THE SHEFFIELD AREA PRESCRIBING GROUP

Shared Care Protocol

For

Mercaptopurine Tablets

Shared care protocol developed by:

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Shared Care Protocol for Mercaptopurine Tablets in Inflammatory Bowel Disease

Statement of Purpose

This shared care protocol (SCP) has been written to enable the continuation of care by primary care clinicians of adult patients initiated and stabilised on mercaptopurine by gastroenterologists at STH.

The use of mercaptopurine in acute leukaemias and chronic myeloid leukaemia is outside of the shared care protocol.

Indication

Mercaptopurine is used to influence the immune response in treatment of severe acute Crohn’s disease, maintenance of remission of Crohn’s disease and ulcerative colitis (unlicensed indications). The main role of mercaptopurine is steroid sparing.

Selection of patients

All patients should be assessed for thiopurine methyltransferase (TPMT) activity before offering mercaptopurine. Patients will not be offered mercaptopurine if TPMT activity is deficient (very low or absent). Mercaptopurine may be considered at a lower dose if TPMT activity is below normal but not deficient. (As per local laboratory reference values).

All adult patients will be treated and stabilised on mercaptopurine by a secondary care specialist. Patients initiated on therapy are suitable for referral to a primary care service once stabilised on treatment.

Patients with the following conditions are excluded from this protocol:

- Severe hepatic impairment
- Severe pleural effusion or ascites
- On more than the maximum recommended therapy
- Children under 16 years
- Patients who prefer to attend the hospital
- Interstitial lung disease

Dosage

1-1.5mg/kg/day
The maximum dose will differ between individuals. Some patients may respond to lower doses.
Mercaptopurine is available as 50mg scored tablets.

NB. Caution needed in patients with renal and hepatic impairment, consider using lower doses.
Contra Indications

TPMT deficiency homozygous state

Hypersensitivity to azathioprine, 6-mercaptopurine or to any of the excipients.

Malignant disease

Severe infections

Severely impaired hepatic or bone-marrow function.

Pancreatitis

Lactation (refer to secondary care if patient breast feeding).

Pregnancy- unless the benefits outweigh the risks. If a patient falls pregnant or wishes to conceive refer to secondary care.

Live vaccines, e.g. VZV, MMR, BCG, small pox, yellow fever, etc. should not be given to patients taking mercaptopurine (refer to Green book for further advice on individual vaccines as the list is not exhaustive).

Live oral polio should not be given to patient or household contacts.

**NB. Pneumovax II® and annual flu vaccine should be given**

**Side–effects**

The details below are not a complete list and the BNF and the SPC remain authoritative.

Very common: bone marrow function suppression, infections, leucopenia, thrombocytopenia, nausea, vomiting

Common: pancreatitis, hepatotoxicity, biliary stasis, anaemia

Uncommon / rare / very rare: new rashes (consider herpes zoster), diarrhoea, hypersensitivity reactions, alopecia, anorexia

Patients must be advised to inform their doctor immediately about sore throat with mouth or throat ulcers, fever, infections, unexplained bruising / bleeding or other signs of myelosuppression.

**Monitoring**

**Secondary care:**
All patients should have their TPMT level checked prior to starting mercaptopurine.
Baseline FBC, full LFTs (including GGT), U&E/creatinine, CRP then FBC, full LFTs, U&E/creatinine at 2 and 4 weeks, then monthly for 3 months or until stable.
Baseline virology screening if not done previously (to include varicella zoster, cytomegalovirus, Epstein Barr virus, Hepatitis B and C and HIV).
Primary care:
FBC, full LFTs, U&E/creatinine 3 monthly once care shared.

Ask about rash, oral ulceration or sore throat, infections, or evidence of bruising or bleeding each time. Also ask patients to report these symptoms immediately if they occur while on mercaptopurine.

Revert to initial monitoring advice if any increase in dose.

Stop mercaptopurine and contact help line if:

- WCC <3.5 x 10^9/l
- Neutrophils <2 x 10^9/l
- Platelets <150 x 10^9/l
- AST/ALT >2 x increase on 2 occasions, or significant rise from baseline

Sore throat with oral or pharyngeal ulceration, fever, dizziness;
Nausea, vomiting or diarrhea;
Unexplained bruising/bleeding, new rash;
Non compliance with monitoring.

Check FBC if significant infection present withhold treatment until results are known.

Overdose – refer directly to secondary care.

Interactions

The details below are not a complete list and the [current BNF](#) and the [SPC](#) remain authoritative.

**Allopurinol** - decreases the rate of catabolism of mercaptopurine. Reduce dose of mercaptopurine to one quarter of usual dose.

Mercaptopurine interacts with febuxostat, warfarin, trimethoprim, co-trimoxazole, aminosalicylates, clozapine.

Dairy products possibly reduce plasma concentration of mercaptopurine—manufacturer of mercaptopurine advises to take at least 1 hour before or 2 hours after dairy products.

Additional information

*Chicken pox/varicella zoster can be fatal in immunosuppressed patients:* if contact suspected check antibody status, stop mercaptopurine and contact relevant secondary care department. Varicella zoster immunoglobulin may be given where contact occurs, preferably within 3 days but up to 10 days after exposure. Systemic antivirals may be needed if infection is suspected. Follow current advice in the [Green Book](#).

Responsibilities of consultant clinician / secondary care clinician

- To discuss benefits and side effects of treatment with the patient/carer and obtain informed consent. This is particularly important for unlicensed indications.
- Carry out pre-treatment tests
- To initiate mercaptopurine in appropriate patients and issue patient with patient information leaflet and counsel on contraceptive advice, if applicable
- To prescribe and monitor for the first three months or until patient stable
- To refer patients to their GP for shared care once stabilised on treatment
- To contact patient’s GP to request prescribing under shared care using Shared Care Transfer form\(^6\). Send a link to or copy of the shared care protocol to the patient’s GP.
- To advise the GP regarding continuation of treatment, including the length of treatment
- To discuss any concerns with the GP regarding the patient’s therapy
- To monitor disease appropriately whilst the patient is under shared care. Whilst on mercaptopurine, the patient must not be discharged from the consultant’s care.
- To issue the patient with a blue blood monitoring booklet once shared care is agreed.

**Responsibilities of the primary care clinician**

- To refer appropriate patients to secondary care for assessment
- To agree to prescribe mercaptopurine for patients in line with the shared care agreement and return completed Shared Care Transfer form to relevant department
- To report any adverse reaction to the CHM and the referring consultant
- To continue to prescribe for the patient as advised by the consultant
- To undertake monitoring as per shared care protocol, see above
- To inform the consultant if the patient discontinues treatment for any reason
- To seek the advice of the consultant if any concerns with the patient’s therapy
- To conduct an annual face to face medication review or more frequent if required
- In the event that the GP is not able to prescribe, or where the SCP is agreed but the consultant is still prescribing certain items e.g. Hospital only product; the GP will provide the consultant with full details of existing therapy promptly by fax on request
- Check for possible drug interactions
- For hospital prescribed drugs GP are advised to follow recommendations for [Recording Hospital-Only Drugs on Clinical Practice Systems](#)

**Re-Referral guidelines**

See under monitoring section above.

Pregnancy and / or preconception advice/ management.

Deterioration of disease.

**Financial implications**

If mercaptopurine is issued under the shared care arrangements then drug costs will move from secondary to primary care. In primary care mercaptopurine will be issued on FP10 prescriptions. Out patient appointments at STH will be reduced, but there will be an increase in payments to GPs under the DMARD for locally commissioned services.

**Support, education and information**

A drug information sheet and shared care booklet has been issued to your patient.

Inflammatory Bowel Disease nurse advice line RHH (0114) 2712209

Inflammatory Bowel Disease nurse advice line NGH (0114) 2269031

On call specialist via RHH switchboard: (0114) 2711900

Secondary care assumes responsibility for the monitoring and re-prescription of mercaptopurine until stable dosage has been successfully achieved.

*Clinicians are reminded that the prescriber is responsible for monitoring the patient on the medication being prescribed.*
Patient information leaflets

These are provided to patient by secondary care, but can also be downloaded from -

References

1. Puri- Nethol summary of product characteristics (SPC)
   Available from www.emc.medicines.org.uk


   Available from: http://publications.nice.org.uk/crohns-disease-cg152

   Available from: http://publications.nice.org.uk/ulcerative-colitis-cg166

5. BNF at: http://www.bnf.org/bnf/index.htm

6. For “Azathioprine, Mercaptopurine and Methotrexate transfer form” see:

Full list of side-effects is given in the mercaptopurine summary of product characteristics (SPC), available from www.emc.medicines.org.uk.

This SCP has been updated from the SCP for Mercaptopurine Tablets approved by Sheffield Area Prescribing Committee, January 2010.