Mesalazine for use in Inflammatory Bowel Disease

This document provides guidance on the prescribing and monitoring of mesalazine in Primary Care. These recommendations are primarily based on the latest British Society of Gastroenterology (BSG) guidance and BNSSG gastroenterology teams' consensus.

This monitoring guidance is an aid for prescribing and in no way obligates the GP to prescribe these drugs. As always GPs should prescribe only when they feel confident to do so.

Background

Mesalazine is a 5-ASA (5-aminosalicylic acid) used to treat inflammatory bowel disease (IBD), primarily ulcerative colitis (UC). It is licensed for the treatment of mild to moderate acute exacerbations of ulcerative colitis and for the maintenance of remission. It is also licensed for the maintenance of remission of Crohn's ileo-colitis but less commonly used. It can be given orally or topically.

Oral 5-ASA is the standard therapy for mild to moderately active UC. National guidance based on evidence from meta-analyses support the efficacy of oral 5-ASA for induction therapy for mild to moderately active UC. The majority of patients with mild to moderate UC will respond to 2–3 g 5-ASA (depending on formulation used) and higher doses can be used in those with more severe symptoms or those not responding initially.

Salofalk® granules is the first line oral mesalazine product on BNSSG Joint Formulary. Salofalk® retention enema/suppositories/foam enema are the first line topical products.

See formulary for alternative brands (TLS Blue) for use in established patients or where Salofalk® has failed / inappropriate. Clinicians should initiate the most cost-effective preparation available. Not all products are considered interchangeable. Switching between brands should be discussed with the relevant clinician. [6]

Treatment schedule

Preparation	Acute treatment dose	Maintenance dose
Oral: Salofalk® Granules	1.5g–3 g, once daily, dose preferably taken in the morning, alternatively 0.5g–1 g, 3 times a day	500mg TDS
Topical: Salofalk® Rectal Foam	2 g once daily, dose to be administered at bedtime.	Unlicensed
Topical: Salofalk® Enema	2 g once daily, dose to be administered at bedtime.	Unlicensed
Topical: Salofalk® Suppositories	0.5−1g BD- TDS, adjusted according to response, dose to be given using 500 mg suppositories, alternatively 1 g once daily, preferably at bedtime, dose to be given using 1 g suppositories.	Unlicensed

Other products may have different dosing schedules. See BNF and SPC for further details

Most patients are established on oral therapy with additional topical therapy added in for 4-8 weeks during flares. A small number of patients may be on topical therapy only. Although patients on topical therapy will have very little/negligible absorption, there is sometimes higher than expected absorption from suppositories due to the blood flow around the rectum, therefore monitoring (as detailed below) is still required for those small number of patients using only topical mesalazine.

Cautions and special recommendations

Cautions
Elderly; risk of mesalazine-induced renal toxicity-maintain adequate fluid intake; pulmonary disease, previous adverse drug reactions to sulfasalazine

Contra-indications
Known hypersensitivity to salicylates; severe renal or hepatic impairment; blood-clotting abnormalities.

See BNF and SPC for full list of cautions and contraindications

Adverse effects
The main adverse effect of concern with mesalazine is impairment of renal function including acute and chronic interstitial nephritis and renal insufficiency. These occur at a frequency of between 1:5000 and 1:10,000 which makes it a rare adverse effect. Although 5-ASA therapy is associated with renal complications, these may also be a primary complication of IBD itself, therefore baseline monitoring of renal function is recommended.
Given the unpredictable nature of this occurrence, BSG guidance suggests that patients on long-term 5-ASA therapy should have renal function checked, including eGFR before starting, after 2–3 months, and then annually long-term, although there are no data to support a particular surveillance interval.

Other common adverse effects include arthralgia, cough, diarrhoea, dizziness, fever, gastrointestinal discomfort including nausea and vomiting; headache, leukopenia, proteinuria, skin reactions.

See BNF and SPC for a full list of adverse reactions.

Drug interactions
Beware concomitant use of medications which may increase the risk of nephrotoxicity. There is weak evidence that mesalazine might decrease the anticoagulant effect of warfarin.

See BNF and SPC for a full list of interactions.

Monitoring

Pre-treatment assessment:

- Full blood count (FBC)
- Renal function (Serum creatinine (for creatinine clearance) or Estimated glomerular filtration rate)
- Liver Function (ALT and/or AST and albumin).

Ongoing monitoring:

- Check renal function (Serum creatinine (for creatinine clearance) or Estimated glomerular filtration rate) at 3 months then annually thereafter.

More frequent monitoring may be appropriate in patients at higher risk of toxicity or impaired renal function - to be directed by gastroenterology team.

Actions to be taken

Adverse effect	Action
Rise of creatinine level above the normal range (or rise of > 20% compared to baseline)	Withhold until discussed with gastroenterology team. Exclude other causes of raised creatinine
Any signs or symptoms of severe skin reactions, such as rash, mucosal lesions or other signs of hypersensitivity	Withold, seek specialist advice
Abnormal bruising or severe sore throat	Check FBC immediately and withhold until the result is available. Discuss with gastroenterology team.
Nausea, dizziness, headache, worsening diarrhoea	If troublesome and other causes are excluded, reduce or stop treatment and consider alternative refer to gastroenterology team

Gastroenterology departments' contact details

Trust	Contact	Contact details
University Hospitals Bristol and Weston Foundation Trust	For patients known to Gastroenterology- IBD Advice Line If patient is not yet under secondary care- Gastroenterology A&G https://remedy.bnssg.icb.nhs.uk/adults/gastroenterology-and-colorectal-surgery/advice-guidance-services/	0117 3421100 IBDnurses@UHBW.nhs.uk
North Bristol Trust, Southmead Hospital	For patients known to Gastroenterology- IBD Advice Line If patient is not yet under secondary care- Gastroenterology A&G	0117 4146354 ibdnurses@nbt.nhs.uk

	https://remedy.bnssg.icb.nhs.uk/adults/gastroenterology-and-colorectal-surgery/advice-guidance-services/	

References

1. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults, 2019 https://gut.bmj.com/content/68/Suppl_3/s1
2. NICE Guideline NG130: Ulcerative colitis: management, 2019: https://www.nice.org.uk/guidance/ng130/chapter/Recommendations#treating-acute-severe-ulcerative-colitis-all-extents-of-disease
3. BNF https://bnf.nice.org.uk/drugs/mesalazine/#indications-and-dose
4. Salofalk Summary of Product Characteristics https://www.medicines.org.uk/emc/product/139/smpc#gref
5. Octasa Summary of Product Characteristics https://www.medicines.org.uk/emc/product/10803/smpc
6. SPS guidance on Mesalazine Using mesalazine tablets appropriately – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice