115FM.2.1 MERCAPTOPURINE FOR USE IN GASTROENTEROLOGY
Shared care protocol

This protocol provides prescribing and monitoring guidance for mercaptopurine therapy. It should be read in conjunction with the Shared Care Responsibilities document, the Summary of Product Characteristics (SPC) available on http://www.medicines.org.uk/emc/ and the BNF.

BACKGROUND FOR USE

- Mercaptopurine use in this protocol is limited to severe inflammatory bowel disease.
- Mercaptopurine is an immunosuppressant which is a metabolite of azathioprine. It has been used for over 25 years in inflammatory bowel disease and has a historical track record of use under shared care in Aylesbury Vale and Chiltern CCGs (and their prior organisations).

In the BNF it is recommended for use:

- In unresponsive and chronically active Crohn's disease.
- For refractory fistulating Crohn's disease.
- For maintenance of remission in ulcerative colitis.

It is recommended for use by the gastroenterology societies. Although it is unlicensed for these inflammatory bowel indications, it has had many years of experience in use both in hospital and in the community (both locally and nationally) and its use is considered routine.

CONTRAINDICATIONS AND PRECAUTIONS

Avoid in porphyria.

Dosage reductions are needed in renal impairment (see below).

Liver impairment – as the drug has hepatotoxic side effects moderate/severe hepatic impairment is a contraindication. Mild liver impairment requires dosage adjustment.

Avoid in pregnancy and in breastfeeding. Patient should be advised on adequate contraceptive precautions (for both males and females). If patient becomes pregnant, mercaptopurine should be stopped immediately and medical advice should be sought.

Hypersensitivity to any component of the preparation.

DOSAGE[2]

1 to 1.5 mg per kg daily (usual doses 50 mg, 100 mg or 150 mg).

Tolerated dose varies because bioavailability varies between individuals.

Reduce dose in moderate and severe renal impairment (see below).

Tablets are scored 50 mg tablets and so minimum dose adjustments are in 25 mg steps.

The dose may need to be reduced when mercaptopurine is combined with other drugs which can cause myelosupression.

In renal impairment[3]

GFR ml/min >50: No dose adjustment.

GFR ml/min 10 – 50: Reduce dosing interval to every 48 hours.

TIME TO RESPONSE: Up to 3 months.

Pharmacy Duration of Supply

The hospital pharmacy will supply 8 weeks of medication against the hospital prescription.

PRE-TREATMENT ASSESSMENT BY THE SPECIALIST

- Before starting, check FBC, U&Es and LFTs.

MONITORING during first 8 - 10 weeks (by the specialist)

- FBC weekly for one month, fortnightly for two months.
- LFTs at two weeks, four weeks, eight weeks and then three monthly.

ONGOING MONITORING SCHEDULE (by GP)

Parameter	Frequency and Result
FBC	Every 3 months
LFTs	Every 3 months

In addition to absolute values for haematological indices, a rapid fall or consistent downward trend in any value should prompt caution and extra vigilance. In order to monitor trends, it is recommended that all blood test results are entered in the patient held monitoring booklet.

SIDE EFFECTS AND ACTIONS TO BE TAKEN[1]

Side Effects	Action
WBC <3.5 x 10^9/l Neutrophils <2 x 10^9/l	Withhold and discuss with specialist/IBD nurse.
Platelets <150 x 10^9/l	Withhold until discussed with specialist/IBD nurse.
Liver impairment Cholestatic jaundice >2 fold rise in ALT/AST from upper limit of reference range	Withhold. Look for alternative cause. Repeat LFTs. If abnormal discuss with specialist/IBD nurse.
Abnormal bruising	Check FBC immediately. Withhold until discussed with specialist/IBD nurse.
Sore mouth/oral ulcers *rare*	Stop and rechallenge at a lower dose. Telephone advice available if needed (IBD nurse).
Nausea and vomiting *common*	Stop and rechallenge at a lower dose. Telephone advice available if needed (IBD nurse).
Diarrhoea *a common sign of a not tolerated dose*	Stop and rechallenge at a lower dose. Telephone advice available if needed (IBD nurse).
Skin rash	Stop drug until rash clear – rechallenge at a lower dose. Telephone advice available if needed (IBD nurse).
Hypersensitivity reactions including: Malaise, dizziness, nausea, vomiting, fever, rigors, rash, myalgia *rare*	Stop and consider rechallenge at a lower dose (or if symptoms severe seek advice).
Hypersensitivity to excipients which include: Lactose, maize starch, hydrolysed starch, stearic acid, Mg stearate	If severe symptoms stop drug.
Alopecia *rare*	If severe stop drug.
Pancreatitis *common*	Stop drug.
Lymphoma *very rare*	Stop drug (all cases were when used in combination with an anti-TNF).

DRUG INTERACTIONS[1]

- When co-prescribed with allopurinol/oxipurinol/thiopurinol, the dose of mercaptopurine should be reduced to one quarter of the original dose.
- Inhibition of the anticoagulant effect of warfarin has been reported.[2] Monitor INR more closely at initiation of treatment in patients taking warfarin.
- There is increased risk of haematological toxicity when mercaptopurine is given with trimethoprim or co-trimoxazole.
- There is *in vitro* evidence that aminosalicylate derivatives, e.g. olsalazine, mesalazine, sulphasalazine inhibit the TPMT enzyme. If this enzyme is inhibited, this would make patients

more susceptible to toxic side effects of mercaptopurine and caution is advised by the manufacturers.[1]

- Avoid live vaccines.
- The manufacturers of febuxostat and ribavirin advise to avoid co-administration with mercaptopurine.
- Possible increased risk of lymphoma when used in combination with anti-TNFs. For this reason, these combinations should be managed by the specialist and are not suitable for shared care.

BACK-UP ADVICE AND TREATMENT

Contact Details	Wycombe and Amersham	Stoke Mandeville
Gastroenterology	Via switchboard 01494 526161 Registrar: Bleep 6582, 6583 Consultant secretary: Dr Cullen 01494 425959 Dr Gorard 01494 425267 Dr Johns 01494 425267 Dr Maggs 01494 425267 Dr Helmer 01494 425267	Via switchboard 01296 315000 Registrar: Bleep 992 Consultant secretary: Dr Sekhar 01296 315299 Dr Hossain 01296 315299 Dr Khan 01296 315299
Medicines Resource Centre	01494 425355	

SHARED CARE AGREEMENT FORM

Available on DocGen. When not available, use the Word version linked here.

References

1. SPC for mercaptopurine available on http://www.medicines.org.uk/emc/ last updated 13/11/2015 (accessed on 05/05/2017).
2. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press http://www.medicinecomplete.com (Accessed on 05/05/2017).
3. Renal Drug Database (online) available at https://renaldrugdatabase.com/ (Accessed on 05/05/2017).

See also:

Guideline 280FM Management of Patients on Immunosuppressants admitted with Suspected Infections

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Area Prescribing Committee	28th June 2017
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SDU(s)/Department(s) responsible for updating the guideline	Gastroenterology
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