Northern Lincolnshire
Area Prescribing Committee

Shared Care Guideline for the Treatment of Inflammatory Bowel Disease with Azathioprine or 6-Mercaptopurine in Adult Patients

Patient Details *(Attached patient label if appropriate)*
Patient Name: _____ NHS No: _____
Patient Address: _____ DOB: _____
_____
_____
_____

GP Name*: _____ Specialist Name: _____
GP Signature: _____ Specialist Signature: _____
Specialist Contact N^{o}: _____

*If the GP is unwilling to accept prescribing responsibility for this patient, the Secondary Care Specialist must be informed within one week of receipt of this document and letter from Secondary Care Specialist.

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Shared Care Guideline for the Treatment of Inflammatory Bowel Disease with Azathioprine or 6-Mercaptopurine in Adult Patients

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1. Introduction

With all Shared Care Guidelines (SCGs) in use across Northern Lincolnshire, the initiating clinician is responsible for ensuring that the patient receives relevant counselling, including warnings, potential side effects and interactions prior to initiating treatment. All baseline checks must be done by the specialist prior to requesting shared care. Continued monitoring e.g. blood tests and ECGs remain the responsibility of the initiating clinician. A management plan for the duration of treatment must be created at the point of initiation, which the patient must be aware of and agree to.

This SCG aims to provide a framework for the shared prescribing and monitoring of azathioprine by General Practitioners (GPs) and Secondary Care Specialists.

If the GP is unwilling to accept prescribing responsibility for the patient, the Secondary Care Specialist should be informed within one week of receipt of the consultant's letter. In such cases the GP must inform the consultant of all relevant medical information regarding the patient and any changes to the patient's medication irrespective of the indication.

2. Indication

The indication that this SCG covers is:

Steroid dependant / resistant inflammatory bowel disease (Crohns disease, ulcerative colitis, microscopic colitis). This is an unlicensed indication.

3. Patient Inclusion and Exclusion Criteria

<u>Inclusion</u>

The patient will be diagnosed by a specialist as suffering from inflammatory bowel disease (IBD) as outlined above.

Exclusion

Do not prescribe to patients with severe hepatic or renal impairment. Exclude patients with creatinine clearance of less than 30ml/minute.

Patients will not be pregnant or breast feeding when being treated as part of this Shared Care Guideline.

Patients over the age of 65 years are excluded from this Shared Care Guideline.

Patients with porphyrias (acute or cutaneous) are excluded from this Shared Care Guideline.

Patients being prescribed warfarin are excluded from this Shared Care Guideline.

4. Form, Dose and Route of Administration

These medicines will be given in tablet form.

- **Azathioprine** dosage: Usually 2mg/kg/day in a single dose; dosage range may vary from 1-2.5mg/kg/day in single dose. Initial prescription is usually half of the target dose if thiopurine s-methyltransferase (TMPT) level unknown (common initial dosage regimen: 50-100mg daily).
- **6-Mercaptopurine** dosage: Usually 1mg/kg/day in a single dose. Initial prescription is half target dose if TPMT level unknown.

Treatment is usually continued for a minimum of two years, subject to adequate response. Specialists will promptly provide advice to GPs regarding any dose changes.

5. Contraindications

Not to be used in patients with hypersensitivity to azathioprine or 6-mercaptopurine. Patients with pre-existing severe hepatic or renal impairment are contraindicated. There must be no contemporaneous use of live vaccines.

6. Interactions

Allupurinol significantly inhibits the metabolism of azathioprine; if it is co-prescribed the dose of azathioprine must be reduced by 75% (one quarter of the original dose). Patients who are taking allopurinol are not excluded from this guideline, however caution must be used in the group and shared care arrangements made only when fully stabilised.

With co-trimoxazole or trimethoprim, there is an increased risk of haematological toxicity and therefore these must not be used whilst a patient is taking azathioprine.

The effects of warfarin potentially reduced and patients who are taking warfarin are excluded from this guideline.

Patients taking aminosalicylates (eg sulfasalazine or mesalazine) have a theoretical risk of leucopenia.

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7. Side Effect Profile

Mucocutaneous: urticaria, erythematous pruritus, oral ulceration, alopecia (rarely: erythema nodosum)

Haematological: Leucopenia (including potentially life-threatening neutropenia), anaemia, macrocytosis (mild; if severe seek other causes), thrombocytopenia, erthroid hyperplasia.

Gastrointestinal: nausea, vomiting, loss of appetite, diarrhoea, colitis

Hepatic: deranged liver function tests, cholestatic hepatitis

Musculoskeletal: myalgia, arthralgia

Other: rare (but potentially serious) side effects include pancreatitis (reversible) pneumonitis, cardiac dysarrhythmias, interstitial nephritis, opportunistic infections

Infection risk: opportunistic infections can occur, outwith the context of leucopenia/neutropenia. These can require early and vigorous treatment; azathioprine 6-mercaptopurine may need to be stopped until the infection has cleared. Live vaccines are contra-indicated; vaccination against influenza is recommended.

8. Clinician Responsibilities for Assessment, Prescribing and Monitoring for Primary and Secondary Care

Stage of Treatment	Hospital Specialist	General Practitioner
Pre-Initiation	TPMT, Hep B & C, HIV , EBV and HVZ serology may be done in advance if time permits, If not at initiation of treatment	
Initiation	Initial supply via hospital for patient Assess patient following referral from GP Recommend appropriate treatment to the GP Carry out baseline U&Es, LFTs and FBCs FBC & LFT weekly for at least 4 weeks and until dosage regime stable	Maintain prescribing on FP10 after a period of stabilisation.
Maintenance	Assess clinical response to treatment Provide adequate advice and support to GPs Inform GP of dose amendments as appropriate	Prescribe suggested medication. Monitor patient for adverse effects: FBC & LFT weekly for 8 weeks, fortnightly for 2 months then monthly; reduce frequency to 3

		monthly on specialist advice. Refer to consultant where necessary.

9. Monitoring

Disease monitoring:

Clinical response to therapy

Drug monitoring:

Baseline

FBC, BCP (for renal function & LFTs) and TPMT assay

On-going

FBC & LFT should be checked once weekly for at least 4 weeks then fortnightly for 2 months, if stable the monitoring may be reduced to monthly. Once the dose, disease and blood monitoring is stable the frequency of monitoring may be reduced to 3 monthly on advice of specialist.

If doses are changed then monitoring should done as if the drug has been started.

Monitoring parameter	Recommended response
WBC 3.0-3.5 x 10 9/l < 3.0 x 10 9/1	Recheck FBC. Inform consultant within 72 hours Stop Drug and refer back to consultant within 24 hours
Neutrophils 1.5-2.0 x 10 9/l <1.5 x 10 9/l	Recheck FBC. Inform consultant within 72 hours Stop Drug and refer back to consultant within 24 hours
Platelets <100 x 10 9/l	Stop Drug and refer back to consultant within 24 hours
ALT> twice normal limit (or if baseline ALT is abnormal, twice baseline level increase)	Recheck if not settling within two weeks or if worsening refer back to consultant (initial temporary increase is normal)
Alk Phos >200 i.u./L	Stop drug and refer back to consultant within 24 hours **In Autoimmune Hepatitis, to only stop if 25% increase in ALP**
MCV > 100 fl	Check **serum folate** and **B12 & TSH**. and alcohol consumption

> 105 fl	Notify consultant within 72 hours
Creatinine Increase above normal range, or above baseline in patients with renal impairment	Stop drug and refer back to consultant within 24 hours
Rash or oral ulceration	Withhold **until discussed** with specialist team within 24 hours
Abnormal bruising or **severe** sore throat or throat ulceration	Withhold **until FBC results** available & discuss with the specialist team within 24 hours
Pregnancy	Continue but refer to gastroenterologist within 72 hours

Refer back to the Consultant using the contact number on the first page of this document.

Details of contraindications, cautions, drug interactions and adverse effects listed above are not exhaustive. For further information always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).

10. Patient Information

Patients should be informed about benefits and risks of treatment and need for monitoring.

Patients should report, immediately, any fever, rash, bruising, bleeding, sore throat, oral ulceration, jaundice, infection or new abdominal pain.

In the event of any serious concerns, abnormalities or symptoms not specified above, please contact the Gastroenterology Department.

11. Resources and Guidance

http://www.nice.org.uk/nicemedia/live/13936/61002/61002.pdf
http://www.medicinescomplete.com/mc/bnf/current/PHP527-azathioprine.htm
http://www.medicinescomplete.com/mc/bnf/current/PHP531-mercaptopurine.htm?q=6-mercaptopurine&t=search&ss=text&p=2#_hit
http://www.medicines.org.uk/emc/medicine/24688/SPC
http://www.medicines.org.uk/emc/medicine/26877

12. References

1. Muller, Dr A.F.. (2012). Disease Modifying Drugs in Inflammatory Bowel Disease (IBD). *Inflammatory Bowel Disease Committee of the British Society of Gastroenterology (BSG).* 1 (1), p2-24.
2. National Clinical Guideline Centre (2012). *Crohn's disease, Management in adults, children and young people.* London: National Institute for Clinical Excellence. p46-392.