Shared Care Guidelines:
Azathioprine / 6-Mercaptopurine in Inflammatory Bowel Disease (IBD)

Indication:

Azathioprine is an immuno-modulatory agent that is used to induce and maintain remission in ulcerative colitis and Crohn's disease. Azathioprine is a pro-drug, which is cleared rapidly in the liver to 6-mercaptopurine. 6-mercaptopurine is also available as a tablet and although it is currently unlicensed in the UK to treat ulcerative colitis and Crohn's disease, its use is widely established in inflammatory bowel disease (see BNF Section 1.5).

Azathioprine is the first choice agent, but a minority of patients (10-20%) do not tolerate azathioprine, but are able to tolerate 6-mercaptopurine. It is anticipated that GP's will prescribe 6-mercaptopurine for those patients that are genuinely intolerant to azathioprine.

The main role of thiopurines (azathioprine/ 6-mercaptopurine) is steroid sparing and should be considered for patients who:

- Require two or more corticosteroid courses for IBD within a calendar year.
- Relapse as the dose of prednisolone is reduced below 15mg daily.
- Relapse within six weeks of stopping steroids.
- Require post-operative prophylaxis of complex Crohn's disease (fistulating / extensive).

Dose & Administration:

The maintenance dose for azathioprine for adults > 18 years is: 2 - 2.5mg/kg per day.
The maintenance dose for 6-mercaptopurine for adults > 18 years is: 1-1.5mg/kg per day.
(note: some patients may respond to lower doses).

Clinical response can usually be expected within 6-12 weeks.

Before treatment is commenced the following should be completed:

- Baseline FBC, LFT's, U&E's, and TPMT
- Vaccinations for opportunistic infections two weeks before treatment – pneumonia, seasonal flu, & swine flu. Varicella antigen should be checked if unsure of exposure from chickenpox and consider subsequent vaccination if appropriate.

Adverse Effects:

- Flu-like symptoms (sore throat, sweats, joint pains)
- Allergic type reactions (e.g. rash)
- Fever
- Jaundice
- Nausea, diarrhoea, mild aches & pains
- Bone marrow suppression
- Potential increased risk of malignancies such as lymphomas & skin cancer (although the risk is deemed low).
- Occasional report of mild to moderate hair loss
- Potential risk of pancreatitis

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Author: Sister Joy Mason, Inflammatory Bowel Disease Nurse (CHUFT)
Reviewed by: Dr Ian Gooding (Consultant Gastroenterologist), Jackie Wallis (Pharmacist)
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Contraindication:

Thiopurine methyltransferase (TPMT) deficiency. Patients with a deficiency may be unusually sensitive to myelo-suppressive effects of azathioprine and 6-mercaptopurine.

Hypersensitivity to azathioprine or 6-mercaptopurine

Cautions & Drug Interactions:

Drug	Interaction
Captopril	Increased risk of leucopoenia
Allopurinol (greatly affects)	**Increased toxicity (reduce to 1/3 to 1/4 usual dose)**
Anticoagulants	Possible reduced anticoagulant effect
Antibacterials (Co-trimoxazole & Trimethoprim)	Possible haematological toxicity increased
Phenytoin	Possibly reduces absorption of phenytoin
Clozapine (avoid)	**Increased risk of agranulocytosis**

- Patients should avoid 'live' vaccinations such as oral polio, oral typhoid, Varicella (chickenpox/shingles), MMR, BCG, & yellow fever whilst on immunosuppressant therapy.
- Patients should try to avoid contact with people who have active chickenpox or shingles and should report any such contact to their GP or hospital specialist.
- Careful assessment of risk versus benefit should be carried out before use during pregnancy and breast feeding. Consult hospital specialist or IBD Specialist Nurse.
- Patients with renal or hepatic insufficiency may need reduced doses and more frequent monitoring.
- Risk of significant haematological impairment – patients should be warned of signs / symptoms.

Monitoring Requirements:

- FBC at week 1, 2, and 4 (this will be arranged by the hospital and results copied to the GP).
- FBC 3-monthly thereafter as long as values remain within normal limits.
- LFT's once a year as long as values remain within normal limits.
- Clinical review by the IBD Specialist Nurse or Gastroenterologist one month after starting treatment followed by review as clinically indicated.
- Once stable refer to primary care for monitoring and prescribing.

Parameters for Intervention:

Please refer to the IBD Specialist Nurse or Gastroenterologist according to the detailed guidance below if any of the following occur:

- WBC $< 4 \times 10^9$ /l
- Neutrophils $< 2 \times 10^9$ /l
- Platelets $< 150 \times 10^9$ /l
- Haemoglobin Any value below normal range
- AST / ALT > 2 x increase on 2 occasions or significant rise from baseline
- MCV > 110 f/L
- Sore throat or oral ulceration, fever, or dizziness
- Nausea, vomiting, or diarrhoea
- Unexplained bruising or hypersensitivity reactions (i.e. rash)
- Non-compliance with monitoring

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Shared Care Responsibilities:

Consultant and/or IBD Nurse Specialist Nurse

1. Send a letter to the GP with Shared Care Guidelines requesting shared care for the patient.
2. Initiate treatment & prescribe until GP formally agrees to shared care.
3. Send a letter to the GP after each clinic attendance ensuring that correct dose, most recent blood results, and frequency of monitoring are stated.
4. Evaluation of any reported adverse effects by GP or patient.
5. Advise GP on review, duration or discontinuation of treatment where necessary.
6. Inform GP of patients who do not attend clinic appointments.
7. Ensure that back-up advice is available at all times.

General Practitioner (GP)

1. Letter of reply confirming acceptance / rejection of shared care for patient.
2. Organise vaccination requirements before treatment commences.
3. Monitor patient's overall health and wellbeing.
4. Prescribe the drug treatment as described.
5. Monitor blood results (FBC, U&E's, LFT's, & CRP) in line with recommendations from hospital specialist.
6. Report any adverse events to the hospital specialist, where appropriate.
7. Help in monitoring the progression of disease.

Patient Information:

1. Full discussion with the patient about the needs for the drug, benefits and potential side effects.
2. Information leaflet explained and provided to patient before treatment starts.
3. Discuss importance of blood monitoring.
4. Advise on vaccination requirements and avoidance of live vaccines.
5. Advice to report promptly signs of on-going or recurrent infection.

Contact Numbers for Advice and Support:

Colchester Hospital University NHS Foundation Trust	(01206) 747474 (Switchboard)
Consultant Gastroenterologists:	
Dr Ian Gooding	(01206) 744233 Ian.gooding@colchesterhospital.nhs.uk
Dr Mary McStay	(01206) 745210 Mary.mcstay@colchesterhospital.nhs.uk
Dr Donagh O'Riordan	(01206) 742085 Donagh.o'riordan@colchesterhospital.nhs.uk
Dr Achuth Shenoy	(01206) 742382 Achuth.shenoy@colchesterhospital.nhs.uk
IBD Specialist Nurse:	
Sister Joy Mason	(01206) 744231 / (01206) 745210 Fax: (01206) 742931 Joy.mason@colchesterhospital.nhs.uk

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Colchester Hospital University NHS
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CHUFT Medicines Information: (01206) 742161

Colchester General Hospital
Gastroenterology Department
Turner Road
Colchester
Fax: (01206) 742931 Essex CO4 5JL

Section A (to be completed by Secondary Care):

Hospital Number:	
NHS No:	
Date:	
GP Courier No:	
GP Name:	

Name of patient:	
Date of Birth:	
Address:	

Background:

Medications:

Dear GP,
Please see attached clinic letter. Please can you sign and return (using the above fax number) to indicate you are in agreement with the Shared Care Guidelines.

Yours sincerely,

Section B (to be completed by General Practitioner):

The above patient has been accepted into our monitoring service.

Practice date for next blood test:	
Accepting GP Name:	
Accepting GP Signature:	
Date:	

Practice Stamp:

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