Mesalazine (5-aminosalicylate) is a locally-acting anti-inflammatory agent for the treatment of ulcerative colitis (UC). Enemas, foams and suppositories deliver mesalazine to the terminal colon or rectum. The oral molecules and formulations deliver the drug to the terminal ileum and colon, reducing systemic absorption from more proximal sites by different mechanisms (see Table 1). The prescribing cautions and contraindications therefore apply to all drugs in this BNF category and, with the exception of sulfasalazine, the small differences in efficacy between the six brands but their release characteristics vary. Patients who are prescribed a product different from their usual brand should be advised to report any changes in symptoms but brand prescribing is not recommended.

**Dosage**

The precise dose varies depending on the preparation prescribed. For oral preparations, the daily dose of mesalazine or balsalazide (Colazide) for an acute attack may be twice the dose for maintenance; for olsalazine (Dipentum) it may be three times higher and four times higher for sulfasalazine.

Only sulfasalazine has specific recommendations for children’s doses. The BNF for Children suggests a dose of mesalazine for children aged two years or older; mesalazine is contraindicated in children under two years old.

**Adverse effects**

The more frequent adverse effects of mesalazine include gastrointestinal symptoms (diarrhoea, nausea, vomiting, abdominal pain, exacerbation of symptoms of colitis), headache and hypersensitivity reactions such as rash and urticaria. Gastrointestinal effects are common with sulfasalazine at doses exceeding 4g per day (as used in acute treatment).

Serious adverse effects may be associated with inflammatory and/or
Immunological disorders and include acute pancreatitis, hepatitis, myocarditis, pericarditis, lung disorders (including eosinophilia and fibrosing alveolitis), peripheral neuropathy, myalgia, arthralgia, serious skin reactions (including lupus erythematosus-like syndrome and Stevens-Johnson syndrome) and alopecia. Mesalazine is associated with renal dysfunction, including severe events such as interstitial nephritis and nephrotic syndrome, and severe blood dyscrasias (agranulocytosis, aplastic anaemia, leucopenia, neutropenia, thrombocytopenia) and methaemoglobinaemia. Adverse effects additionally reported with sulfasalazine include severe skin reactions, crystalluria, anaemia, depression, disturbances of smell and taste, discoloration of skin, urine and tears, photosensitivity, oligospermia and infertility. Toxicity is more likely in patients with G6PD deficiency or slow acetylator status.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of delivery</th>
<th>Ulcerative colitis*</th>
<th>Crohn’s disease*</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfasalazine</td>
<td>Combination of mesalazine and sulfapyridine; the molecule is split into its components in the colon</td>
<td>Induction and maintenance of remission</td>
<td>Treatment of active disease</td>
<td>Tablets, enteric-coated tablets, suppositories, suspension</td>
</tr>
<tr>
<td>Mesalazine</td>
<td>pH dependent and non-pH dependent modified/ prolonged release</td>
<td>Treatment of mild-to-moderate acute exacerbations and maintenance of remission</td>
<td>Maintenance of remission of ileo-colitis</td>
<td>Enteric-coated tablets, modified release tablets, rectal foam, retention enema, suppositories, modified-release granules</td>
</tr>
<tr>
<td>Olsalazine</td>
<td>Mesalazine dimer split by bacterial enzymatic action in the colon</td>
<td>Treatment of mild active disease and maintenance of remission</td>
<td>Not licensed</td>
<td>Capsules, tablets</td>
</tr>
<tr>
<td>Balsalazide</td>
<td>Mesalazine prodrug split by bacterial enzymatic action in the colon</td>
<td>Treatment of mild-to-moderate active disease and maintenance of remission</td>
<td>Not licensed</td>
<td>Capsules</td>
</tr>
</tbody>
</table>

* Check the licensed indications for each product before prescribing: the wording of the licensed indications varies and not all brands are licensed for all indications

Table 1. Variations of 5-aminosalicylates
Cautions and monitoring
Patients with severe allergies or asthma should be alert to worsening of symptoms during treatment.

Mesalazine and its precursor compounds should be used with caution in patients with renal impairment, including the elderly, and in those with impaired hepatic function. Renal function should be assessed before treatment, after three months and then annually, and more frequently if renal function is impaired. Mesalazine is contraindicated in severe renal impairment and should be discontinued if renal function deteriorates during treatment. Other drugs that are potentially nephrotoxic, including NSAIDs, may increase the risk of adverse renal effects.

Patients should be advised to report any unexplained bleeding, bruising, purpura, sore throat, fever or malaise. If a blood dyscrasia is suspected a blood count should be performed and, if confirmed, treatment should be stopped immediately. Concurrent use of azathioprine or other myelotoxic agents may increase the risk of blood dyscrasias.

A full blood count and liver function tests should be carried out before starting sulfasalazine and every second week during the first three months of therapy, repeated once after three months then every three months. Patients taking sulfasalazine should be warned that contact lenses and urine may be discoloured; they should be encouraged to have a high fluid intake.

Pregnancy and lactation
Mesalazine is not known to cause problems during pregnancy. Balsalazide should be avoided during pregnancy because experience is limited. Large doses of olsalazine impaired foetal development in rodents; the manufacturer advises avoiding its use during pregnancy unless the benefits outweigh the possible risks. There is no evidence that sulfasalazine is teratogenic though it may cause folate deficiency and neonatal haemolysis.

Breast-feeding infants whose mothers are taking mesalazine, olsalazine or balsalazide should be monitored for diarrhoea. Small amounts of sulfasalazine occur in breast milk and there is a theoretical risk of neonatal haemolysis (especially in infants who are G6PD deficient).

Declaration of interests
Steve Chaplin has none to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics

Place in therapy

Emma Johnston and Peter Irving

Mesalazine is the first-line treatment for the induction and maintenance of remission in patients with mild to moderate ulcerative colitis (UC).

Patients with left-sided or extensive UC should take ≥2g per day of oral mesalazine to induce remission. The addition of topical mesalazine to oral therapy has been shown to be beneficial even in patients with extensive colitis (at least with a non-colonic release preparation) and this can be a useful adjunct in patients not responding to oral therapy.

In patients with proctitis, mesalazine suppositories 1–2g per day are first-line therapy. Enemas are useful for left-sided disease proximal to the rectum but deliver less drug to the rectum than suppositories. Oral mesalazine (≥2g per day) can be added if there is no response to topical treatment alone.

Currently there is limited evidence to suggest there are large differences in efficacy between the various oral preparations, although as their release characteristics vary, the delivery of drug to different parts of the colon may also be variable. Thus, in patients not responding to one preparation, it is often worth swapping to another. In addition, most available preparations have been found to be at least as effective when used on a once-daily basis as when used with split-dosing regimens; this is likely to improve adherence.

Whether mesalazine significantly reduces the risk of colorectal cancer in patients with UC remains unclear. However, it undoubtedly reduces the risk of relapse of colitis. As with most chronic diseases, the greatest challenge is adherence and this should be discussed with all patients on long-term treatment.

References

Declaration of interests
Peter Irving has received honoraria for acting in an advisory capacity for, or speaking on behalf of, Warner Chilcott, Ferring, Shire, Ferring and Octasa. Emma Johnston has no interests to declare.

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