

HEALTH TECHNOLOGY BRIEFING SEPTEMBER 2020

Budesonide granules for induction of remission in lymphocytic colitis – first line

NIHRI ID	9568	NICE ID	10456
Developer/Company	Dr Falk Pharma UK Ltd	UKPS ID	372705

Licensing and market availability plans

Completed phase III clinical trials

SUMMARY

Budesonide 9mg gastro-resistant granules are in clinical development for the induction of remission in patients with lymphocytic colitis. Lymphocytic colitis is an inflammatory bowel disease that causes bouts of severe diarrhoea. Certain medications, viruses and bacteria can trigger lymphocytic colitis, however the cause of the disease is not known; it is thought that genetic and environmental factors may be involved.

Budesonide is a corticosteroid that exerts anti-inflammatory effects in the gastrointestinal tract. The treatment works by binding with high affinity to intracellular glucocorticoid receptors. In one phase III clinical trial, budesonide was shown to be significantly effective in inducing clinical remission in lymphocytic colitis patients in comparison to a placebo. If licensed, budesonide will offer a treatment option for patients with lymphocytic colitis.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

PROPOSED INDICATION

First line treatment for the induction of remission in lymphocytic colitis.^a

TECHNOLOGY

DESCRIPTION

Budesonide (Budenofalk) is a second-generation corticosteroid that allows local, selective treatment of the gastrointestinal tract and the liver, exerting potent anti-inflammatory effects at the site of inflammation by high-affinity binding to the intracellular glucocorticoid receptor. Extensive (90%) pre-systemic metabolism within the mucosa of the small intestine and the liver results in low systemic availability.¹

Budesonide completed clinical development for the induction of remission in lymphocytic colitis in June 2017. In the phase III clinical trial (NCT01209208), patients are given budesonide 9mg gastro-resistant granules orally once a day.²

INNOVATION AND/OR ADVANTAGES

Entocort 3mg capsules and Budenofalk 3mg gastro-resistant capsules are licensed treatments for microscopic colitis; lymphocytic colitis is a type of microscopic colitis.^{3,4} Expert guidelines recommend budesonide as first-line therapy for induction of remission in microscopic colitis.⁵

In a recent phase III study (NCT01209208), budesonide achieved clinical remission in lymphocytic colitis significantly more frequently than placebo and adverse event rates were similar. Therefore, 9mg daily budesonide taken for eight weeks could be considered the treatment of choice for patients with active lymphocytic colitis.⁶

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Budesonide 9mg gastro-resistant granules are licensed in the UK for the following indications:⁷

- Induction of remission in patients with mild to moderate active Crohn's disease affecting the ileum and/or ascending colon
- Induction of remission in patients with active collagenous colitis

Budesonide 3mg gastro-resistant capsules and Entocort CR 3mg capsules are already licensed budesonide products that are licensed for the induction/maintenance of remission in patients with microscopic colitis.^{3,4}

Common side effects affecting 1 in 10 people include Cushing's syndrome, dyspepsia, abdominal pain, increased risk of infection, muscle and joint pain, brittle bones, headache, allergic exanthema, petechiae, delayed wound healing, contact dermatitis and mood changes.⁷

^a Information provided by Dr Falk Pharma UK Ltd on UK PharmaScan

PATIENT GROUP

DISEASE BACKGROUND

Lymphocytic colitis is a type of microscopic colitis which is an inflammatory bowel disease.⁸ In lymphocytic colitis, the inner lining of the bowel becomes inflamed and has more white blood cells than in a healthy bowel lining. Because of this, the large bowel is unable to absorb as much liquid from the waste. Lymphocytic colitis is distinguished from collagenous colitis by the presence of an increased number of intraepithelial lymphocytes (≥ 20 per 100 epithelial cells) and the absence of a markedly thickened subepithelial collagen band.⁹

Chronic, non-bloody, watery diarrhoea is the main symptom of lymphocytic colitis. These incidences occur more than 3 times a day for longer than 4 weeks; for some people this can be as many times as 15 times a day. Other symptoms can include abdominal pain, fatigue, joint pain and bloating.⁸

There is no known cause of lymphocytic colitis however it is thought to be due to a combination of genetic factors, environmental factors and also possible damage to the lining of the gut by viruses, bacteria or medication.⁸

Lymphocytic colitis is more common in those over 50 years old, those who smoke cigarettes, have an autoimmune condition such as type 1 diabetes, use certain medications such as SSRI's or are female.⁸

CLINICAL NEED AND BURDEN OF DISEASE

The estimated incidence of lymphocytic colitis in the UK is 4.2 per 100,000, although this is thought to be higher due to misdiagnosis and underreporting.¹⁰

According to hospital episode statistics for England in 2018-19 there were a total of 54,798 finished consultant episodes for other noninfective gastroenteritis and colitis (ICD-10 code K52) recorded as primary diagnosis of which 47,140 were recorded as admissions with a total of 37,476 day cases.¹¹

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

Before being offered any treatment for lymphocytic colitis, a doctor will review current medications that could have triggered the colitis. The doctor will then encourage lifestyle changes. Reducing caffeine intake, drinking less alcohol and stopping smoking are all suggested to reduce symptoms. Depending on the severity of your symptoms, a patient could then be offered different medications to improve their symptoms and therefore, improve their quality of life.⁸

CURRENT TREATMENT OPTIONS

The following medications are currently offered for lymphocytic colitis:⁸

- Budesonide

- Loperamide which slows down muscle contractions of the gut allowing more liquid to be absorbed
- Bile acid sequestrants such as colestyramine, colestipol or colesevelam
- Infliximab/adalimumab/vedolizumab
- Immunosuppressants such as azathioprine and mercaptopurine have been shown to be effective where budesonide hasn't worked.

PLACE OF TECHNOLOGY

If licensed, budesonide 9mg gastro-resistant granules would provide a first-line treatment for the induction of remission in patients with lymphocytic colitis.^b

CLINICAL TRIAL INFORMATION

Trial	NCT01209208 ; 2008-005994-36 (EudraCT Number) ; Double-blind, Double-dummy, Randomised, Placebo-controlled, Multi-centre Phase III Study on the Efficacy and Tolerability of a 8-week Treatment With Budesonide vs. Mesalazine vs. Placebo in Patients With Lymphocytic Colitis Phase III - completed Location(s): Germany Study completion date: June 2017
Trial design	Randomised, parallel assignment, quadruple-blinded, placebo-controlled
Population	N = 57; 18-90 years of age; have symptoms and signs of lymphocytic colitis
Intervention(s)	Budesonide; 9mg per day; oral
Comparator(s)	- Mesalamine; 3mg per day; oral - Placebo
Outcome(s)	Rate of clinical remission (Time frame: 8 weeks)
Results (efficacy)	- Proportion of patients in clinical remission at week 8 was significantly higher in the budesonide group than in the placebo group (intention-to-treat analysis, 79% vs 42%; P = .01) - The difference in proportions of patients in clinical remission at week 8 between the mesalamine (63%) and placebo groups was not significant (P = .09). - The proportion of patients with histologic remission at week 8 was significantly higher in the budesonide group (68%) vs the mesalamine (26%; P = .02) or placebo (21%; P = .008) groups. ⁶
Results (safety)	The incidence of adverse events was 47.4% in the budesonide group, 68.4% in the mesalamine group, and 42.1% in the placebo group. ⁶

ESTIMATED COST

Budenofalk 9mg granules cost £135.00 for 60 sachets.¹²

^b Information provided by Dr Falk Pharma UK Ltd. on UK PharmaScan.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE interventional procedure guidance. Computed tomographic colonography (virtual colonoscopy). (IPG129). June 2005.
- NICE interventional procedure guidance. Leukapheresis for inflammatory bowel disease. (IPG126). June 2005.
- NICE diagnostic guidance. Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel. (DG11). October 2013.
- NICE quality standard. Inflammatory bowel disease. (QS81). February 2015.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

NHS England. 2013/14 NHS Standard Contract for Colorectal: Complex Inflammatory Bowel Disease (Adult). A08/S/c.

OTHER GUIDANCE

American Gastroenterological Association Institute. Guideline on the Medical Management of Microscopic Colitis. 2016.⁵

ADDITIONAL INFORMATION

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