

Mesalazine modified release (MR) prescribing

Mesalazine (5-aminosalicylic acid), is indicated for the treatment of mild to moderate ulcerative colitis and the maintenance of remission in ulcerative colitis.¹ The brands Asacol® modified release (MR) and Octasa® MR are also licensed for the maintenance of remission in Crohn's ileo-colitis.²⁻⁵

Nationally the prescribing of generic mesalazine and branded Asacol® MR 400mg and 800mg tablets costs the NHS over £30 million per year (ePACT January-March 2014). Both strengths of MR tablets are category C in the Drug Tariff and the reimbursement price to community pharmacy is based on the Asacol® MR brand. Branded Asacol® MR is more expensive than the equivalent dose of Octasa® MR tablets.⁶ If a prescription for mesalazine is written generically it will have a greater cost implication to the NHS prescribing budget than if Octasa® MR is prescribed by brand name.

Following a review of the literature, changes have been made to the recommendations on interchangeability of oral mesalazine preparations. The BNF now states that there is **no evidence** to show that any one oral preparation of mesalazine is more effective than another. This bulletin reviews the cost of prescribing mesalazine MR generically and as the Asacol® brand, and offers guidance and support to organisations who wish to recommend the prescribing of branded Octasa® MR tablets.¹

Recommendations

- Prescribe mesalazine MR 400mg and 800mg by brand name for all new patients, in-line with National Institute for Health and Care Excellence (NICE) Clinical Guidance (CG), 166 ulcerative colitis, CG 152 Crohn's disease and guidance from the British Society of Gastroenterology. Currently Octasa MR tablets 400mg and 800mg is the least costly brand.⁷⁻⁹
- Review all patients currently prescribed generic mesalazine MR 400mg and MR 800mg tablets for suitability for switching to branded Octasa® MR 400mg and MR 800mg tablets. **As with all switches this should be tailored to the individual patient.**
- Review all patients prescribed Asacol® MR 400mg tablets and MR 800mg tablets by brand name with a view to a potential switch to Octasa® MR 400mg tablets and MR 800mg tablets. This should be conducted and managed in conjunction with gastroenterologists.
- If switching a patient to a different brand of mesalazine, the patient should be advised to report any changes in symptoms.¹

National guidance

Mesalazine is indicated for:

- The treatment of mild to moderate ulcerative colitis.¹
- The maintenance of remission in ulcerative colitis.¹
- The brands Asacol® MR and Octasa® MR are also licensed for the maintenance of remission in Crohn's ileo-colitis.²⁻⁵

The NICE CG 166 '*Ulcerative colitis; Management in adults, children and young people*' recommends oral mesalazine as step one therapy for treating mild to moderate ulcerative colitis. It is recommended in addition to topical aminosalicylate (suppository or enema), or as monotherapy if preferred to induce remission in people with mild to moderate first presentation or inflammatory exacerbation of proctitis or proctosigmoiditis. Oral mesalazine is also recommended for adults (high induction dose), children and young people to induce remission in mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis. In both instances after the induction of remission oral mesalazine is recommended to maintain remission.⁷

NICE CG 152 '*Crohn's disease; Management in adults, children and young people*' recommends mesalazine as monotherapy to induce remission after the first presentation or a single inflammatory exacerbation in a 12-month period if glucocorticosteroid treatment is declined, not tolerated or is contraindicated and as a consideration to maintain remission after surgery.⁸

The guidelines for the management of inflammatory bowel disease in adults from the British Society of Gastroenterology⁹ recommends mesalazine use in two indications:

1. For the treatment of active (left-sided or extensive) ulcerative colitis:
 - » Oral mesalazine 2.4 - 4.8g daily for the treatment of active (left-sided or extensive) ulcerative colitis is effective first-line therapy for mild to moderately active disease.
 - » Topical mesalazine combined with oral mesalazine >2g/day is more effective than oral therapy alone for both left-sided and extensive colitis.
 - » Once daily dosing with mesalazine is at least as effective as twice or three times daily regimes.
 - » Prednisolone 20 - 40mg daily is appropriate for those patients with moderately active disease, in whom mesalazine in appropriate dose and route has been unsuccessful.
2. For the treatment of active proctitis:
 - » In mild to moderate disease, topical mesalazine 1 - 2g daily (in appropriate form for extent of disease) may be effective alone. Combination with oral mesalazine 2 - 4g daily, or balsalazide 6.75g daily, may be useful in resistant cases.
 - » Topical corticosteroids are less effective than topical mesalazine, and should be reserved as second-line therapy for patients who are unresponsive to topical mesalazine.
 - » Patients who have failed to improve on a combination of oral mesalazine with either topical mesalazine or topical corticosteroids should be treated with oral prednisolone 40mg daily. Topical agents may be used as adjunctive therapy in this situation.⁹

Clinical effectiveness

Mesalazine is commonly prescribed as a modified release (MR) preparation to allow drug delivery to target the diseased area of the bowel. This offers optimal treatment for the patient by providing topical anti-inflammatory action. Commonly the modified release mechanism used is enteric coating of the tablets to influence the site of drug release.¹⁰

There are several brands of mesalazine MR oral tablets currently available in a variety of strengths including Asacol® MR, Ipocol MR, Mezavant XL, Octasa® MR, Pentasa Slow Release and Salofalk.¹⁰ The brands Asacol® MR, Ipocol MR and Octasa® MR are all available in 400mg strength tablets. Asacol® MR and Octasa® MR are also available as an 800mg MR tablet.¹

For adults the dosage ranges from 2.4 - 4.8g once daily or in divided doses depending on the preparation.¹

Previously it was recommended that mesalazine should be prescribed by brand name, however following a review of the literature, changes have been made to the recommendations on interchangeability of oral mesalazine preparations. The BNF now states that 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.¹

Octasa® MR tablets are a rebranded version of Mesren MR tablets which were discontinued in December 2012. They have exactly the same formulation. To obtain a license as a generic, products only have to demonstrate bioequivalence to the brand leader and therefore Octasa® MR is a generic version of Asacol® MR.¹⁰ It has not been compared to other brands of mesalazine in clinical trials.

Asacol® MR and Octasa® MR have very similar pharmacokinetic release characteristics.¹⁰

Table 1: Comparison of the release characteristics of the 400mg MR tablets

	Asacol® 400mg MR	Octasa® MR
pH 1.0-1.2 for 2 hours	0% release	0% release
pH 6.4 for 1 hour	<1% released	<1% released
pH 7.2 for 1 hour	~98% released in 30 - 60 minutes	~99% released in 30 - 60 minutes

Octasa® MR 400mg tablets and Asacol® MR tablets 400mg have a virtually identical in vitro dissolution profile, optimal pH for release, site of drug release and similar formulations as they both have an enteric coating of Eudragit S.¹⁰

Table 2: Comparison of formulations and release characteristics of all mesalazine MR tablets

Drug	Formulation	Optimal drug release pH	Site of drug release
Asacol MR	400mg: Enteric coated with Eudragit S	>7	Terminal ileum & large bowel (colon & rectum)
	800mg: Enteric coated with Eudragit S and Eudragit L	>6-7	
Ipocol (Urotir) MR	Enteric coated with Eudragit S	>7	Terminal ileum & colon
Mezavant XL	Film coated with Eudragit S and Eudragit L	>6-7	Colon
Octasa MR	Enteric coated with Eudragit S	>7	Terminal ileum & colon
Pentasa Slow Release	Ethylcellulose coated microgranules to allow slow continuous release	Enteral pH	Duodenum to rectum
Salofalk	Enteric coated with Eudragit L	>6	Terminal ileum & colon

Safety

Mesalazine should be used with caution in patients with decreased renal function. Renal function should be monitored before starting treatment with mesalazine, again after three months of treatment, and then annually during treatment (more frequently in renal impairment).¹

Blood disorders can occur with aminosaliclates and patients receiving mesalazine 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.¹

Aminosaliclates are contra-indicated and should be avoided in patients with salicylate hypersensitivity.¹

Mesalazine intolerance can occur in up to 15% of patients, with diarrhoea (3%), headache (2%), nausea (2%) and rash (1%) reported, but a systematic review has confirmed that all currently marketed 5-ASA agents are safe, with adverse events that are similar to placebo.⁹

Common side effects include diarrhoea, nausea, vomiting, abdominal pain, exacerbation of symptoms of colitis, headache and hypersensitivity reactions (including rash and urticaria).¹

Rare side effects include acute pancreatitis, hepatitis, myocarditis, pericarditis, lung disorders (including eosinophilia and fibrosing alveolitis), peripheral neuropathy, blood disorders (including agranulocytosis, aplastic anaemia, leucopenia, methaemoglobinaemia, neutropenia, and thrombocytopenia - see also recommendation above), renal dysfunction (interstitial nephritis, nephrotic syndrome), myalgia, arthralgia, skin reactions (including lupus erythematosus-like syndrome, Stevens-Johnson syndrome), alopecia.¹

Costs

There is a significant difference in cost between prescribing generic mesalazine or branded Asacol® and Octasa® MR 400mg and 800mg tablets. Table 3 below illustrates the cost differences.

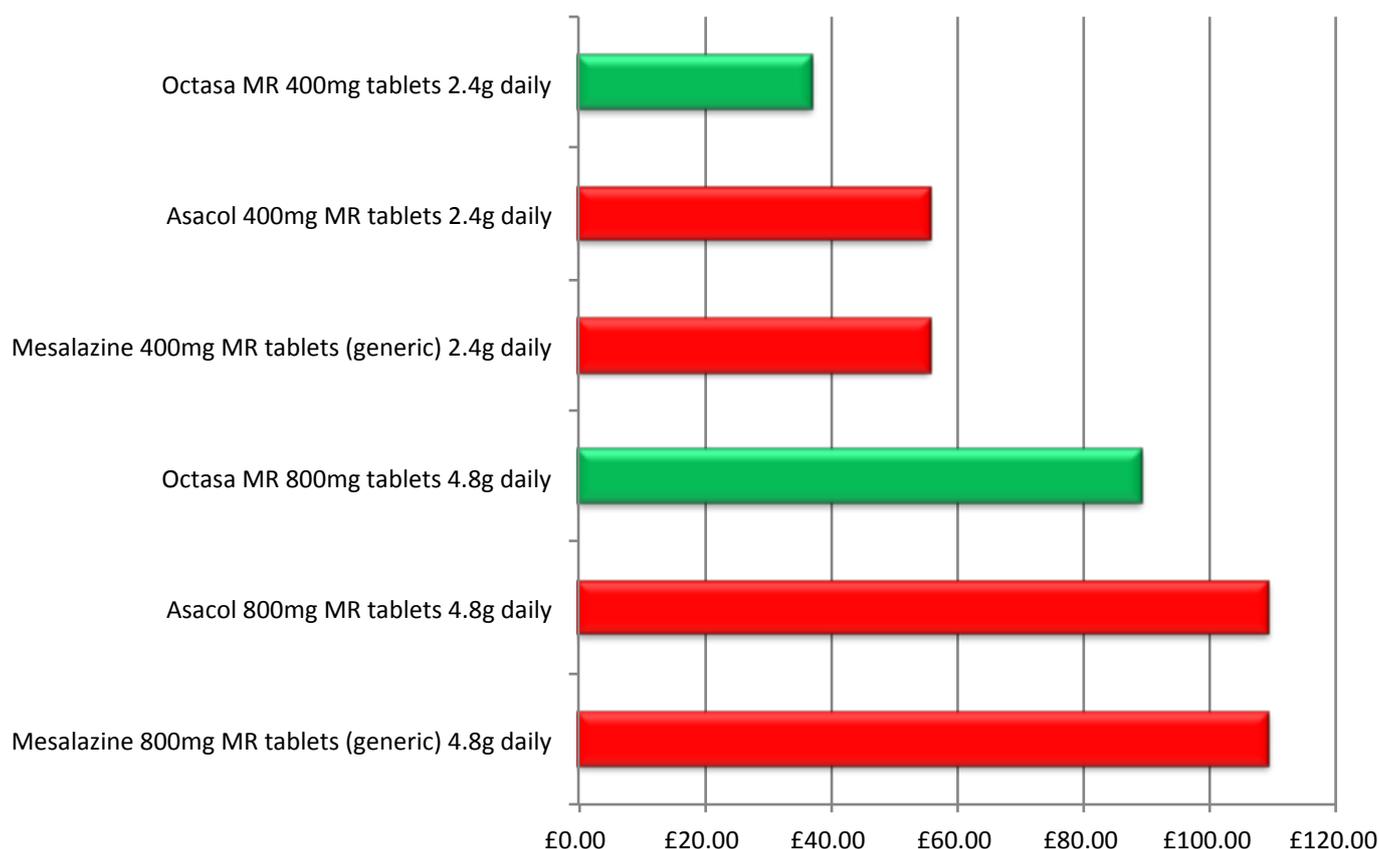
Table 3: Asacol® and Octasa® MR tablet price comparison^{6,11}

Product	Cost per pack/pack size	Cost per MR tablet
Octasa® 400mg MR tablets	£19.50/90	0.22p
Asacol® 400mg MR tablets	£29.41/90	0.33p
Octasa® 800mg MR tablets	£95.00/180	0.53p
Asacol® 800mg MR tablets	£117.62/180	0.65p

Mesalazine 400mg MR tablets prescribed generically or as Asacol® brand is £9.91 more expensive for a pack of 90 tablets than the equivalent Octasa® MR 400mg tablets.

Mesalazine 800mg MR tablets prescribed generically or as Asacol® brand is £22.62 more expensive for a pack of 180 tablets than the equivalent Octasa® MR 800mg tablets.

Chart 1, on the following page, illustrates the cost differences between mesalazine MR tablets prescribed generically, as Asacol® and as Octasa®. It looks at cost comparisons for prescribing the maximum daily dose of 2.4g for the 400mg tablets and 4.8g for the 800mg tablets for 28 days.

Chart 1: 28 day cost for prescribing mesalazine MR tablets at the maximum daily dose

Nationally, around £5.7 million is spent on generic mesalazine per year and £25 million on prescribing Asacol® by brand (ePACT January to March 2014). Switching from prescribing generic mesalazine and Asacol® brand to Octasa® MR 400mg and 800mg tablets could release **savings of up to £6.7 million per year nationally. This equates to £11,771 per 100,000 patients.**

Table 4: Savings from switching generic mesalazine and Asacol® to Octasa® MR tablets

Switch	Saving per 28 days at maximum dose	Switch to Octasa® national savings per year
Generic mesalazine MR 400mg to Octasa® MR tablets 400mg	£18.48	£1,176,566
Generic mesalazine MR 800mg to Octasa® MR tablets 800mg	£20.16	£173,851
Asacol® 400mg to Octasa® MR tablets 400mg	£18.48	£4,051,857
Asacol® 800mg to Octasa® MR tablets 800mg	£20.16	£1,250,650
Total savings		£6,652,924

Switching options

There are four potential switch options for mesalazine MR 400mg or 800mg tablets (although clinicians may choose other options according to the clinical need of the patient). These include:

1. Review patients currently prescribed generic mesalazine MR tablets 400mg for suitability for switching to branded Octasa® MR tablets 400mg.

2. Review patients currently prescribed generic mesalazine MR tablets 800mg for suitability for switching to branded Octasa® MR tablets 800mg.
3. Review patients prescribed Asacol® MR 400mg tablets by brand name with a view to a potential switch to Octasa® MR 400mg tablets. This should be conducted and managed in conjunction with gastroenterologists.
4. Review patients prescribed Asacol® MR 800mg tablets by brand name with a view to a potential switch to Octasa® MR 800mg tablets. This should be conducted and managed in conjunction with gastroenterologists.

If switching a patient to a different brand of mesalazine, the patient should be advised to report any changes in symptoms.¹

For all new patients who require oral mesalazine MR 400mg and MR 800mg tablets prescribe Octasa® MR by brand name.

Summary

- There is no evidence to suggest that any one oral preparation of mesalazine is more effective than another.
- Octasa® MR 400mg tablets and 800mg tablets are a branded generic version of Asacol® branded tablets. They have virtually the same in vitro dissolution profile, pH for release, site of drug release and same formulation, however the Asacol® brand is significantly more expensive than Octasa® brand.
- The Drug Tariff bases the payment for generic prescribing of mesalazine MR 400mg and 800mg tablets on the higher cost Asacol® brand and therefore in this instance generic prescribing has a greater cost implication than Octasa® brand prescribing.
- Switching from prescribing generic mesalazine and Asacol® brand to Octasa® MR 400mg and 800mg tablets could release savings of up to £6.7 million per year nationally.

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Additional PrescQIPP resources



Briefing



Data pack



Patient letter

Available here:

<http://www.prescqipp.info/resources/viewcategory/259-branded-mesalazine-prescribing>

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Non-subscriber publication December 2014.

Minor update February 2015 and September 2015.