Mesalazine and other aminosalicylates (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:
Aminosalicylates and corticosteroids form the basis of drug treatment of inflammatory bowel disease. Mesalazine is licensed for the treatment of mild to moderate ulcerative colitis and the maintenance of remission. It is indicated for the maintenance of remission in Crohn’s ileocolitis and is also used locally in the treatment of active disease.

### Dosage and administration:
- **Mild to moderate ulcerative colitis attack:** Mesalazine (Asacol MR) 400 to 800mg orally three times daily. This dose can be continued to maintain remission.
- **Active Crohn's disease, second-line, added to systemic corticosteroids:** Asacol MR 400 to 800mg orally three times daily OR Pentasa orally up to 4g daily in divided doses (for full bowel disease). The treatment initiated for active disease can be continued to maintain remission, if appropriate.

### Additional Information
- Mesalazine is the formulary choice of aminosalicylate and is the active metabolite of all aminosalicylates. 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).
- Sulfasalazine is metabolised to mesalazine and sulfapyridine. Sulfapyridine is responsible for most of the additional adverse effects of sulfasalazine.

### Monitoring requirements:

**Mesalazine:**
- Before treatment:
  - Urea and electrolytes (U&Es)
- During treatment:
  - U&Es every 3 months for the first year, every 6 months for the next 4 years, then annually if stable
  - Full blood count (FBC) including platelets and liver function tests (LFTs) if haematological or hepatic adverse effects are suspected

**Sulfasalazine:**
- Before treatment:
  - FBC including platelets, U&Es and LFTs
- During treatment:
  - FBC and LFTs monthly for 3 months, then every 3 months thereafter.
  - If stable after 2 years, monitoring can be discontinued

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

### Action to be taken if abnormal results/adverse effects:
- **WBC< 4 x 10^9/l** Check neutrophil count
- **Neutrophils < 2.0 x 10^9/l** Monitor weekly. If it falls below 1.5 x 10^9/l STOP DRUG and contact GI consultant.
- **Platelets < 150 x 10^9/l** Monitor weekly. If drop below 100 contact hospital
- **3 fold rise in ALT/AST** Monitor weekly. If ALT continues to rise, contact hospital
- **Rash** STOP DRUG and contact hospital for advice
- **Oral ulceration** Severe – STOP DRUG, Corlan pellets and contact hospital
- **MCV > 105fl** Check B12 and Folate and, if low, start appropriate supplements
- **Abnormal bruising** Repeat FBC 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 (CKD stages 4 and 5 with a GFR less than 20ml/minute).
- Children under 2 years of age.
- Acute intermittent porphyria (sulfasalazine).

Drug interactions:
- Asacol MR should not be given with lactulose or similar preparations which lower the stool pH and may prevent the release of mesalazine.
- 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.

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):
Commonly GI, including nausea, diarrhoea and abdominal pain. Headache. Rarely, leucopenia, thrombocytopenia, agranulocytosis, aplastic anaemia, hepatic abnormalities, renal impairment, interstitial nephritis and nephrotic syndrome. Very rarely, exacerbation of colitis, SJS, 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 aminosalicylate.
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 2 months of mesalazine or other aminosalicylate during the trial period and discontinue if no response or significant adverse effect.
5. Provide the patient with a shared care booklet and enter the blood results into the booklet.
6. Regularly review the patient to monitor treatment efficacy tolerability, and to consider whether continuation of treatment is appropriate.
7. Communicate promptly with the GP when treatment is changed and each time the patient is seen.
8. Undertake any necessary monitoring at review appointments.
9. Ensure clear backup arrangements exist for GPs for advice and support.
10. 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. The patient should allow at least 48 hours for the prescription from the GP to be generated once they have agreed to take on prescribing.
3. Continue monitoring as outlined on the first page and document results in the shared care booklet.
4. Report any adverse effects to the consultant.
5. Refer back to the consultant if the patient’s condition deteriorates or if there is a change in the patient’s status.
6. 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:
Report any adverse effects, concerns or lack of understanding of the treatment to the GP or specialist. Attend for blood tests and take the monitoring booklet to all appointments.

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

Mesalazine availability: Asacol MR 400mg tablet: 90 = £31.22  800mg tablet: 180 = £124.86
Pentasa MR 500mg tablet: 100 = £25.48  1g sachets: 50 = £30.02  (see BNF for sulfasalazine, olsalazine, balsalazide)

Written By: Helen Dingle, Clinical Effectiveness Pharmacist, Medicines Management Team, Wirral PCT
Dr J Dawson, Consultant Gastroenterologist, Wirral University Teaching Hospital NHS Trust

Back up advice and support: IBD Specialist Nurse
Telephone: 0151 604 7459

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