Amber with Guidance (Amber-G) = To be recommended or initiated by a specialist with follow up prescribing and monitoring by primary care clinicians.*
**Specialist is defined by the APC as a clinician who has undertaken an appropriate formal qualification or recognised training programme, or who has the appropriate knowledge and competencies within the described area of practice.*

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Oral Mesalazine Preparations for Ulcerative colitis and Crohn's disease

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (https://www.medicinescomplete.com/#/) and the SPC (https://www.medicines.org.uk/emc/) remain authoritative.

Background Information	• To be recommended or initiated by the specialist team with follow up prescribing and monitoring by primary care clinicians. • The Amber-G guideline covers the care of adults only.
BNF therapeutic class	1.3 Inflammatory Bowel Disease Aminosalicylates https://www.medicinescomplete.com/#/content/bnf/_552641254?hspl=mesalazine
Indication	• To induce and maintain remission in ulcerative colitis and maintenance of remission in Crohn's ileo-colitis. • Mesalazine has an anti-inflammatory effect. • All preparations are licensed for the treatment of mild to moderate acute exacerbations of ulcerative colitis. All except Salofalk® 1g tablets* are licensed for maintenance of ulcerative colitis remission. Asacol® MR and Octasa® MR (400mg and 800mg) are licensed for the maintenance of remission in Crohn's ileo-colitis. *Note that Salofalk® tablet formulation is non-formulary in Barnsley. • To be prescribed by brand • 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.
Dosage and administration	• Commonly given as oral gastro-resistant tablet. It may also be given orally in the form of granules. • To be discontinued on the advice of the specialist • Oral dose for acute flares of IBD in adults ranges between 2.4g-4.8g daily. For maintenance; 1.2g-2.4g daily. Consult the BNF and SPC for the dose information for the brand prescribed. • The preferred oral brand in Barnsley is Octasa® • Octasa® is available as 400mg MR tablets, 800mg MR tablets and 1600mg MR tablets. To be swallowed whole, not to be chewed or crushed. • The second line choice is Salofalk® granules. • Pentasa® tablets/sachets, Mezavant XL® tablets and Asacol MR® tablets are only for patients already stabilised on these brands. Not to be used for new patients. • Guidance on the prescribing of oral mesalazine preparations is available: http://barnsleybest.nhs.sitekit.net/clinical-support/medicines/prescribing-guidelines/Mesalazine%20oral%20preparations.pdf
Cautions and Contraindications	Mesalazine is contraindicated in; • Patients with a known hypersensitivity to salicylates • Blood clotting abnormalities • Severe liver impairment • Severe renal impairment (GFR less than 30 mL/min/1.73 m^2)

	Renal Impairment Caution should be exercised in patients with raised serum creatinine or proteinuria. The possibility of mesalazine-induced nephrotoxicity should be suspected in patients developing impairment of renal function during treatment. Patients need to remain well hydrated whilst taking mesalazine to reduce the risk of crystalluria and consequential kidney damage. Treatment with mesalazine should be stopped immediately if there is evidence of renal impairment and patients should seek immediate medical advice. Nephrolithiasis Cases of nephrolithiasis have been reported with the use of mesalazine including stones with a 100% mesalazine content. It is recommended to ensure adequate fluid intake during treatment. Severe cutaneous adverse reactions Severe cutaneous adverse reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported in association with mesalazine treatment. Mesalazine should be discontinued, at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity. Blood dyscrasia Serious blood dyscrasia have very rarely been reported. Mesalazine therapy should be stopped immediately if there is a suspicion or evidence of blood dyscrasia (signs of unexplained bleeding, bruising, purpura, anaemia, persistent fever or sore throat), and patients should seek immediate medical advice. Hepatic impairment There have been reports of increased liver enzyme levels in patients taking preparations containing mesalazine. Caution is recommended if mesalazine is administered to patients with mild to moderate liver impairment. Avoid in severe impairment. Cardiac hypersensitivity reactions Mesalazine-induced cardiac hypersensitivity reactions (myo- and pericarditis) have rarely been reported with mesalazine. In case of previous mesalazine-induced cardiac hypersensitivity mesalazine must not be reintroduced. Caution should be taken in patients with previous myo- or pericarditis of allergic background regardless of its origin. Pulmonary disease Patients with pulmonary disease, in particular asthma, should be very carefully monitored during treatment with mesalazine. Adverse drug reactions to Sulfasalazine Patients with a history of adverse drug reactions, to sulfasalazine therapy should be kept under close medical supervision. Treatment must be stopped immediately if acute symptoms of intolerance occur such as abdominal cramps, acute abdominal pain, fever, severe headache and rash. Gastric and duodenal ulcers In case of existing gastric or duodenal ulcers treatment should begin with caution based on theoretical grounds. Elderly population Use in the elderly should be handled with caution and should only be prescribed to patients having a normal or non-severely impaired liver and renal function

Pregnancy and breast feeding	• Pregnancy- BNF advises negligible amounts of drug cross the placenta. SPC advises to only use if the potential benefit outweighs the risk. • Breast feeding- BNF advises the diarrhoea has been reported in breast-fed infants, but negligible amounts of drug are detected in breast milk. SPC advises only using mesalazine during breast feeding if potential benefit outweighs possible risk. If the infant develops diarrhoea, the breast feeding should be discontinued.
Adverse Drug Reactions	• The details below are not a complete list and the BNF and SPC remain authoritative. Listed side-effects are common (1 in 10 to 1 in 100) • Gastrointestinal Disorders Nausea, gastrointestinal discomfort, diarrhoea, vomiting, and dyspepsia • Blood and Lymphatic System disorders Leucopenia. A FBC should be performed and the medication stopped immediately if there is a suspicion of blood dyscrasia. • Nervous System Disorders Dizziness and headache • Respiratory Disorders Cough • Skin Disorders Skin reactions, rash • Musculoskeletal and Connective Tissue Disorders Arthralgia • General Disorders Fever • ***Patients and their carers should be advised to report any unexplained bleeding, bruising, purpura, sore throat, fever or malaise that occurs during treatment.*** • Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme: www.mhra.gov.uk/yellowcard
Monitoring	• Baseline tests (to be undertaken by specialists if providing first prescription OR to be undertaken in primary care following a recommendation to prescribe by secondary care); FBC, U&Es, LFTs, Serum creatinine (for creatinine clearance) or eGFR, and urine dipstick. • Monitoring until stable (to be undertaken in primary care); FBC, U&Es, serum creatinine (for creatinine clearance) or eGFR , LFTs and urine dipstick. *14 days after starting; then at 4, 8 and 12 weeks; then 3 monthly* • Routine tests once stable (to be undertaken in primary care); FBC, U&Es, LFTs and urine dipstick. Serum creatinine (for creatinine clearance) or eGFR *Every 6 months or annually depending on risk factors for toxicity.* *Serum creatinine (for creatinine clearance) or eGFR to be checked 6 monthly for first 4 years and then annually.* • If patients present with symptoms of potential adverse effects (sore throat, fever, anaemia, pallor, bruising or unexplained bleeding) perform an urgent blood test. • Stop if suspicion or evidence of blood dyscrasia and contact the specialist. • Stop if renal function deteriorates and contact the specialist. • If AST or ALT are greater than twice the upper limit of the reference range, stop and discuss with the specialist. *(Standard LFT monitoring in Barnsley only includes ALT and ALP enzymes unless additional tests are requested).*
Interactions	The list below is not exhaustive and includes common interactions only. Please refer to the BNF and SPC for the complete list. Weak evidence that mesalazine might decrease the anticoagulant effect of warfarin. In patients who are concomitantly treated with azathioprine, 6-mercaptopurine or thioguanine, a possible increase in the myelosuppressive effects of azathioprine, or 6-mercaptopurine or thioguanine should be taken into account. As a result, life-threatening infection can occur. Patients should be closely observed for signs of infection and myelosuppression. Specialist to advise on monitoring.

Additional information	• Reports of intact tablets in the stool have been recorded. What appear to be intact tablets may in some cases be empty shells of the coated tablets. If intact tablets are observed in the stool repeatedly, the specialist should be consulted • Vaccines are safe and recommended with mesalazine and should be offered in line with the standard schedule. Refer to Green Book Chapter 6 for further details.

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- BHNFT Gastroenterology Department: https://www.barnsleyhospital.nhs.uk/service/gastroenterology/
- Crohn's and Colitis UK: https://www.crohnsandcolitis.org.uk/

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Development Process

This guidance has been produced by Laura White, Clinical Pharmacist SY ICB Barnsley Place following an AMBER-G classification status of oral mesalazine preparations by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by the gastroenterologists and was ratified by the Area Prescribing Committee on 11th January 2023.