-Mercaptopurine may possibly reduce the effect of warfarin.

## AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

Shared care agreement is one of the suggested ways in which the responsibilities for management of disease shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them. **The clinician who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.**

### Aspects of Care for which the Hospital Specialist is Responsible:

- Initiation of treatment and monitor patient for the initial 4 months period
- Discussion with the patient regarding the benefits and side effects of treatment
- Ask the GP whether they are willing to participate in shared care and communicate with the GP any changes in treatment
- Guidance to GP of time scale of treatment, doses, action if abnormal result
- Regular review of patient's condition and of response to treatment
- Monitoring of the FBCs and LFTs before and during initial treatment period
- Advice to GPs on what to do when test results above normal levels
- Advice to GPs on when to stop treatment
- Upon discovering adverse event related to drug, to complete MHRA Yellow card report online or via BNF
- Ensure clear arrangements for back up, advice and support

**Aspects of Care for which the General Practitioner is Responsible:**

- Replies to request for shared care as soon as practicable
- Prescribing of treatment after communication with specialist
- Prompt referral to specialist when any clinical suspicion of adverse effects, loss of efficacy, worsening of disease related symptoms
- Report adverse events to the specialist team and CSM
- Reporting to and seeking advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment
- Stopping treatment on advice of specialist
- Upon discovering adverse event related to drug, to complete MHRA Yellow card report online or via BNF

**Aspects of Care for which the Patient is responsible:**

- Report any adverse effects to their GP
- Ensure they have a clear understanding of their treatment & adhere with blood monitoring arrangements
- Report suspicious skin lesions ( increased lifetime risk of skin cancer )
- Attend Hospital outpatient clinic appointments and follow-ups

Contact Details	Telephone No.	Extension	Fax or email address
<b>Consultants</b> Dr Awasthi, Dr Cox, Dr Hughes, Dr Desai, Dr Shekhar	01922 721172	Ext 7151/7449/ 6975/7197	01922 656226 <a href="mailto:sec.awasthi@walsallhealthcare.nhs.uk">sec.awasthi@walsallhealthcare.nhs.uk</a> <a href="mailto:sec.cox@walsallhealthcare.nhs.uk">sec.cox@walsallhealthcare.nhs.uk</a> <a href="mailto:sec.hughes@walsallhealthcare.nhs.uk">sec.hughes@walsallhealthcare.nhs.uk</a> <a href="mailto:sec.desai@walsallhealthcare.nhs.uk">sec.desai@walsallhealthcare.nhs.uk</a> <a href="mailto:sec.shekhar@walsallhealthcare.nhs.uk">sec.shekhar@walsallhealthcare.nhs.uk</a>

Contact Details	Telephone No.	Extension	Fax or email address
<b>Specialist Nurse</b> Jasbir Nahal	01922 721172	Ext 7527	Mobile:07775 824468 <a href="mailto:jasbir.nahal@walsallhealthcare.nhs.uk">jasbir.nahal@walsallhealthcare.nhs.uk</a>
<b>Hospital Pharmacy</b> Dept: Kai-Yee Chan	01922 721172	Ext 6841	<a href="mailto:KaiYee.Chan@walsallhealthcare.nhs.uk">KaiYee.Chan@walsallhealthcare.nhs.uk</a> Bleep 2367

These guidelines have been written in collaboration by the Department of Gastroenterology and Pharmacy Department, Walsall Manor Hospital NHS Trust.

**References:**

Summary of Product Characteristics (SPC) of Azathioprine (Imuran®), 6-Mercaptopurine (Puri-Nethol®)  
BNF 72 BMA/RPS, March 2017, Pages 757 & 806-807.

The treatment of IBD with 6-Mercaptopurine or Azathioprine. Hielsen,OH. Alimentary Pharmacology & Therapeutics 2001; 15; 1699-1708

Toronto consensus statements for the management of inflammatory bowel disease in pregnancy, Gastroenterology 2016, 150: 734-757

JN/ 2017