Budesonide [Budenofalk®] foam enema for the treatment of active rectal and rectosigmoid disease in ulcerative colitis

This review discusses the evidence in support of the use of budesonide [Budenofalk®] foam enema for the treatment of active rectal and rectosigmoid disease in ulcerative colitis (UC). Budesonide is a synthetic steroid with potent local anti-inflammatory effects and is well tolerated due to low systemic bioavailability, with less effect on plasma cortisol levels and potentially minimising side effects reported with traditional corticosteroids.

Budesonide foam enema was registered for the treatment of active rectal and rectosigmoid disease in ulcerative colitis by Australia's Therapeutic Goods Administration on 12 June 2012 and the product has been listed on the Pharmaceutical Benefits Scheme (PBS) since 28 February 2014.

Background

Ulcerative colitis (UC) is a chronic idiopathic inflammatory bowel disease (IBD) characterised by unpredictable relapsing and remitting episodes of intestinal inflammation primarily affecting the mucosal layer and occasionally the submucosa of the colon. The inflammation may involve the rectum only, the distal colon or the entire colon, typically in a contiguous fashion. The symptoms include bloody diarrhea, abdominal pain or discomfort, tenesmus and urgency, rectal bleeding and fatigue. The cause of UC is unknown but is thought to be due to a combination of genetic factors, host environment, dysbiosis and abnormal host immune responses. Treatment can result in mucosal healing, but as yet, no cure exists for the condition.

Management of ulcerative colitis

Management aims at inducing and maintaining remission and suppressing inflammation. Severe and prolonged inflammation of the colonic mucosa is a significant risk factor for the development of colonic carcinoma. Various therapeutic options are available – the choice of medication depends on the severity of inflammation as well as the extent of the disease. First-line therapy for inducing remission during acute disease flares include aminosalicylates (such as sulfasalazine or mesalazine [5-aminosalicylic acid]), with mesalazine being the preferred initial treatment, oral corticosteroids (such as prednisone or prednisolone), immunomodulators (such as thiopurines and methotrexate) and biological therapies (such as tumour necrosis factor alpha [TNF-α] inhibitors and vedolizumb), a selective antibody against 4ß7-integrin; aminosalicylates, immunomodulators and TNF inhibitors are also used as maintenance therapy. Patients with ongoing, severe inflammation, unresponsive to medical therapy, or those who are steroid-dependent may have to be considered for colectomy.

These treatments are associated with considerable adverse effects. Mesalazine intolerance occurs in up to 15% of patients. Diarrhoea (3%), headache (2%), nausea (2%), rash (1%) and thrombocytopenia (<1%) have been reported with aminosalicylate agents in the treatment of patients with UC, although a recent systematic review of the evidence found that 5-aminosalicylic acid agents are safe, with adverse events that are similar to placebo for mesalazine.

In common with other biological therapies, TNF inhibitor treatment is accompanied by a risk of serious infection, demyelinating disease and associated mortality.

While conventional corticosteroids are frequently used to induce clinical remission in UC and are recommended by current guidelines when treatment with aminosalicylates has been unsuccessful, these agents fail to achieve mucosal healing and their long-term use is limited by a large range of adverse effects including hypothalamic-pituitary-adrenal axis suppression and the possible development of steroid-dependent disease, hypertension, diabetes, osteopenia and osteoporosis, cataracts and glaucoma, as well as the risk of opportunistic infection. Maintenance corticosteroid therapy is therefore not recommended.

New formulations of corticosteroids have been developed for the treatment of UC, as a means of limiting systemic activity and reducing the likelihood of treatment-related adverse events. These second-generation topical oral or rectal preparations have high local efficacy in the gut and low systemic bioavailability due to first-pass hepatic inactivation, such as budesonide, a non-halogenated gluco-corticosteroid that binds with the gluco-corticoid receptor with 195-fold greater affinity than hydrocortisone.

The efficacy of budesonide in ulcerative colitis

Budesonide was originally developed as an inhaled treatment for inflammatory airway diseases. Nowadays, several formulations of budesonide exist. Enteric-coated formulations of budesonide resist degradation by gastric acid and deliver active drug to the small intestine and proximal colon. A once-daily, oral, extended-release formulation of budesonide that extends release throughout the colon using matrimax (MMX) technology (budesonide MMX) induced a fast and significant clinical improvement of active left-sided UC without suppression of adrenocortical functions and without important toxicity, compared with placebo. Similarly, three other randomised, double-blind trials have reported that oral budesonide MMX 9 mg once daily is significantly more effective than placebo for the induction of remission in UC. In these studies, no between-group differences were observed in the frequency of treatment-related and serious adverse events. In another trial, an oral controlled-release formulation of budesonide was as effective and well tolerated as prednisolone in patients with extensive or left-sided, mild-to-moderate active UC. In Australia, budesonide MMX is only approved for induction of remission in patients who fail to respond to or are unable to tolerate 5-ASA.

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Treatment may be continued in patients showing progressive improvement, but it should not be persisted with if the response has been inadequate. Once-daily actuation of budesonide 2 mg, morning or evening.

Suppositories and liquid enemas are recommended for inducing remission in patients with active distal UC and proctitis, budesonide enema (2 mg/100 mL) was as efficient and well tolerated as mesalazine enema. However, the clinical remission rate at 4 weeks in this study was much lower with budesonide than with mesalazine (38% vs 60%, respectively; p=0.03). Notably, budesonide foam and enemas have shown comparable clinical efficacy to other steroid foam and enema preparations, with less effect on the plasma cortisol level and thus potentially cause fewer steroid side effects. Limitations with suppositories and liquid enemas include difficulty of administration, retention, and limited proximal spread. Suppositories do not disperse beyond the rectum, and although liquid enemas can spread to the splenic flexure, patients have to successfully retain the liquid and remain recumbent for a specified period of time after administration.

The foam formulation (Budenofalk®) was specifically designed to improve both the patient’s ability to retain the drug in the rectum following administration as well as distribution of the active drug to the rectum and sigmoid colon. Rectally administered budesonide foam addresses the potential limitations of oral budesonide formulations, as it spreads to a maximum of 40 cm, thereby reaching the sigmoid colon in all patients and even extending into the distal third and the middle of the descending colon in some patients. In one study, budesonide foam demonstrated similar efficacy to that of budesonide enema in the treatment of active ulcerative proctitis or proctosigmoiditis, and both budesonide formulations were safe, with no drug-related serious adverse events. Patients cited better tolerability and easier application with the foam formulation, and the majority preferred foam.

Recent clinical trial evidence suggests that twice-daily budesonide foam is superior to once-daily budesonide foam for inducing complete mucosal healing in patients with distal UC (see a detailed discussion of study results in the Clinical Trials section). Moreover, twice-daily treatment was also superior when the analysis was restricted to patient with no prior use of 5-aminosalicylic acid enema or suppository. Clinical remission rates were similar after 6 weeks of twice-daily and once-daily treatment, both were significantly better than with placebo. There were no serious problems relating to safety or application.

Ulcerative colitis: a significant national health burden
In Australia, an estimated 75,000 Australians have UC or Crohn’s disease (i.e. about 1 in 250 people aged 5–49 years nationally), with this number projected to increase to 100,000 by 2022. Worryingly, Australia has one of the highest rates of prevalence and incidence of IBD worldwide and each year more and more young people are being diagnosed. Budesonide has numerous, major impacts on all facets of a sufferer’s life: development, psychological wellbeing, education and employment productivity, family life and relationships. Management of IBD is associated with substantial annual costs, both in human and monetary terms. Direct costs resulting from hospitalisation are also increasing, with a significant cost burden related to healthcare utilisation. In 2013, national total hospital costs for IBD were estimated to be around $AU100 million per annum. In 2012, productivity losses in Australia attributable to IBD are estimated at over $AU330 million. Moreover, management of IBD has been associated with an additional $AU2.7 billion of financial and economic costs.

Optimal management is essential in IBD, to help prevent comorbid conditions and minimise the impact of the disease on patients, the healthcare system and the economy. Typically, however, the medical approach concentrates on the acute flares and fails to address the long-term management needs of this chronic condition.

Australians currently experience inequitable access to quality IBD care. Those hospitals and clinics that have implemented an integrated and formal IBD care model have produced significant benefits to patients and cost savings to the healthcare system, including increased adherence and compliance to medication, decreased hospitalisations and emergency department presentations, reduced need for surgery, less morbidity, improved quality of life and work productivity. However, funding for this care model remains disparate and insecure. Moreover, care is difficult to access for those patients living in remote areas and those who lack dedicated IBD resources. Clearly, much needs to be done to improve treatment options for patients with UC.

Pharmacological properties of budesonide foam enema
Budesonide is a glucocorticoid with a high local anti-inflammatory effect. At a dosage of 2 mg budesonide, applied rectally, leads to practically no suppression of the hypothalamus-hypophysis-adrenal cortex axis. Budesonide 2 mg foam enema investigated up to the daily dosage of 4 mg budesonide had essentially no effect upon basal plasma cortisol levels. The AUC of a rectally administered dose of budesonide is about 1.5-fold higher than in historical controls considering the identical oral budesonide dose. Peak levels occur on average 2–3 hours after a single rectal dose of budesonide 2 mg foam enema. Budesonide has a high volume of distribution (about 3 L/kg). Plasma protein binding is estimated to be 85–90%, independent of gender. Budesonide undergoes extensive biotransformation in the liver (approximately 90%) to metabolites of negligible glucocorticoid activity. The average elimination half-life is about 3–4 hours. The mean clearance rate is about 10–15 L/min for budesonide, determined by HPLC-based methods. Pharmacokinetic data after single and multiple dosing of budesonide 2 mg foam suggest there is no potential accumulation of the drug in serum.

Budesonide foam enema is contraindicated in the following patients:
- those who are hypersensitive to budesonide or any of the ingredients
- those with hepatitis

Drug-drug interactions:
Inhibitors of cytochrome p450 3A4 (CYP3A4) activity (such as ketoconazole, ritonavir, itraconazole, clarithromycin, and grapefruit juice) may increase systemic budesonide concentrations. Concomitant use of CYP3A4 inhibitors should be avoided with budesonide foam enema. Inducers of CYP3A4 activity (such as carbamazepine and rifampicin) may reduce systemic budesonide concentrations. The budesonide dose might need to be adjusted accordingly.

Use in specific populations:
Severely impaired hepatic function affects the pharmacokinetics of oral preparations of budesonide, reducing the elimination rate and increasing oral systemic availability. However, oral budesonide is safe and well tolerated in daily doses of 3 mg three times daily in patients with liver disease without hepatic cirrhosis. The effects of hepatic impairment on the pharmacokinetics of budesonide foam enema have not been studied. The recommendation is that as plasma levels of budesonide appear to be generally slightly higher with rectal budesonide, the foam enema preparation should be used only with caution in patients with hepatic impairment.

Adverse effects:
In clinical trials of budesonide foam enema, budesonide foam enema has shown good tolerability, with undesirable effects in 14% of study participants. Burning in the rectum or pain were common, while nausea, headache and an increase in liver enzymes were uncommon. Caution is recommended in patients where administration of glucocorticoids may have undesirable effects, including the masking of infections. No long-term data exist on the long-term use of budesonide foam enema in patients with UC and long-term use is not recommended. The local action of budesonide foam enema means that this product has a generally lower risk of undesired effects as compared with systemically-acting glucocorticoids.

Dosage and administration
Budesonide foam enema is delivered from a metered-dose aerosol canister containing 14 doses of budesonide 2 mg in 20 mL foam. For adults aged >18 years:
- Once-daily actuation of budesonide 2 mg, morning or evening.
- The attending physician determines the duration of use. An acute episode generally subsides after 6 to 8 weeks.
- Treatment may be continued in patients showing progressive improvement, but it should not be persisted with if the response has been inadequate.
- Continuous treatment beyond 8 weeks has not been assessed. Budesonide 2 mg foam enema should not be used after this time.

In Australia, budesonide foam enema has been listed since 28 February 2014 on the Pharmaceutical Benefits Scheme.

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Clinical trial evidence for budesonide foam enema

**Budesonide foam versus budesonide enema in active ulcerative proctitis and proctosigmoiditis**

**Summary:** Budesonide foam (Budenofalk™) was as effective as budesonide enema in patients with active distal UC. Budesonide foam was well tolerated and the vast majority of the patients preferred the administration of a rectal foam when compared with a rectal enema.

**Methods:** This multinational study enrolled patients aged between 18 and 70 years with active ulcerative proctitis or proctosigmoiditis (clinical activity index [CAI] >4 and endoscopic index ≥4) and randomised them to receive 2 mg/25 mL budesonide foam and placebo enema (n=265), or 2 mg/100 mL budesonide enema and placebo foam (n=268) for 4 weeks. The primary endpoint was clinical remission (CAI ≤4) at the final/withdrawal visit (per protocol).

**Results:** Rates of clinical remission (CAI) in the per protocol (PP) analysis set were 60% for budesonide foam and 66% for budesonide enema. Budesonide foam was proven to be not inferior to budesonide enema at the experiment-wise significance level of 0.025 using a noninferiority margin of 15%. In an analysis of the influence of baseline covariates on the clinical remission rates, only baseline CAI had a statistically significant effect on the response to rectal budesonide. Patients with a CAI of >6 achieved clinical remission significantly less frequently than those with a CAI ≤6. Patients who were previous nonresponders to oral or rectal 5-aminosalicyclic acid agents showed a tendency towards a lower remission rate than those who had previously responded to oral or rectal 5-aminosalicyclic acid. Nevertheless, endoscopic remission was obtained with budesonide foam in 49% and 41% and with budesonide enema in 50% and 62% of the non-responders to oral or rectal 5-aminosalicyclic acid, respectively. Most patients (84%) preferred the foam, while only 6% preferred the enema; 10% expressed no preference.

**Expert commentary:** Increasing attention towards medication adherence supports the role for selecting treatments that are effective, acceptable to patients and have minimal adverse effects. Patients’ concerns over side effects and in particular Cushinoid features, mood disruption and insomnia due to systemic corticosteroid effects can result in loss of confidence amongst patients taking induction and maintenance IBD therapies. Non-persistence to treatment increases the risk of relapse and in the long term, IBD-associated dysplasia. As such, new treatments aim to be more specific to the pathogenic mechanism of IBD and more tolerable. Budesonide, a commonly-used topical steroid in the treatment of asthma, is almost entirely metabolised on first-pass hepatic metabolism. It meets the treatment goal of acceptable tolerability for patients and minimising corticosteroid side effects. Being listed on the PBS means Budesonade™ foam enema is an easy-to-prescribe and affordable treatment option for patients. Efficacy has been demonstrated in published data and clinical experience confirms the rapidity of induction of remission. Whilst not as effective in more severe UC, it may effectively stratify patients to those with easy-to-control distal UC versus those with moderate-to-severe UC requiring rapid escalation towards more potent treatments.

The options in the treatment of mild-to-moderate left-sided colitis now include oral 5-ASA, topical 5-ASA, topical budesonide and oral MMX-budesonide. Budesonide is a good option especially for patients failing or intolerant to 5-ASA. Although the systemic bioavailability of budesonide is low (approximately 10%), it is not negligible. Prolonged use is still associated with detectable effects on the hypothalamic-pituitary-adrenal axis. As such, budesonide is for short-term treatment only (maximum of 2 months) and maintenance therapy should be with 5-ASA.

Safety and efficacy of budesonide rectal foam was established based on the following pivotal phase III studies and one long-term safety trial.

**Budesonide foam induces remission in patients with mild to moderate ulcerative proctitis and ulcerative proctosigmoiditis**

**Summary:** Budesonide rectal foam was superior to placebo in inducing remission in patients with active, mild-to-moderate ulcerative proctitis and ulcerative proctosigmoiditis. Moreover, the safety profile of budesonide foam was consistent with that observed with the oral formulation of budesonide.

**Methods:** Two replicate 6-week, phase III, multicentre, randomised, double-blind, placebo-controlled trials were designed to assess the efficacy of budesonide 2 mg rectal foam (dosed twice daily for 2 weeks, followed by once daily for 4 weeks) in 546 patients aged >18 years with active, mild-to-moderate distal UC. Study participants had a baseline Modified Mayo Disease Activity Index (MMDAI) score between 5 and 10, with a score of ≥2 on the MMDAI rectal bleeding component and ≥2 on the MMDAI endoscopy or sigmoidoscopy component. The primary outcome was the proportion of patients who achieved remission after 6 weeks of treatment. Remission was defined as an endoscopy subscore of ≤1, a rectal bleeding subscore of 0, and improvement or no change from baseline in the stool frequency subscore of the MMDAI after 6 weeks of treatment. Demographic and baseline characteristics were similar between the groups in both studies (i.e. mean number of daily normal stools, duration and extent of disease). Over half of the patients in both studies were concomitantly oral mesalazine. Most (>80%) patients were exposed to study drug for 29–44 days, with a mean duration of 38.8 days and 39.1 days for budesonide foam and placebo, respectively, for the combined studies. Overall compliance was high and comparable between the budesonide foam and placebo groups overall (94% vs 97%), during twice-daily dosing (through week 2; 94% vs 97%, respectively) and once-daily dosing (week 3 to week 6; 94% vs 97%, respectively).

**Results:** After 6 weeks, remission rates were significantly higher with budesonide foam than with placebo in both studies (see Table 1), with combined rates of 41% and 24% for the budesonide foam and placebo treatment groups (p<0.0001). However, there were also large numbers of nonresponders with each treatment. At week 6, a significantly greater percentage of budesonide-treated patients compared with placebo recipients achieved rectal bleeding resolution (Study 1: 47% vs 28%; p=0.002; Study 2: 50% vs 29%; p=0.0002) and endoscopic improvement (Study 1: 56% vs 43%; p=0.05; Study 2: 56% vs 37%; p=0.001). Most adverse events occurred at similar frequencies between groups, although events related to changes in cortisol values occurred more often with budesonide foam. There were no cases of clinically symptomatic adrenal insufficiency.

**Table 1. Remission rates after 6 weeks of budesonide foam enema or placebo.**

<table>
<thead>
<tr>
<th>Efficacy endpoint</th>
<th>Study 1</th>
<th>Study 2</th>
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<tbody>
<tr>
<td></td>
<td>Budesonide foam (n=133)</td>
<td>Placebo (n=132)</td>
</tr>
<tr>
<td>Achieved remission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responder</td>
<td>51 (38%)</td>
<td>34 (26%)</td>
</tr>
<tr>
<td>Nonresponder</td>
<td>82 (62%)</td>
<td>98 (74%)</td>
</tr>
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</table>

**Expert commentary:** These data support the role of budesonide foam enema in the induction of remission of mild-to-moderate distal UC. Remission was defined in objective terms with both mucosal healing and improvement of PR bleeding. The most important aspect of this treatment was the safety, showing no symptomatic adrenal insufficiency. Changes to serum cortisol values, although detectable, are unlikely to be significant with short-term treatment. The incremental response rate, however, was not high and might be best suited to milder disease. Whether treatment can improve in conjunction with 5-ASA treatment and / or addition of immunomodulator therapy remains to be tested. Certainly a step-up approach is appropriate in non-responders after 6 weeks of treatment.
The safety and tolerability of budesonide foam in subjects with active ulcerative proctitis or proctosigmoiditis

Summary: Repeat cycles of budesonide foam for recurrent flares had a favourable safety profile for the treatment of patients with ulcerative proctitis or proctosigmoiditis.

Methods: This was an open-label, multicentre, extension safety study (BFPS3073; Clinical Trials.gov identifier NCT01349673) conducted in the USA involving 114 patients who completed the above-mentioned two replicate studies and had recurrent flares of ulcerative proctitis or proctosigmoiditis. These patients were permitted to receive additional 6-week treatment cycles of budesonide foam. When a flare occurred, budesonide foam 2 mg was administered rectally twice daily for 2 weeks followed by 2 mg once-daily administration for 4 weeks. Safety data from this extension study were pooled with data from the two above placebo-controlled studies, an open-label study (once-daily treatment for 8 weeks) and an active-comparator study (once-daily treatment for 4 weeks).

Results: In the integrated analysis, adverse events were reported by similar percentages of patients in the budesonide foam and placebo groups (41% and 36%, respectively). The majority of adverse events were mild or moderate in intensity. Budesonide foam had no clinically relevant effects on the hypothalamic-pituitary-adrenal axis. A population pharmacokinetic analysis revealed low systemic exposure after budesonide foam administration.

Expert commentary: This is an open-labelled study recruiting from different sources and was not powered for long-term outcomes. Due to patient drop outs it might not be possible to detect meaningful differences between groups. However, it indicates the treatment to be tolerable over time. Adherence is not mentioned and might be expected in those who enter remission.

Twice-daily budesonide 2-mg foam induces complete mucosal healing in patients with distal ulcerative colitis

Summary: Twice-daily budesonide foam is superior to once-daily budesonide foam for inducing complete mucosal healing in patients with distal UC.

Methods: This phase II study enrolled 165 Japanese patients aged 16–69 years with active, mild-to-moderate distal UC and randomised them to 3 groups: once-daily budesonide 2 mg/25 mL foam (n=55), twice-daily budesonide 2 mg/25 mL foam (n=56), or placebo foam (n=54), for 6 weeks. Disease activity was assessed using the MMDAI score. At baseline, patients had an endoscopic subscore of 2, rectal bleeding subscore of 1 or 2, stool frequency subscore of 0–2, lesions restricted to the segment from the rectum to the sigmoid colon, and it was ≥12 weeks since the confirmed diagnosis of UC. Complete mucosal healing and the safety profile were assessed at week 6. Complete mucosal healing was defined as an endoscopic subscore of 0. Clinical remission was defined as a rectal bleeding subscore of 0 and endoscopic subscore ≤1, and a stool frequency subscore of 0 or a decrease from baseline of ≥1 in the stool frequency subscore.

Results: At 6 weeks, significantly greater proportions of patients in the budesonide foam groups compared to placebo achieved complete mucosal healing compared with patients in the placebo foam group (see Table 2). Twice-daily administration also demonstrated superiority for complete mucosal healing over once-daily administration and placebo when the analysis was restricted to patients with no prior use of 5-aminosalicylic acid enema or suppository. Clinical remission rates were similar after 6 weeks of twice-daily and once-daily budesonide foam treatment, both of which were significantly better than placebo.

A total of 164 patients completed a questionnaire on acceptability of once-daily and twice-daily administration of budesonide foam; 96% of respondents reported that handling the device was very easy to use. The responses demonstrated that budesonide foam was generally accepted by patients, as either once- or twice-daily dosing regimens, and was not associated with any serious problems relating to safety and application. No serious adverse event occurred in any group. Although plasma cortisol and corticotrophin levels decreased during treatment in both budesonide foam groups, all recovered to normal levels after completing treatment.

Table 2. Efficacy endpoints after 6 weeks of budesonide foam enema (twice-daily or once-daily) or placebo.

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Budesonide foam QD</th>
<th>Budesonide foam BD</th>
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<tbody>
<tr>
<td>Complete mucosal healing (full analysis set), n (%)</td>
<td>54 (5.6%)</td>
<td>55 (24%)*</td>
<td>56 (46%)**</td>
</tr>
<tr>
<td>Complete mucosal healing (no previous use of 5-aminosalicylic acid enema or suppository), n (%)</td>
<td>33 (6%)</td>
<td>32 (34%)*</td>
<td>31 (58%)**</td>
</tr>
<tr>
<td>Complete mucosal healing (previous use of 5-aminosalicylic acid enema or suppository), n (%)</td>
<td>21 (5%)</td>
<td>23 (9%)*</td>
<td>25 (32%)**</td>
</tr>
<tr>
<td>Clinical remission, (%)</td>
<td>20%</td>
<td>51%</td>
<td>48%*</td>
</tr>
<tr>
<td>Endoscopic subscore ≤1, n (%)</td>
<td>25 (46%)</td>
<td>38 (69.1%)*</td>
<td>43 (77%)*</td>
</tr>
<tr>
<td>MMDAI ≤1, n (%)</td>
<td>6 (11%)</td>
<td>21 (38%)</td>
<td>28 (50%)**</td>
</tr>
<tr>
<td>Rectal bleeding subscore 0, n (%)</td>
<td>19 (37%)</td>
<td>38 (70%)†</td>
<td>37 (70%)†</td>
</tr>
</tbody>
</table>

QD = once-daily administration; BD = twice-daily administration; MMDAI = Modified Mayo Disease Activity Index.

*p<0.02 vs placebo; **p≤0.0001 vs placebo; †p<0.05 vs budesonide foam QD; ‡p=0.0774 vs placebo; ‡p=0.0763 vs budesonide foam QD; ‡p=0.0699 vs placebo; ‡p=0.0774 vs placebo.

Expert commentary: This large prospective controlled trial demonstrated twice-daily budesonide foam enema could significantly improve mucosal healing above once-daily treatment (46% BD versus 24% QD versus 5.6% placebo). The benefit was observed in those with previous use of 5-ASA and those without previous use of 5-ASA. Clinical remission rates and rectal bleeding subscores, however, were similar between the two treatment doses but superior over placebo. The study therefore supports a proportion of patients who would benefit with twice-daily administration of Budesonalk® foam enema. The foam consistency may permit better tolerability over liquid enemas and allow for twice-daily application.

Concluding remarks and take-home messages

Budesonalk® foam enema is easy to prescribe and listed with the PBS. It is safe and does not demonstrate clinically relevant adverse events, at least in short-term usage. When given twice daily it demonstrates higher mucosal healing rates over once-daily administration in distal mild-to-moderate ulcerative colitis. It is at least additive to the effects of 5-ASA. Budesonalk® foam enema is undoubtedly a good first-line agent for induction of remission in mild-to-moderate distal UC, along with 5-ASA administered either once or twice daily. Due to its safety profile it is likely to replace Predsol® enema in this respect.

An alternative and speculative use of this agent may be as an adjunct in patients who have not quite achieved mucosal healing where short-term treatment escalation using budesonide might help to achieve this endpoint. This might include patients on higher efficacy treatments such as immunomodulators and even biological agents. This approach, however, should be studied as part of a controlled clinical trial.
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1. Product Information. Budenofalk® (budesonide) foam enema. Orphan Australia Pty Ltd. Date of most recent update: 12 June 2012.


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