

## Mesalazine and other aminosaliclylates in Inflammatory Bowel Disease (Adults)

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs). This guideline reinforces the basic premise that: When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the "sharing of information with the individual GP and their mutual agreement to the transfer of care."

These are not rigid guidelines. On occasions, Consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

### Indications:

#### Ulcerative Colitis

Mesalazine is licensed for the treatment of mild to moderate ulcerative colitis and the maintenance of remission.

#### Crohn's disease\*

Mesalazine can be prescribed for patients with one or more of distal ileal, ileocaecal or right-sided colonic disease for a first presentation or a single inflammatory exacerbation in a 12-month period who decline, cannot tolerate or in whom glucocorticosteroid treatment is contraindicated. Mesalazine can also be considered for maintenance of remission of Crohn's disease.

#### Other

Mesalazine may be considered as monotherapy or as part of combination therapy in those with isolated colonic or ileocolonic disease in certain circumstances.

\*NB Pentasa® does not have a UK licence for this specific indication

### Dosage and administration:

#### Treatment

Mesalazine: (Pentasa® SR 500mg/1g) 2-4g once daily or in two or three divided doses.

Mesalazine MR (400/800mg) up to 4.8g in divided doses.

#### Maintenance/remission

Mesalazine (Pentasa® SR 500mg/1g) 2g once daily.

Mesalazine MR (400/800mg) up to 2.4g once daily or in divided doses.

NB Pentasa® is 1<sup>st</sup> line treatment for all new patients. Some patients may be on other brands of mesalazine. For patients prescribed mesalazine MR 400/800mg, the Octasa® brand is the cost effective brand of choice in primary care.

Sulfasalazine - see SPC for dosing schedules.

### Additional Information

- Mesalazine is the formulary choice of aminosaliclylate and is the active metabolite of all aminosaliclylates. This guideline also applies to sulfasalazine (licensed for the same indications and olsalazine and balsalazide (licensed for mild and mild to moderate ulcerative colitis respectively)). Please refer to [www.bnf.org](http://www.bnf.org) for further prescribing information.
- Sulfasalazine is metabolised to mesalazine and sulfapyridine. Sulfapyridine is responsible for most of the additional adverse effects of sulfasalazine.

### Monitoring requirements:

#### Mesalazine/Sulphasalazine:

Before treatment:

- FBC, U&Es, LFTs

During treatment:

- FBC, U&E, LFTs after 1 month, 3 months and 12 months. Then every 12 months unless concern

For patients with Crohn's disease and Ulcerative Colitis, responsibility for monitoring, once stable, rests with the GP.

It is acknowledged that monitoring requirements vary according to the Summary of Product Characteristics for different aminosaliclylates as well as for different brands of the same drug ([www.medicines.org.uk](http://www.medicines.org.uk)).

### Action to be taken if abnormal results/adverse effects:

- WBC < 3.5 x 10<sup>9</sup>/l Check neutrophil count
- Neutrophils < 2.0 x 10<sup>9</sup>/l Monitor weekly. If it falls below 1.5 x 10<sup>9</sup>/l STOP DRUG and contact GI consultant.
- Platelets < 150 x 10<sup>9</sup>/l Monitor weekly. If it falls below 100 contact hospital
- 3 fold rise in ALT/AST Monitor weekly. If ALT continues to rise, contact hospital
- >20% SrCr baseline rise Withhold until discussed with specialist team.
- Rash STOP DRUG and contact hospital for advice
- Oral ulceration Severe – STOP DRUG and contact hospital
- MCV > 105fl Check B12 and Folate and, if low, start appropriate supplements
- Abnormal bruising Repeat FBC, LFT and Clotting and act on results as above
- Sore throat Repeat FBC and act on results as above
- Nausea and dizziness If possible continue, may have to reduce dose or stop
- GI side effects Try symptomatic measures first

**Please note that 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.**

**Contraindications:**

- A history of sensitivity to salicylates or where there is renal sensitivity to sulfasalazine.
- Severe renal impairment (GFR less than 20ml/minute).
- Severe hepatic impairment
- Acute intermittent porphyria (sulfasalazine).
- Hypersensitivity reaction to sulphonamides / co-trimoxazole (sulfasalazine)

**Drug interactions:**

- Concurrent use of other known nephrotoxic agents, such as NSAIDs and azathioprine, may increase the risk of renal reactions.
- Sulfasalazine may reduce absorption of digoxin and folate.
- Concomitant treatment in patients receiving azathioprine/mercaptopurine can increase the risk of blood dyscrasias.

**Cautions:**

- Discontinue mesalazine if renal function deteriorates.
- Use with caution in the elderly and only when renal function is normal.
- Use of mesalazine during pregnancy should be with caution, and only if the potential benefits are greater than the possible hazards. Unless essential, it should be avoided by nursing mothers.
- Haematological and hepatic side effects are more common with sulfasalazine.

**Adverse Effects (mesalazine):**

Common GI: Nausea, diarrhoea, abdominal pain, headache.

Rare: Leucopaenia, neutropenia, thrombocytopenia, agranulocytosis, aplastic anaemia, hepatic abnormalities, renal impairment, interstitial nephritis, nephrotic syndrome.

Very rare: Exacerbation of colitis, Steven Johnson Syndrome, erythema multiforme.

Depression of sperm count and function occurs with sulfasalazine but not with mesalazine.

**Specialist responsibilities:**

1. Confirm the diagnosis of Inflammatory Bowel Disease (IBD) and discuss with the patient the benefits and side effects of treatment with an aminosaliclylate.
2. Ensure baseline monitoring of full blood count and biochemical profile.
3. Review the patient after one month (this can be in the gastroenterology specialist nurse clinic) and if the patient is tolerating and benefiting from the medication, a written request should be made to the GP to continue prescribing the medication and to continue the monitoring.
4. Prescribe the initial month of mesalazine or other aminosaliclylate during the trial period and discontinue if no response or significant adverse effect.
5. Regularly review the patient to monitor treatment efficacy tolerability, and to consider whether continuation of treatment is appropriate.
6. Communicate promptly with the GP when treatment is changed and each time the patient is seen.
7. Undertake any necessary monitoring at review appointments.
8. Ensure clear backup arrangements exist for GPs for advice and support.
9. Report serious adverse events to the Committee on Safety of Medicines (CSM)

**GP's responsibilities:**

1. Initial referral to a Consultant Gastroenterologist raising the possibility of IBD.
2. Provide the patient with monthly repeat prescriptions of medication once the specialist has recommended continuation therapy.
3. Continue monitoring as outlined on the first page and document results on the practice computer.
4. Ensure practice computer is updated with any dose changes.
5. Report any adverse effects to the consultant.
6. Refer back to the consultant if the patient's condition deteriorates or if there is a change in the patient's status.
7. Contact the consultant if they do not agree with the treatment recommendation, or if there is a perceived problem with compliance or concordance, or if they have any questions about the management plan.

**Patient's responsibilities:**

1. Read the written information provided about the drug and have a clear understanding of the risks / benefits of oral mesalazine / aminosaliclylate therapy.
2. Attend for blood tests.
3. Allow at least 48 hours for the prescription from the GP to be generated (once the GP has agreed to take on the prescribing).
4. Report any adverse effects, concerns or lack of understanding of the treatment to the GP or specialist.
5. Take monitoring booklet every time the patient sees their GP, has a hospital appointment or visits the pharmacist

**Secondary care review:** Patients will be reviewed one month after starting mesalazine or other aminosaliclylate, and thereafter at a frequency determined by the clinical need by the consultant clinic, or if requested to review by the GP.

Mesalazine availability: Pentasa MR 500mg tablet: 100 = £30.74 1g sachets: 50 = £30.74

Octasa MR 400mg tablet: 90 = £ 19.50 800mg tablet: 180 = £ 95.00 (see BNF for sulfasalazine, olsalazine, balsalazide)

*Prices from September 2016 Drug Tariff (online)*

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