Central Manchester University Hospitals NHS
NHS Foundation Trust

NHS

Greater Manchester Interface Prescribing Group

On behalf of the Greater Manchester Medicines Management Group

Shared Care Guideline for **Azathioprine / 6 Mercaptopurine for the treatment of chronic inflammatory bowel disease (unlicensed use)**	**Reference Number**
Author(s)/Originator(s): (please state author name and department) **Dr Simon Campbell, Consultant Gastroenterologist, CMFT**	**To be read in conjunction with the following documents:** Current Summary of Product characteristics (http://www.medicines.org.uk) BNF
Date approved by Interface Prescribing Group: (to be completed by Interface Group)	**Review Date: July 2015**

Please complete all sections

1. Licensed Indications	Azathioprine / 6 Mercaptopurine in IBD is an unlicensed off label indication
2. Therapeutic use & background	Inflammatory bowel disease (IBD) affects one in 10,000 of the UK population of whom less than 20% have such severe of refractory disease that immunosuppressive therapy is required as maintenance therapy. Given the significant adverse effects of long-term corticosteroid therapy, immunosuppressant therapy has been shown to be effective in reducing the requirement for steroid therapy and the complications of the disease.(1,2)
3. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).	Hypersensitivity to Azathioprine or 6-Mercaptopurine. Patients receiving azathioprine must NOT receive immunisation with LIVE vaccines. Inactivated polio is available although sub-optimal response may be seen. LIVE vaccines e.g. Rubella, BCG, yellow fever should not be given.
4. Prescribing in pregnancy and lactation	This drug can be prescribed in the pregnant patient. Under these circumstances prescribing should be the responsibility of the specialist. Azathioprine use in breast feeding is documented in the literature and the levels in breast milk are thought to be safe. Prescribing during breast feeding should be done only by the specialist in conjunction with appropriate patient counselling.

5. Dosing regimen for continuing care	Route of administration	Oral
	Preparations available (include in this section any necessary information relating to availability of special preparations for children or those with swallowing difficulties) Tablets	
	Please prescribe _____as a single daily dose or as divided daily dose	
	Is titration required? **No - titration to approximately 2mg/kg will be performed by the Hospital Consultant or in the case of 6 Mercaptopurine titration to 1-1.5mg/kg**	
	Titration – see above	
	Adjunctive treatment regime Annual flu, swine flu and pneumococcal vaccinations are safe and recommended. There may be reduced efficacy and swine flu DoH recommendations are 2 inoculations 3 weeks apart.	
	Conditions requiring dose reduction Renal, hepatic impairment and elderly patients. The dose used in these patient groups should be at the lower end of the normal range and the haematological response should be monitored carefully	
	Usual response time Usually 8-12 weeks	
	Duration of treatment At least 5 years	
	Treatment to be terminated by Hospital Consultant if indicated	
	NB. All dose adjustments will be the responsibility of the initiating specialist care unless directions have been specified in the medical letter to the GP.	
6.Drug Interactions ***For a comprehensive list consult the BNF or Summary of Product Characteristics***	The following drugs must **NOT** be prescribed without consultation with the specialist: **Co-trimoxazole** and **Trimethoprim** - increased risk of haematological toxicity **Clozapine** - avoid concomitant use, there is an increased risk of agranulocytosis	
	The following drugs may be prescribed with caution:	

Allopurinol - enhancement of effect with increased toxicity, the dose of allopurinol should be reduced to one quarter of the original dose.
Warfarin - anticoagulant effect possibly reduced.
ACE inhibitors - co-prescription may cause anaemia
Phenytoin, **Sodium Valproate**, **Carbamazapine** - there is reduced absorption of these drugs]

Adverse event	Action to be taken	By whom
malaise, dizziness, vomiting, diarrhoea, fever, rigors, myalgia, arthralgia, rash, hypotension and interstitial nephritis	withdraw immediately and contact specialist	GP
dose-related bone marrow suppression	Contact specialist	GP

The patient should be advised to report any of the following signs or symptoms to their GP without delay:

Infection, unexplained bleeding or bruising

Other important co morbidities (e.g. Chickenpox exposure). Include advice on management and prevention and who will be responsible for this in each case:
Patients suffering from chickenpox or active skin lesions in shingles; withhold Azathioprine / 6 Mercaptopurine and inform the gastroenterologist.
Exposure to chickenpox or shingles; passive immunization should be carried out using varicella zoster immunoglobulin (VZIG), by GP.

Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the “Yellow Card” scheme.

8.Baseline investigations	FBCs, LFTs and U&Es, weekly for four weeks until target dose is reached. This will initially take place at CMFT, thereafter by the GP.				
9. Ongoing monitoring requirements to be undertaken by GP	**Is monitoring required?**	**Yes or No (if yes complete following section)** **Yes**			
	Monitoring	**Frequency**	**Results**	**Action**	**By whom**
	FBC, LFTs and U&Es	Monthly for two months Then every three months for duration of treatment	**If WCC<3.5, neutrophils<2 or platelets <150**	***Repeat test after two weeks. If abnormal results on two successive occasions withhold azathioprine and contact the specialist***	**GP**
	FBCs	Monthly for two months Then every three months for duration of treatment	**If WCC<3.5, neutrophils<2 or platelets <150**	**Repeat test after two weeks, if abnormal results on two successive occasions withhold azathioprine and contact the specialist**	**GP**
	LFTs	Monthly for two months Then every three months for duration of treatment	**If levels exceed twice the upper limit of normal or increase significantly**	**Contact the specialist**	**GP**
	Renal function U&Es	Monthly for two months Then every three months for duration of treatment	**If renal function decreases significantly**	**Contact the specialist**	**GP**
10. Pharmaceutical aspects	*e.g. special storage requirements, washout periods Or where there are "no special considerations"*				
11. Secondary care contact information	**If stopping medication or needing advice please contact:**				
	Inflammatory Bowel Disease Specialist Nurses				
	Contact number: 0161 276 3429 / 4048				
	Hospital: Central Manchester University Hospitals NHS Foundation Trust				

12. Criteria for shared care	**Prescribing responsibility will only be transferred when** ▪ Treatment is for a specified indication and duration. ▪ Treatment has been initiated and established by the secondary care specialist. ▪ The patient's initial reaction to and progress on the drug is satisfactory. ▪ The GP has agreed in writing in each individual case that shared care is appropriate. ▪ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements
13. Aspects of care for which the Specialist is responsible	Initiate treatment and prescribe until dose is stable Undertake baseline monitoring. Dose adjustments. Monitor patient's initial reaction to and progress on the drug. Ensure that the patient has an adequate supply of medication until GP supply can be arranged. Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP Provide GP with diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient *or* inform GP if the patient does not attend appointment Provide GP with advice on when to stop this drug. Provide patient with relevant drug information to enable Informed consent to therapy Provide patient with relevant drug information to enable understanding of potential side effects and appropriate action Provide patient with relevant drug information to enable understanding of the role of monitoring.
14. Aspects of care for which the GP is responsible	--- Initiate treatment as directed by the specialist Ensure no drug interactions with concomitant medicines To monitor and prescribe in collaboration with the specialist according to this protocol To ensure that the monitoring and dosage record is kept up to date To undertake vaccination as directed by the initiating consultant, the BNF or Green Book Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary. ---
15. Aspects of care for which the patient	To take medication as directed by the prescriber, or to contact the GP if not taking medication To attend hospital and GP clinic appointments, bring monitoring booklet (if

<table>
<tr><td>is responsible</td><td colspan="4">issued)

Failure to attend will result in medication being stopped (on specialist advice).

To report adverse effects to their Specialist or GP</td></tr>
<tr><td>16.Additional Responsibilities</td><td>List any special considerations:</td><td>Action required</td><td>By whom</td><td>Date</td></tr>
<tr><td>17. Supporting documentation</td><td colspan="4">The SCG must be accompanied by a patient information leaflet.</td></tr>
<tr><td>18. Shared care agreement form</td><td colspan="4">Attached below</td></tr>
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Shared Care Agreement Form

Specialist request

IMPORTANT: ACTION NEEDED

Dear Dr _____

Attach patient Label

Patient name: _____

Date of birth: _____

Diagnosis: _____

This patient is suitable for treatment with Azathioprine / 6 Mercaptopurine for the treatment of chronic inflammatory bowel disease

This drug has been accepted for Shared Care according to the enclosed protocol (as agreed by Trust / LHB / AWMSG). I am therefore requesting your agreement to share the care of this patient.

Treatment was started on _____ Dose _____

If you are in agreement, please undertake monitoring and treatment from

Date _____

NB: date must be at least 1 month from initiation of treatment.

Blood tests required: FBC, LFTs monthly for two months, three monthly thereafter for the duration of treatment.

Next review with this department: Date _____

The gastroenterology medical staff will be available Monday to Friday 9am to 5pm to give you advice.

Please contact the Gastroenterology Specialist Nurses on 0161 276 3429/4048

Please use the reply slip overleaf and return it as soon as possible.

Thank you.

Shared Care Agreement Form

GP Response

Dear Dr: _____

Patient: _____

Address and DOB: _____

I have received your request for shared care of this patient who has been advised to start Azathioprine / 6 Mercaptopurine

A I am willing to undertake shared care for this patient as set out in the protocol

B I wish to discuss this request with you

C I am unable to undertake shared care of this patient.

General Practitioner signature: _____ Date: _____

General Practitioner address/practice stamp