Section 1.5  Chronic Bowel Disorders (including IBD)

Aminosalicylates:
Mesalazine 400mg and 800mg MR Tablets (Octasa)
Mesalazine 400mg and 800mg MR Tablets (Asacol)
Mesalazine 1.2g MR Tablets (Mezavant XL)
Mesalazine 500mg Tablets (Pentasa)
Mesalazine 1g and 2g Sachets (Pentasa)
Mesalazine 1g Foam Enema (Asacol)
Mesalazine 500mg Suppositories (Asacol)
Mesalazine 1g in 100ml Enema (Pentasa)
Mesalazine 1g Suppositories (Pentasa)
Sulphasalazine 500mg EC Tablets
Balsalazide 750mg Capsules

Corticosteroids:
Hydrocortisone 10% Foam Enema
Prednisolone 20mg in 100ml Enema
Prednisolone 20mg Foam Enema
Prednisolone 5mg Suppositories
Prednisolone 5mg Tablets
Budesonide 3mg MR Capsules

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Prescribing Guidance:

See also the British Society of Gastroenterologists (BSG) Guidelines for the Management of Inflammatory Bowel Disease in Adults available at:


More recent guidance is available from the ECCO or European Crohn’s and Colitis Organisation website (via www.ecco-ibd.eu) in the publications section.
Aminosalicylates:
Aminosalicylates have a role in maintenance of remission in ulcerative colitis (UC). Topical treatment is more beneficial for left sided and distal colitis. Systemic or oral treatment, with or without topical treatment, is most beneficial where there is extensive colonic involvement. Maintenance therapy may reduce the risk of colorectal cancer by up to 75% and therefore long-term therapy is indicated in those patients with extensive UC.

The role of aminosalicylates in acute severe Crohn’s disease (CD) flare is unclear. There may be a role for mesalazine at a higher dose (3g or more) having some beneficial effect in small bowel Crohn’s disease although this has to be weighed against the small benefit margin.

The most effective intervention for maintenance of remission of Crohn's disease in patients who smoke is to stop smoking. This reduces likelihood of flare ups, complications, surgery and post-operative recurrence by up to threefold.

Higher doses are also used in mild active disease (UC and CD) where they have been shown to have some effect in placebo-controlled clinical trials. However, doses used in this indication are again generally higher than those that are licensed for use by the drug company – for specialist advice, contact a Consultant Gastroenterologist.

Mesalazine is now frequently used as the first-line aminosalicylate despite sulfasalazine showing a modest therapeutic advantage in one meta-analysis. The main reason for this is improved tolerability, as mesalazine is tolerated by 80% of those unable to tolerate sulfasalazine.

Which Mesalazine Preparation?
There is no evidence to show that any one oral preparation of mesalazine is more effective than another; however, the delivery characteristics of oral mesalazine preparations may vary. If it is necessary to switch a patient to a different brand of mesalazine, the patient should be advised to report any changes in symptoms. Where clinically appropriate, the more cost-effective preparations, such as Octasa and Pentasa, should be used first-line for new patients.

The appropriate preparation to use depends on the site of involvement. When given by mouth in uncoated preparations, mesalazine is rapidly absorbed from the jejunum and does not progress more distally. Several mechanisms are used to ensure delivery of oral preparations more distally. These include release in a controlled time-dependent manner (e.g. Pentasa), coating to modify release so that it only occurs when bowel pH rises to 7 (e.g. Asacol, Octasa), or diazo-bonding which leading to release predominantly in the left colon (e.g. balsalazide, sulfasalazine). Loose stools can occasionally be a problem with all preparations although they are less likely to occur if the dose is built up gradually and taken with food. Whichever drug or preparation is used, it should be used indefinitely because aminosalicylates exert their suppressive effects on colitis over many years.
Other mesalazine preparations include enemas and suppositories enabling delivery to left colon or rectum. Topical mesalazine is at least as effective as topical steroids in the management of distal disease and a combination of both appears to have a greater benefit than either approach alone.

Patients on aminosalicylates also have a small risk of interstitial nephritis and should have their blood pressure and renal function checked annually.

**CSM Recommendation - Blood Disorders:**

Patients receiving aminosalicylates should be advised to report any unexplained bleeding, bruising, purpura, sore throat, fever or malaise that occurs during treatment. A blood count should be performed and the drug stopped immediately if there is suspicion of a blood dyscrasia.

**Corticosteroids:**

Corticosteroids are the mainstay of treatment for moderate to severe attacks of both ulcerative colitis and Crohn’s disease. They have no role in the maintenance of remission.

Prednisolone is standard first line oral therapy with a recommended starting dose of 40mg. Initial doses are generally maintained for one to three weeks depending on response, before being reduced over around two months (by around 5mg per week). Patients who have previously had difficulties reducing should be tapered more slowly. Up to 80% of CD and UC patients will either respond or go in remission with steroid treatment. However, recurrence and long term steroid dependence remains a problem. Patients who have difficulty weaning off steroids should be considered for azathioprine.

Budesonide may have similar efficacy to prednisolone in moderate disease (it is less effective in severe disease) with a favourable systemic side effect profile and therefore may be appropriate in patients troubled by these effects. It is indicated in patients with disease affecting the ileum or ascending colon for short-term treatment (up to eight weeks).

Intravenous steroids (hydrocortisone 100mg qds) are appropriate for severe disease. Here, a five day regime should be completed prior to restarting oral steroids.

Oral and topical preparations are only usually combined in severe disease. Topical steroid preparations (e.g. prednisolone suppositories, enemas) may be useful in mild to moderate proctitis and sigmoiditis where response should be reviewed after a six week course.

The preparation should be appropriate for the area of bowel affected:
- Suppositories for disease confined to the rectum
- Enemas for left sided disease limited to the distal and splenic flexure
**Drugs Affecting the Immune Response:**

Patients should not be prescribed these products unless they are under the care of a Consultant Gastroenterologist. They should be counselled regarding the side effects associated with these medicines.

Azathioprine (AZT) or 6-mercaptopurine (6-MP) may be useful second-line therapies for active disease and maintaining remission in ulcerative colitis and Crohn’s disease (both unlicensed). They can normally be maintained for several years. Recent meta-analyses suggest that the odds ratio (OR) of response to be approximately 2.5 compared with placebo for both AZT and 6-MP. The standard doses are 2 to 2.5mg/kg for AZT and 1.5mg/kg for 6-MP.

Methotrexate (MTX) can also be used as a second or third line drug in patients with Crohn’s disease. There are few good quality trials but intramuscular MTX (15mg/week) in particular does seem to have beneficial role (OR=3) in maintenance of remission in CD.

Ciclosporin is increasingly being used in severe ulcerative colitis (unlicensed). Intravenous use (up to 4mg/kg daily – see protocol) can used in patients with severe active colitis who fail to respond to intravenous glucocorticoids. This can be tapered down and changed to oral preparation for up to 6 months. A protocol is available via the following [link](#).

Infliximab and adalimumab, both within their licensed indications, are recommended as treatment options for adults with severe active Crohn’s disease whose disease has not responded to conventional therapy (including immunosuppressive and/or corticosteroid treatments), or who are intolerant of or have contraindications to conventional therapy. *Infliximab* or *adalimumab* should be given as a planned course of treatment until treatment failure (including the need for surgery), or until 12 months after the start of treatment, whichever is shorter. *Infliximab* is a chimeric monoclonal antibody that binds to TNF-α and inhibits its functional activity. It can be used for:

- fistulising, active Crohn’s disease or
- severe, active Crohn’s disease.

The most common adverse events reported during *infliximab* therapy include acute infusion-related reactions, infections and delayed hypersensitivity reactions. *Infliximab* is contraindicated in people with moderate or severe heart failure and active infections. Before treatment is started, patients must be screened for active and inactive tuberculosis. For severe, active Crohn’s disease, *infliximab* is given as a 5mg/kg intravenous infusion over a 2 hour period followed by another 5mg/kg infusion 2 weeks after the first. If the disease does not respond after two doses, no additional treatment with infliximab should be given. In people whose disease responds, *infliximab* regimens include maintenance treatment (another 5mg/kg infusion at 6 weeks after the initial dose, followed by infusions every 8 weeks) or re-administration, otherwise known as episodic treatment (an infusion of 5mg/kg if signs and symptoms of the disease recur).
Adalimumab is a recombinant human monoclonal antibody that binds specifically to TNF-α, blocking interaction with its cell-surface receptors and thereby limiting the promotion of inflammatory pathways. Adalimumab is indicated for the treatment of severe, active Crohn’s disease in people whose disease has not responded despite full and adequate treatment with an immunosuppressant and/or corticosteroid, or who are intolerant to or have contraindications to such therapies. For induction therapy, adalimumab should be given in combination with corticosteroids. Adalimumab can be given as monotherapy if a person is intolerant to corticosteroids or when continued treatment with corticosteroids is inappropriate. Common adverse events associated with adalimumab include injection site reactions and infections. Before therapy is started, all patients must be screened for active and inactive tuberculosis. Adalimumab is contraindicated in patients with moderate to severe heart failure, active tuberculosis and other severe infections. The adalimumab induction treatment dose regimen for adults with severe Crohn’s disease is 80mg via subcutaneous injection, followed by 40mg 2 weeks later. If there is a need for a more rapid response to therapy, a dose of 160mg followed by 80mg 2 weeks later can be used, though the risk of adverse events with this higher dose is greater during induction. After induction treatment the recommended dose is 40mg every other week. This can be increased to 40mg every week in people whose disease shows a decrease in response to treatment.