Working in Partnership

SHARED CARE PRESCRIBING GUIDELINE

Azathioprine and Mercaptopurine in Inflammatory Bowel Disease (IBD) and Autoimmune Hepatitis

General Shared Care Guideline (SCG) Principles

- Medicines considered suitable for shared care are those which should be initiated by a Specialist, but where prescribing and monitoring responsibility may be transferred to Primary Care. Due to their potential side effects, shared care medicines usually require significant regular monitoring, and regular review by the Specialist is needed to determine whether the medicines should be continued. The best interest, agreement and preferences of the patient should be at the centre of any shared care agreement.

- The transfer of prescribing responsibility from the Specialist to the patient's General Practitioner (GP) or Primary Care prescriber should occur when both parties are in agreement that the patient's condition is stable or predictable, and that the Primary Care prescriber has the relevant knowledge, skills and access to equipment to allow them to monitor treatment as indicated in this shared care prescribing guideline.

- The aim of this guideline is to equip Primary Care prescribers with the information to confidently take on clinical and legal responsibility for prescribing the medication under a shared care agreement within their own level of competence.

- Within the Bedfordshire, Luton and Milton Keynes (BLMK) Integrated Care System (ICS), shared care guidelines are produced and updated through a robust governance process, following consultation with a wide range of key stakeholders. On this basis for BLMK ICS approved shared care guidelines, it is anticipated that Primary Care prescribers, upon individual assessment, will accept shared care for the patient if they felt it was clinically appropriate to do so and seek patient consent.

- If the Primary Care prescriber feels that a request for shared care cannot be accepted, i.e. falls outside of their own level of competence, they should initially seek further information or advice from the clinician who is sharing care responsibilities or from another experienced colleague in line with the General Medical Council (GMC) guidance.

- If the Primary Care prescriber is still not satisfied clinically to accept shared care, they should make appropriate arrangements for the patient's continuing care where possible. This may include asking another colleague in their practice to undertake the shared care. In the event that other colleagues in the practice also decline to share care, the Primary Care prescriber could seek assistance and advice from their Primary Care Network (PCN) (e.g. PCN Pharmacist).

- If the decision, after discussion with the PCN, is to decline shared care, the Primary Care prescriber must notify the Specialist clinician of their decision and reason (See appendix 1) to decline as soon as they can and in a timely manner (within a maximum of 14 to 21 days upon receipt of request) in writing and ensure the patient is aware of the change. In this scenario, the prescribing responsibility for the patient remains entirely with the Specialist. This principle also applies where shared care needs to be terminated in primary care e.g. due to lack of patient engagement. It is anticipated that these would be very rare events.

- The requirement for the Primary Care prescriber to send confirmation in writing via letter or approved electronic communication to the Specialist team for acceptance of shared care is NOT mandated.

- Where the hospital or Specialist clinician retains responsibility for monitoring drug therapy and/or making dosage adjustments, the Primary Care prescriber must be informed of any dose changes made as soon as possible to avoid medication errors. Similarly, if the Primary Care prescriber makes changes to the patient's medication regimen, the Primary Care prescriber must inform the Specialist in a timely manner. Primary Care prescribers can contact the Specialist team for advice, training and support as required.

- The principles above apply to shared care arrangements that involve the Specialist service sharing care with GPs and/or other Primary Care prescribers, e.g. Community Nursing Services. Where patient care is transferred from one Specialist service or GP practice to another, a new shared care agreement request must be commenced.

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Date of Next Review: (Unless clinical evidence changes)	April 2025		

Azathioprine and Mercaptopurine in Inflammatory Bowel Disease and Autoimmune Hepatitis

Introduction and Aims of Shared Care

This guideline has been developed to assist primary and secondary providers to monitor patients taking azathioprine or mercaptopurine (thiopurines) for Inflammatory Bowel Disease (IBD) or Autoimmune Hepatitis

It was a recommendation of the 2nd National IBD Audit action plan to achieve Standard B local Care Delivery – develop shared care between hospitals and primary care, where care is delivered as locally as possible with rapid access to specialist services when needed (IBD Standards Group, 2013).

This guideline seeks to establish a clear and comprehensive process to ensure a consistent standard is achieved. It is the responsibility of General Practitioners, Gastroenterologists and IBD Specialist Nursing staff to follow the document. The professional who prescribes the medication assumes legal clinical responsibility for the specific medication and consequences of its use.

This shared care agreement outlines suggested ways to which the responsibilities for managing the prescribing and monitoring of azathioprine and mercaptopurine with patients who have IBD or autoimmune hepatitis can be shared between the hospital specialist team and general practitioner (GP).

1. AREAS OF RESPONSIBILITY

Secondary/Tertiary Care Prescribers or Specialist Team

- To obtain patient informed consent for sharing of care between the Specialist, Primary Care prescriber and patient. Consenting parties must have sufficient, accurate, timely information in an understandable form. Consent must be given voluntarily and must be documented in the patient's notes.
- To confirm the working diagnosis.
- To confirm that the patient's condition has a predictable course of progression and the patient's care can be suitably maintained by Primary Care, following their medicine being optimised with satisfactory investigation results for at least 4 weeks.
- If shared care is considered appropriate for the patient, the patient's treatment regimen is confirmed, and benefit from treatment is demonstrated, the Specialist will contact the Primary Care prescriber to initiate shared care.
- At the point of initial contact, the Specialist should check if the Primary Care prescriber can access blood test results electronically. If access is unavailable, the Specialist and the Primary Care prescriber should agree a process of communication to ensure blood test results and relevant results of investigations can be accessed by both parties in a timely manner.
- Following the request to the patient's Primary Care prescriber to initiate shared care; to ensure that the patient has an adequate supply of medication until shared care arrangements are in place. Further prescriptions will be issued if, for unforeseen reasons, arrangements for shared care are not in place by the anticipated start date of the shared care (usually within 28 days or once the patient is stabilised on the medication). Patients should not be put in a position where they are unsure where to obtain supplies of their medication.
- To ensure that the Primary Care prescriber has sufficient information to enable them to monitor treatment, identify medicines interactions, and prescribe safely. This should include access or direction to a current copy of the SCG and contact details for the initiating Specialist. As a partner in the shared care agreement,

the patient should, where appropriate, be provided with access or direction to a copy of the shared care guideline.

- The Specialist will provide the patient's Primary Care prescriber with the following information:
  - diagnosis of the patient's condition with the relevant clinical details
  - details of the patient's specialist treatment to date
  - details of treatments to be undertaken by the Primary Care prescriber (including reasons for choice of treatment, medicine or medicine combination, frequency of treatment, number of months of treatment to be given before review by the Specialist)
  - the date from which the Primary Care prescriber should prescribe the treatment
  - details of other specialist treatments being received by the patient that are not included in shared care
  - details of monitoring arrangements required
- Whenever the Specialist sees the patient, he/she will:
  - send a written summary to the patient's Primary Care prescriber in a timely manner, noting details of any relevant blood test results or investigations if applicable
  - confirm that ongoing treatment with the monitored medicine is appropriate
  - record test results on the patient-held monitoring booklet if applicable and if this method of communication has been agreed at the onset of shared care
  - confirm the current dosage and clearly highlight any changes made both to the patient and in writing to the patient's Primary Care prescriber who will action any of them as required
- The Specialist team will:
  - provide training, advice and guidance (as appropriate) for Primary Care prescribers if necessary to support the shared care agreement
  - provide contact details for both working and non-working hours
  - supply details for fast track referral back to secondary/specialist care
  - provide the patient with details of their treatment, follow-up appointments, monitoring requirements and, where appropriate, nurse specialist contact details
  - provide continued support for the Primary Care prescriber and answer any questions they may have on the treatment and the condition for which the medicine is being used
- Prior to transfer of prescribing, the Specialist will:
  - Ensure that patients (and their caregivers, where appropriate) are aware of and understand their responsibilities to attend appointments and the need for continued monitoring arrangements.
- The Specialist will document the decision to transfer prescribing of the treatment to the Primary Care prescriber via the shared care guideline in the patient's hospital medical notes. If the Primary Care prescriber declines the request for shared care and the Specialist is therefore responsible for the prescribing of the medication for the patient, the Specialist will document this also in the patient's hospital medical notes.

All of the above information should be provided to the Primary Care Prescriber in writing via a letter or approved electronic communication.

Primary Care Prescribers

- To prescribe within their own level of competence. The (GMC) guidance on "Good practice in prescribing and managing medicines and devices" states that doctors are responsible for the prescriptions they sign and their decisions and actions when they supply and administer medicines and devices, or authorise or instruct others to do so. They must be prepared to explain and justify their decisions and actions when prescribing, administering and managing medicines.
- The same principles apply to non-medical prescribers as well as medical prescribers as outlined in the "Competency Framework for all Prescribers".
- To confirm that the patient or carer consents to sharing of care between the Specialist, Primary Care prescriber and patient. Consenting parties must have sufficient, accurate, timely information in an understandable form. Consent must be given voluntarily and must be documented in the patient's notes.
- If shared care is accepted, commencement of shared care must be clearly documented in the patient's Primary Care medical notes.
- If declining the request for shared care, the decision and rationale should be explained to the Specialist in

writing as soon as is possible and in a timely manner, within a maximum of 14 to 21 days upon receipt of request. The patient should also be informed of the decision.

- Ensure that he/she has the information and knowledge to understand the therapeutic issues relating to the patient's clinical condition.
- Undergo any additional training necessary in order to carry out the prescribing and monitoring.
- Agree that in his/her opinion the patient should receive shared care for the diagnosed condition unless good reasons exist for the management to remain within Secondary/Specialist care.
- Prescribe the maintenance therapy in accordance with the written instructions contained within the SCG or other written information provided, and communicate any changes of dosage made in Primary Care to the patient. It is the responsibility of the prescriber making a dose change to communicate this to the patient.
- Report any adverse effect in the treatment of the patient to the Specialist team, and via the MHRA Yellow Card Scheme https://yellowcard.mhra.gov.uk/.
- The Primary Care prescriber will ensure that the patient is monitored as outlined in the SCG and will take the advice of the referring Specialist if there are any amendments to the suggested monitoring schedule.
- The Primary Care prescriber will ensure a robust monitoring system is in place to ensure that the patient attends the appropriate appointments in Primary Care for follow-up and monitoring, and that defaulters from follow-up are contacted to arrange alternative appointments. It is the Primary Care prescriber's responsibility to decide whether to continue treatment for a patient who does not attend appointments required for follow-up and monitoring, and to inform the Specialist of any action taken.
- Primary Care prescriber are not expected to be asked to participate in a shared care arrangement where:
    - no locally approved SCG exists, or the medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care agreement
    - 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
- Where community nurse involvement is required in the administration of medicines under a SCG, nurses should be provided with adequate information and guidance by the prescriber or the Specialist. Arrangements should be made in good time for any potential problems to be resolved to ensure that patient care is not compromised.

Patient and/or carer

- To provide their informed consent for sharing of their care with the Specialist and Primary Care prescriber. Consenting parties must have sufficient, accurate, timely information in an understandable and accessible format. Consent must be given voluntarily and must be documented in the patient's notes. Supporting information is available from NICE "Making decisions about your care".
- To take their medication as agreed, unless otherwise instructed by an appropriate healthcare professional.
- To meet all necessary monitoring arrangements to ensure the safe prescribing of their medication, and to alert the prescriber where these arrangements are not met.
- To attend all follow-up appointments with the Primary Care prescriber and Specialist. If the patient is unable to attend any appointments, they should inform the relevant practitioner as soon as possible and arrange an alternative appointment.
- Inform healthcare professionals of their current medications prior to receiving any new prescribed or over-the-counter medication.
- Report all suspected adverse reactions to medicines to their Gastroenterology Team or Primary Care prescriber. To note that patients will have received the medication initially from secondary care and most ADRs are commonly associated with the initiation phase so less likely to report to their GP.
- If the reaction is severe, the patient should seek urgent medical attention via A&E.
- Store their medication securely away from children and according to the medication instructions.
- Read the information supplied by their Primary Care prescriber, Specialist and Pharmacist and contact the relevant practitioner if they do not understand any of the information given.
- An agreed method of communication of results of investigations between the Specialist, the Primary Care prescriber, the Community Pharmacist and the patient should be agreed at the onset of therapy.

Community Pharmacist

- Know where to access locally agreed shared care guidelines to aid professional clinical check of prescription prior to dispensing.
- Professionally check prescriptions to ensure they are safe for the patient and contact the Primary Care prescriber if necessary to clarify their intentions. It is good practice to check the patient-held record book if applicable to ensure the correct dose is dispensed*.
  * An agreed method of communication of results of investigations between the Specialist, the Primary Care prescriber, the Community Pharmacist and the patient should be agreed at the onset of therapy.
- Fulfil legal prescriptions for medication for the patient unless they are considered unsafe.
- Counsel the patient on the proper use of their medication.
- Advise patients suspected of experiencing an adverse reaction to their medicines to contact their Primary Care prescriber or Specialist/Specialist nurse team.

2. COMMUNICATION AND SUPPORT

Hospital name and address:	**Out-of-hours contact details & procedures:**
Milton Keynes University Hospital NHS Foundation Trust Standing Way, Eaglestone, Milton Keynes, MK6 5LD **Consultant names:** Dr. George MacFaul, Consultant Physician and Gastroenterologist - (IBD Lead) 01908 997115 George.macfaul@mkuh.nhs.uk Dr, Wamedh Taj-Aldeen Consultant Physician and Gastroenterologist 01908 997103 Wamedh.taj-aldeen@mkuh.nhs.uk Dr Ravi Madhotra, Consultant Physician and Gastroenterologist 01908 997103 Ravi.madhotra@mkuh.nhs.uk Dr Prakash Gupta – Consultant Gastroenterologist and Hepatologist 01908 997115 Prakash.Gupta@mkuh.nhs.uk Inflammatory Bowel Disease Nursing Team 01908 996955 IBDNursingTeam@mkuh.nhs.uk	**Milton Keynes University Hospital NHS Foundation Trust:** Out of hours – contact Medical Registrar via switchboard 01908 660033
Bedfordshire hospitals NHS Foundation Trust Bedford Hospital, South Wing, Kempston Road, Bedford, MK42 9DJ Luton and Dunstable University Hospital, Lewsey Road, Luton, LU4 0DZ **IBD team (Luton)**: **Consultant names:** Dr Matthew Johnson (Lead Consultant for IBD) Dr Steve Shieh (Consultant Gastroenterologist with Special Interest in IBD) Dr Joya Bhattacharyya (Consultant Gastroenterologist with Special Interest in IBD)	**Bedfordshire Hospitals NHS Foundation Trust** Luton contact Medical Registrar via switchboard 01234 355 122 Bedford contact Medical Registrar via switchboard 01582 491 166

Mr Frank Castro (Lead Nurse for IBD) Ms Linda Samuel-Tuck (Clinical Nurse Specialist in IBD) Mrs Susan Nanton (IBD Nurse) IBD helpline - 01582 718368 Email - IBD@ldh.nhs.uk **Hepatology team (Luton)**: Dr Sambit Sen (Consultant Hepatologist) Dr Pooja Khanna (Consultant Hepatologist) Dr Meha Bhuva (Consultant Hepatologist) - coming into post April '23 Mr Luis Neto-Pereira (Clinical Nurse Specialist in Hepatology) Miss Shahnaz Begum (Advanced Care Practitioner in Hepatology) Gastro secretaries - 01582 49(7478/7508) or 718028 **IBD team (Bedford):** **Consultant names:** Dr Javaid Babur (consultant gastroenterologist) IBD nurses IBDNurse@bedfordhospital.nhs.uk	

Specialist support / resources available to Primary Care prescriber including patient information:

This shared care guideline is available online at www.formularymk.nhs.uk then click on shared care guidelines and on the BLMK Medicines website https://medicines.bedfordshirelutonandmiltonkeynes.icb.nhs.uk/. A detailed guidance on prescribing and monitoring azathioprine and mercaptopurine in Inflammatory Bowel Disease is available on the Hospital Trust website. Any dosage adjustments made by the hospital specialist team will be recorded in the electronic medical notes and full details sent to the GP. Blood test results taken by the specialist hospital team will be available on the e-care system, the hospital specialist team will then send a paper copy of the blood test results to the GP in a timely manner. GPs should contact the hospital specialist team if any dose adjustments are required or if the need to discontinue the medication arises. The dosage regime and frequency of blood test monitoring should be clearly explained to the patient. Further information sources: ECCO e-guide http://www.e-guide.ecco-ibd.eu/

3. CLINICAL INFORMATION

Indication(s): **(Please state whether licensed or unlicensed)**	**Azathioprine**: Maintenance therapy in steroid-dependent and steroid-refractory patients with Crohn's Disease, Ulcerative Colitis and Autoimmune Hepatitis **Mercaptopurine** (unlicensed indication): Maintenance therapy in steroid-dependent and steroid-refractory patients with Crohn's Disease, Ulcerative Colitis and Autoimmune Hepatitis
Place in therapy:	**IBD** Azathioprine or Mercaptopurine will be used following 2 or more steroid courses in 12 months; steroid-dependent patients; and those with severe disease especially with adverse prognostic factors. They are also used to enhance anti-TNF therapy, by reducing immunogenicity of biologic

<table>
<tr><td></td><td colspan="3">agents.

Autoimmune Hepatitis
Steroid sparing agent in autoimmune hepatitis to maintain remission after or with steroid use.</td></tr>
<tr><td>Therapeutic summary:</td><td colspan="3">Azathioprine and Mercaptopurine are immune modulators utilized to avoid prolonged steroid use by maintaining patients in remission.

Autoimmune Hepatitis Steroid sparing agent in autoimmune hepatitis to maintain remission after or with steroid use.</td></tr>
<tr><td>Initiation and ongoing dose regime and Route of administration:

Note: Transfer of monitoring and prescribing to Primary Care is normally after the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.

All dose or formulation adjustments will be the responsibility of the initiating Specialist unless directions have been discussed and agreed with the Primary Care prescriber. Termination of treatment will be the responsibility of the Specialist.</td><td colspan="3"><u>Initial stabilisation</u>: (The loading period must be prescribed by the initiating Specialist)
For IBD:
Azathioprine PO 2-2.5mg/kg/day or Mercaptopurine PO 0.75-1.5 mg/kg/day.

For Autoimmune Hepatitis
Azathioprine dose 1-2mg/kg/day and mercaptopurine 25-75mg or up to 1mg/kg/day

Both azathioprine and mercaptopurine are taken by mouth, usually once a day.

<u>Maintenance dose (following initial stabilisation)</u>: As advised by the initiating Specialist)

<u>Conditions requiring dose adjustment</u>:
Doses should be reduced in renal impairment. GFR ml/min>50: no dose adjustment; GFR ml/min 10-50: reduce dose by 25%; GFR <10 ml/min: reduce dose by 50%.</td></tr>
<tr><td>Duration of treatment:</td><td colspan="3">IBD: Consider stopping azathioprine and mercaptopurine after 4 years if patient is in remission. Therapy will be stopped by the consultant specialist following review. Stopping therapy: Caution in withdrawal as may result in worsening of disease. Withdrawal should be a gradual process. Some patients will remain in long term remission. Remission can be reinduced by reinitiating thiopurines in most of those who, having previously responded, relapse.

Autoimmune hepatitis: This will be a Specialist clinical decision as there is a high relapse rate.</td></tr>
<tr><td>Preparations available (Manufacturer):</td><td colspan="3">Azathioprine comes as 25mg and 50mg tablets.
Mercaptopurine comes as 50mg tablets.</td></tr>
<tr><td>Summary of adverse effects:
(See Summary of Product Characteristics for full list)

click link:- <u>SPC</u>

Any serious adverse reactions should be reported to the MHRA via the <u>Yellow Card scheme</u>.</td><td>Adverse effect</td><td>Frequency/ likelihood</td><td>Management</td></tr>
<tr><td></td><td>WBC</td><td>Unknown</td><td><5 x10^9/L Contact the hospital specialist team</td></tr>
<tr><td></td><td>Neutropenia</td><td>Unknown</td><td>If neutrophils <2 x 10^9/L, Contact the hospital specialist
If neutrophils <1.5 x 10^9/L, Stop medication and contact the hospital specialist</td></tr>
<tr><td></td><td>Platelets</td><td>Very common</td><td>If <150 x 10^9/L Contact the hospital specialist</td></tr>
</table>

	Lymphocytes	Very common	If <0.5 x 10^9/L Contact the hospital specialist
	Varicella	Unknown	If in contact with the virus, non-immune patients require two weeks of oral Aciclovir 800mg 5 times daily and inform hospital specialist. Stop Azathioprine until lesions crusted over and Aciclovir completed.
	Nausea, vomiting **Diarrhoea**	Common Unknown	Advice to take medication at night. If persists, identify and ensure that the patient is taking their tablets with food. Advise patient to divide dosage and take with food. If no improvement, reduce dosage and contact hospital specialist if reducing dose ineffective.
	Abnormal bruising/bleeding/fever/ severe sore throat	Very common	Stop Azathioprine until recovery and check FBC and LFTs. Do not restart Azathioprine if blood tests abnormal – discuss with hospital specialist team
	Significant reduction in renal function	Unknown	Any abnormality, attempt to identify alternative cause. Repeat bloods and contact hospital specialist. If grossly abnormal (twice the normal range) Withhold and contact hospital specialist immediately for advice.
	Flu like illness / general aches and pains/ general malaise	Rare	This could possibly be part of a hypersensitivity reaction. Discuss with the gastroenterology specialist team.
	Severe or persistent infection	Unknown	Stop medication, take FBC, CRP and contact hospital specialist. Do not restart until results of FBC known (until it can be shown that there is no neutropenia).
	MCV>105 fl	Uncommon	Check TSH, B12, Folate Start appropriate supplementation. Alert IBD Team
	Rash or Oral Ulceration	Rare	If rash is a significant new rash, stop treatment until resolved and check FBC. If FBC abnormal, contact hospital specialist. Wait until rash resolved and consider restarting at reduced dose provided no blood dyscrasias.

	Liver impairment Cholestatic jaundice Abnormal LFTs, ALT > x2 ULN	Common Unknown	Any abnormality, attempt to identify alternative cause. Repeat bloods and contact hospital specialist. If grossly abnormal (twice the normal range) ALP>250IU/L; ALT>100IU/L Withhold and contact hospital specialist immediately for advice.
	Hair Loss	Rare	Mild - consider dose reduction on advice of hospital specialist team. Severe - stop medication and discuss with hospital specialist team
	Severe abdominal pain	Unknown	Consider pancreatitis, obtain amylase, and contact hospital specialist team.
	Macrocytosis	Unknown	This typically does not signify a medical concern. Check serum folate and B12 & TSH. Treat any underlying abnormality. If results are within normal parameters discuss with hospital specialist team.
	Hypersensitivity reactions- including dizziness, malaise, vomiting, diarrhoea, fever, rigors, myalgia, arthralgia, rash, hypotension.	Unknown	Many respond to taking drug twice daily, dose reduction, or switching to alternative thiopurine.
	Increased non-melanoma skin cancer	Unknown	Advise patients to avoid excess exposure and use high-factor sunscreen.
	Pancreatitis	Rare	Tends to occur within the first two months of use. Discontinue drug and do not re-challenge as pancreatitis often recurs

Other adverse effects:

- Increased risk of opportunistic infections
- Hepatotoxicity (hepatic necrosis, biliary stasis)
- Rarely gastrointestinal ulceration
- Interstitial nephritis, pneumonitis, hepatic veno-occlusive disease, lymphoma, red cell aplasia
- Increased risk of skin cancer
- Other malignancy
- Bone marrow suppression- leucopenia, anaemia, thrombocytopenia is common, and may be associated with improved drug efficacy.
- Severe leucopenia (neutrophil < 1x109/L or lymphocytes < 0.5x109/L) is associated with adverse outcomes (infection). Stop drug; consider lower dose and rechallenge once blood parameters have normalised.

Note: Hepatic toxicity can be abrogated by taking 25% of the daily dose together with 100mg of allopurinol, which requires frequent blood monitoring (similar to those newly commenced on thiopurines +/- thiopurine metabolite monitoring); or switching to alternate thiopurine. This should be done at specialist level.

Switch to Mercaptopurine with intolerance / severe adverse effects to Azathioprine unless these are severe pancreatitis or severe leucopenia.

The British National Formulary should be consulted to review adverse drug reactions and drug interactions.

Adverse effects and advised action to be taken: Careful consideration has been given prior to initiation of therapy and the potential benefits are thought to outweigh any potential adverse effect.

In addition to absolute values for haematological indices a rapid fall or consistent downward trend in any values should prompt caution and extra vigilance. Any increase in LFTs should also be carefully monitored.

Monitoring requirements by Specialist (baseline investigations, initial monitoring and ongoing monitoring):

Baseline investigations:
Varicella status and thiopurine methyltransferase (TPMT) assay prior to starting azathioprine or mercaptopurine.

Initial monitoring: *(Monitoring at baseline and during initiation is the responsibility of the Specialist until the patient is optimised and stabilised on the medicine with no anticipated further changes)*

- FBC, U&Es, LFTs

Ongoing monitoring:
Careful monitoring is essential during treatment as these drugs are potentially toxic immunosuppressants. Please see table below for regimen:

Time period of treatment	Frequency of monitoring	Tests to be done				
		FBC	LFTs	Amylase	CRP	U&Es
0-8 weeks	2 Weekly	√	√	**If symptomatic**	√	√
8 weeks -3months	Monthly	√	√		√	√
>3 months and stable dose for 6 weeks	Every 3 months	√	√		√	√
Any dose change	2 weeks post dose change then monthly	√	√		√	√

Situations where increased frequency of blood monitoring may be required and/or advice from the Specialist team:

- Downward trend in WBC or neutrophil count
- Renal impairment (dose should be adjusted accordingly)
- Following a dose change
- Mild to moderate hepatic impairment
- Concomitant drug therapy (see interaction sections below for details)
- Increased frequency of blood monitoring should be effectively communicated

Clinically relevant drug interactions and advice on management: ***Note: This list is NOT exhaustive and does not replace the SPC. This should be read in conjunction with the SPC.***	Drug interaction	Management / Action for Primary Care prescriber
	Allopurinol	**Should be avoided where possible. If co-prescribed with azathioprine, the dose of azathioprine should be reduced to one quarter of the original dose.** **Due to the severity of interaction, GPs should contact the specialist hospital team for advice before commencing a patient on Allopurinol.**
	Aminosalicylate derivates (e.g. olsalazine, mesalazine, sulfasalazine)	Can increase the bioavailability of mercaptopurine, this would make the patients more susceptible to the toxic side effects and caution is advised by the manufacturers.
	Co-trimoxazole/Trimethoprim	Close monitoring of FBC is required, as it increases the risk of haematological toxicity.
	Warfarin	The dose of Warfarin may require adjustment when initiating or discontinuing treatment with Thiopurines, as the anticoagulant effect of Warfarin and other derivatives may be possibly reduced.
	Phenytoin, sodium valproate, carbamazepine	The dose of these may require adjustment when initiating or discontinuing treatment with Thiopurines, as the absorption may be reduced.
	Febuxostat	Concomitant use should be **avoided**
	Ribavarin	The myelosuppressive effects of Thiopurines are possibly heightened.
	Clozapine	Concomitant use should be **avoided**, as there may be an increased risk of agranulocytosis (mercaptopurine).
	Live Vaccines	**Avoid** – see contraindication section below
	Close monitoring of FBC is required with concomitant use: • **Allopurinol** • **Co-trimoxazole/Trimethoprim** • Aminosalicylates • Indomethacin (contra-indicated in patients with inflammatory bowel disease) • Cytotoxic/myelosuppressive agents	

	• ACE inhibitors • Cimetidine For more detailed information please refer to the BNF **Please see SPC for comprehensive information.**
Clinically relevant precautions and contraindications: *Note: This does not replace the SPC and should be read in conjunction with it.*	**Cautions/Precautions:** **Pregnancy and lactation:** Thiopurines are considered safe to use in pregnancy, following discussion as to their risk / benefit. Low dose excretion occurs into breast milk for four hours following ingestion; therefore, consider advising expressing and wasting milk during this time period. **Surgery:** Thiopurines do not increase the risk of peri- or post-operative complications **Contraindications:** **Live vaccines are contraindicated** during and up to 3 months after treatment. If possible, vaccinate non-immune patients prior to immuno-suppressive treatment dependent on the results of the examinations. This will be performed by the specialist. **Other contraindications** Ensure recent cervical screen performed – Cervical neoplasia is a contra- indication to thiopurine use. Please see SPC for comprehensive information.
Renal impairment:	No specific recommendations in SPC
Hepatic impairment:	No specific recommendations in SPC
Advice to patients and carers: *The Specialist will counsel the patient with regard to 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 if they: • Are feeling extremely tired or dizzy, being sick (vomiting), loose or watery stools (diarrhoea), a high temperature (fever), muscle pain or stiffness, skin rash, kidney problems (such as a change in the amount or colour of your urine) • Are feeling unwell, a high temperature, a sore throat or symptoms of an infection • Experience unexpected bruising or bleeding
Pregnancy, paternal exposure and breastfeeding: *It is the Specialist's responsibility to provide advice on the need for contraception to male and female patients where applicable on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the Primary Care prescriber and the Specialist.*	**Pregnancy:** Thiopurines are considered safe to use in pregnancy, following discussion as to their risk / benefit. **Breastfeeding:** Low dose excretion occurs into breast milk for four hours following ingestion; therefore, consider advising expressing and discarding milk during this time period.
Practical issues and Supply of ancillary equipment (where	If the tablet needs to be halved, the tablet is required to be handled in accordance with guidance for handling cytotoxic agents and the patient

relevant):	should be advised accordingly.
Key references:	• Summary of Product Characteristics http://www.medicines.org.uk/emc/ • IBD Standards Group, 2013 update. Quality Care - Service standards for the healthcare of people who have Inflammatory Bowel Disease (IBD). Available online: https://www.bsg.org.uk/attachments/160_IBDstandards.pdf
This shared care guideline is to be read in conjunction with the following documents: • RMOC Shared Care Guidance – link here • NHSE/NHSCC guidance – items which should not be routinely prescribed in Primary Care: guidance for CCGs – link here • NHSE policy – Responsibility for prescribing between Primary & Secondary/Tertiary Care – link here	

Appendix 1 – Possible Reasons for a Primary Care Prescriber to decline to accept shared care:-

1	I do not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care. I have consulted with other Primary Care prescribers in my practice who support my decision. I have discussed my decision with the patient and request that prescribing for this individual remains with you due to the sound clinical basis given above.
2	The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement (medicine not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine).
3	The patient has not had the minimum duration of supply of medication to be provided by the initiating Specialist. Therefore, please contact the patient as soon as possible in order to provide them with the appropriate length of supply of the medication before transferring the prescribing responsibility to the Primary Care prescriber.
4	The patient has not been optimised/stabilised on this medication. Therefore, please contact the patient as soon as possible in order to provide them with the medication until the patient is optimised on this medication before transferring the prescribing responsibility to the Primary Care prescriber.
5	Shared Care Guideline and/or relevant clinical information as stipulated in the guideline not received. Therefore, please contact the patient as soon as possible in order to provide them with the medication until I receive the appropriate Shared Care Guideline before transferring the prescribing responsibility.
6	Other (Primary Care prescriber to complete if there are other reasons why shared care cannot be accepted or why shared care is to be discontinued if already started, e.g. adverse effects): ……