Cardiff & Vale (C&V) UHB Corporate Medicines Management Group (c MMG)

SHARED CARE AND NEAR PATIENT TESTING

Drug: 6-MERCAPTOPURINE **Protocol number: CV 25**

Indication: **INFLAMMATORY BOWEL DISEASE**

General guidance

This protocol sets out details for the shared care of patients taking **6-mercaptopurine** and should be read in conjunction with the General Guidelines for Shared Care. Sharing of care requires communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **The doctor who prescribes the medication legally assumes responsibility for the drug and the consequences of its use.** The prescriber has a duty to keep themselves informed about the medicines they prescribe, their appropriateness, effectiveness and cost. They should also keep up to date with the relevant guidance on the use of the medicines and on the management of the patient's condition.

Background

6-mercaptopurine is used as second line therapy for patients with steroid-dependent ulcerative colitis or Crohn's disease, or where there are frequent relapses or severe disease (*unlicensed indication*) The drug has immunosuppressive and steroid-sparing properties. It may be used in patients intolerant to azathioprine.

Responsibilities

A. Consultant responsibilities

1. When treatment is **initiated** send Shared Care/Near Patient Testing request form with Shared Care Protocol to GP.
2. Baseline and continued monitoring until patient is stabilised of biochemical and haematological parameters (see page 2) If Near patient Testing not agreed then monitoring will be continued after patient is stabilised.
3. Initiate therapy following full discussion with the patient of benefits and risks.
4. The patient will be informed to contact their GP immediately if any of the following occur: rash, mouth ulcers, bruises, itching, bleeding, fever, sore throat, jaundice or other infection.
5. Check patient's immune status to *herpes zoster* and notify GP to enable coding to occur.
6. When a GP positive response to SC/NPT has been received and patient has been stabilised send a letter to GP "handing over" the Shared Care/Near Patient Testing of the patient to the GP.
7. Respond to any request from GP to review the patient due to adverse effects of therapy.

8. Advise the GP on continuing or stopping 6-mercaptopurine therapy following medical review of the patient and associated drug therapy
9. If Near Patient Testing not agreed notify GP if patient is failing to attend for appropriate monitoring and advise GP on appropriate action.

B. General practitioner responsibilities

1. Within one week of receipt return the completed Shared Care/ Near Patient Testing request form to indicate whether or not willing to undertake Shared Care/Near Patient Testing.
2. Prescribe 6- mercaptopurine as part of the Shared care / Near Patient Testing agreement.
3. Monitor the general health of the patient.
4. Where Near Patient Testing is agreed monitor the parameters indicated (see below), and report to and seek advice from the consultant on any aspect of patient care which is of concern.
5. Report adverse effects of therapy to the consultant and the Medicines and Health Care products Regulatory Agency (MHRA).
6. Recommend that patient receives pneumococcal vaccination and annual influenza vaccination as well as Zostavax as part of the national shingles immunisation programme. (see Special recommendations)
7. If Near Patient Testing not agreed to act on advice provided by the Consultant if patient does not attend for appropriate monitoring.

C. Patient responsibilities

1. Consent to treatment with 6-mercaptopurine.
2. Attend regular appointments with specialist centre and GP.
3. Report any side effects to the specialist or GP whilst taking 6-mercaptopurine.

Dosage Regimen

Usual starting dose 50mg daily. Final dose of 6-mercaptopurine 1.5mg per kilogram. Occasionally higher doses are used for non-responsive patients.

Monitoring

Before treatment Full blood count (FBC), Creatinine and electrolytes and LFTs

Baseline TPMT levels can be checked, but are not a substitute for regular monitoring of FBC. (X2 EDTA tubes, sent to either Purine Research Lab, Guy's Hospital, or Dept Biochemistry, Birmingham City Hospital).

During treatment FBC weekly or fortnightly for first four weeks and then every two months. Check FBC two weeks after any dose increase. LFTs at one month, two months, 4 months and 6 months and then every six months.

Stop 6-mercaptopurine if any of the following occurs: -	
WBC	$< 4x10^9/L$
Neutrophils count	$<1.5x\ 10^9/L$
Platelets	$< 150 \times 10^9/L$
AST/ALT/ Alkaline phosphatase	> 2-fold rise (from upper limit of reference range)

*** patients may continue treatment if WBC is 3.0 - 4.0 x 10^9/L if the neutrophil count is above 1.5 x 10^9/L**

In addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Adverse effects

Bone marrow suppression (see page 2) Nausea, vomiting, headache, joint aches, diarrhoea, fever or malaise usually occur in first four weeks. Pancreatitis, cholestasis, renal failure, pneumonitis, skin rashes and alopaecia are uncommon.

Interactions

Use of allopurinol prevents breakdown of 6-mercaptopurine and dosage of the latter has to be reduced greatly. Allopurinol should be stopped and an alternative agent used.

The anticoagulant effect of warfarin may be reduced by 6-mercaptopurine. Regular INR monitoring should be undertaken if both agents are used.

Sulphasalazine and salicylic acid derivatives inhibit 6-mercaptoprurine in vitro and may result in 6-mercaptopurine toxicity. Therefore, FBC and LFTs should be monitored more closely after the introduction of these drugs by the specialist team.

Special recommendations

- Patients who have not previously had chickenpox should be identified and advised to seek medical attention if they subsequently come into contact with somebody who has chickenpox or shingles.

- The administration of live vaccines should be generally avoided as in the other SCPs. A diminished response to killed vaccines, such as hepatitis B has been observed in patients receiving a combination of azathioprine and corticosteroid therapy. However Department of health guidelines advise that **Zostavax may be given to patients taking 6-mercaptopurine ≤ 1.5mg/kg/day either alone or in combination with prednisolone ≤ 20mg daily.** Specialist advice should be sought for other treatment regimes.

- In patients receiving 6-mercaptopurine exposed to chickenpox or shingles, whose immune status to *Herpes Zoster* is unknown or negative, prophylactic aciclovir

(po) (unlicensed use) should be prescribed 40mg/kg daily in four divided doses for 7 days starting one week after exposure.

- If a patient on 6-mercaptopurine develops chickenpox aciclovir should be started urgently. If the rash is severe and extensive and the patient is systemically unwell then he/she will need to be admitted urgently via the medical assessment unit as intravenous acyclovir and possibly other support will be required. If the patient is well however and the rash is no worse than would usually be seen then there is no indication for urgent admission or referral. The patient can be treated at home with oral aciclovir and advised to seek medical advice if there is any worsening of their condition.

- Patients should also be warned to seek advice if severe abdominal pain develops as 6-mercaptopurine can cause pancreatitis. Serum amylase should be checked urgently in this situation**.**

Female patients considering pregnancy should be advised to discuss with their doctor the benefits and risks of continuing the drug during pregnancy

Contact Details

If you suspect an adverse event, please contact the supervising Gastroenterologist at the relevant hospital. For UHW call 029 20746510 or 029 20742183. For Llandough call 029 20716820.The IBD Nurse Advice line is 029 20716403

Date of next review December 2021