Budesonide orodispersible tablets are a new formulation of budesonide to treat eosinophilic oesophagitis in adults. Eosinophilic oesophagitis is an inflammatory condition that causes problems with eating and swallowing. Budesonide orodispersible tablets are dissolved in the mouth and slowly swallowed. Some studies have suggested that budesonide may reduce the inflammatory reaction that causes the symptoms of eosinophilic oesophagitis.

This briefing is based on information available at the time of research 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.

This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.
**TARGET GROUP**

- Eosinophilic oesophagitis (EoE) – first line.

**TECHNOLOGY**

**DESCRIPTION**

Budesonide orodispersible tablets (BUL) are a new formulation of an established glucocorticoid receptor agonist (corticosteroid). In clinical trials\(^1\), budesonide was administered orally at 1mg, twice daily.

Budesonide is available in several formulations and is currently licensed in the EU for asthma, ulcerative colitis (limited to the rectum and sigmoid colon), Crohn's disease (affecting the ilium and/or the ascending colon), autoimmune hepatitis, collagenous colitis, laryngitis subglottica, seasonal and perennial allergic rhinitis, nasal polyps and chronic obstructive pulmonary disease. Recognised adverse effects for the oral route include: Cushing’s syndrome, indigestion, increased risk of infection, local fungal infection, bruising easily, cough or hoarseness, sneezing and sore throat\(^2\).

Budesonide effervescent is also in phase III clinical trials for graft-versus-host-disease.

**INNOVATION and/or ADVANTAGES**

If licensed, budesonide orodispersible tablets will provide the first specific pharmacological treatment option for patients with eosinophilic oesophagitis.

**DEVELOPER**

Dr Falk Pharma GmbH.

**AVAILABILITY, LAUNCH OR MARKETING**

In phase III clinical trials.

**PATIENT GROUP**

**BACKGROUND**

EoE is a chronic, immune-mediated inflammatory oesophageal disease, characterised by the presence of large numbers of intraepithelial eosinophils in oesophageal biopsies and recurrent symptoms of oesophageal dysfunction\(^3\). Symptoms include dysphagia and food impaction, especially in adults, feeding disorders and vomiting in children and less typical symptoms of abdominal and chest pain in both\(^4\). EoE is strongly associated with atopy and is triggered by food or environmental antigens in genetically predisposed individuals\(^4\). The majority of cases are in children, adolescents and adults under the age of 50, with clinical differences between adults and children\(^5\). The condition is thought to progress from an

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\(^a\) Expert personal opinion.
inflammatory-predominant phenotype (primarily seen in children) to a fibrosis-predominant one (seen in adults).  

**CLINICAL NEED and BURDEN OF DISEASE**

EoE was first recognised as a distinct disorder around 25 years ago, with diagnosis in Westernised countries rising sharply in the last two decades. It is now considered to be the most frequent eosinophilic gastrointestinal disorder. The most recent estimated prevalence for Europe is around 16.1 per 100,000 population (95% CI 7.9-27.1), equating to approximately 823 cases in England. Incidence in Europe is estimated at around 2 per 100,000 population, per year.

Onset of EoE is in childhood, adolescence and young adulthood with a gradually rising incidence from young children to adults, peaking between 20 and 40 years of age. There is a male preponderance, with a male:female ratio of 3:1. It is more common in white ethnic groups. Symptoms of EoE can be unpleasant and socially embarrassing, and have a significant impact on quality of life. People with EoE may modify their social behaviour and what they choose to eat. Eating in company can be stressful due to the risk of bolus obstruction and subsequent retching. EoE is associated with considerable morbidity, with symptoms of dysphagia and food impaction being common. EoE is the most common underlying cause of emergency admission to hospital with food bolus obstruction.

In 2014-15, there were 27,769 hospital admissions in England due to oesophagitis (ICD10 K20), accounting for 32,004 finished consultant episodes and 16,608 bed days. The population likely to be eligible to receive budesonide orodispersible could not be estimated from available published sources.

**PATIENT PATHWAY**

**RELEVANT GUIDANCE**

- **NICE Guidance**
  None identified.

- **NHS England Policies and Guidance**
  None identified.

- **Other Guidance**

**CURRENT TREATMENT OPTIONS**

Treatment of EoE aims to improve clinical symptoms and oesophageal eosinophilic inflammation. Dietary elimination is recommended as an initial therapy option for the management of EoE in children and adults, in conjunction with an allergist to guide
elemental and elimination diets\textsuperscript{11}. Off-licence topical steroids (e.g. spray or suspension) are prescribed as first line pharmacologic therapy\textsuperscript{b}. Where no symptomatic or histologic improvement is achieved following topical steroids, and for patients who require a rapid improvement in symptoms, systemic steroids may be recommended\textsuperscript{11}. Oesophageal dilation may be used in symptomatic patients with strictures that persist in spite of pharmacological and dietary therapy\textsuperscript{11}.

### EFFICACY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>Sponsor</th>
<th>Status</th>
<th>Source of information</th>
<th>Location</th>
<th>Design</th>
<th>Participants</th>
<th>Schedule</th>
<th>Follow-up</th>
<th>Primary outcomes</th>
<th>Secondary outcomes</th>
<th>Key results</th>
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<tbody>
<tr>
<td>EOS-1; NCT02434029; BUL-1/EEA 2014-001484-12; budesonide orodispersible vs placebo; phase III.</td>
<td>Dr. Falk Pharma GmbH.</td>
<td>Complete.</td>
<td>Trial registry\textsuperscript{1}, manufacturer.</td>
<td>EU (incl UK).</td>
<td>Randomised, placebo-controlled.</td>
<td>n=88; aged 18-75 years; active EoE; documented trial of proton pump inhibitors (PPI) to rule out PPI responsive eosinophilia.</td>
<td>Randomised to budesonide orodispersible, 1mg; or placebo, twice daily.</td>
<td>Active treatment for 6 weeks; 4 weeks follow-up, if not continuing in EOS-2 trial.</td>
<td>Clinico-pathological remission.</td>
<td>Histological remission; resolution of symptoms; quality of life.</td>
<td>-</td>
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<tr>
<td>EOS-2; NCT02493335; BUL-2/EER 2014-001485-99; budesonide orodispersible vs placebo; phase III.</td>
<td>Dr. Falk Pharma GmbH.</td>
<td>Ongoing.</td>
<td>Trial registry\textsuperscript{14}.</td>
<td>EU (incl UK).</td>
<td>Randomised, placebo-controlled.</td>
<td>n=204 (planned); aged 18-75; active EoE; documented trial of PPIs to rule out PPI responsive eosinophilia.</td>
<td>Randomised to budesonide orodispersible, 0.5mg or 1mg; or placebo, twice daily.</td>
<td>Active treatment for 48 weeks; 4 weeks follow-up.</td>
<td>Rate of patients free of treatment failure.</td>
<td>Rate of histological and clinical relapse; quality of life.</td>
<td>-</td>
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<tr>
<td>NCT02280616; BUU-2/EEA 2009-016692-29; budesonide orodispersible vs budesonide suspension vs placebo; phase II.</td>
<td>Dr. Falk Pharma GmbH.</td>
<td>Complete.</td>
<td>Publication\textsuperscript{12}, trial registry\textsuperscript{14}.</td>
<td>EU (not incl UK).</td>
<td>Randomised, placebo-controlled.</td>
<td>n=76; aged 18-75 years; active EoE.</td>
<td>Randomised to budesonide orodispersible, 1mg or 2mg with placebo suspension; or budesonide suspension, 5mL (0.4mg/mL) with placebo tablet; or placebo tablet with placebo suspension; all twice daily.</td>
<td>Active treatment for 2 weeks; 2 weeks follow-up.</td>
<td>Histological remission; eosinophilic load.</td>
<td>Endoscopic abnormality score; clinical symptoms; quality of life.</td>
<td>For budesonide 1mg, 2mg, suspension, and placebo respectively: histological remission (%), 100.0 (95% CI 64.7-100.0), 94.7 (95% CI 57.6-99.5), 94.7 (95% CI 57.6-99.5), 0.0. Eosinophilic load (eos/mm\textsuperscript{2}), -120 (p=0.0003), -128</td>
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\textsuperscript{b} Expert personal opinion.
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<th></th>
<th>Mean peak eosinophilic load (eos/mm²)</th>
<th>Improved endoscopic abnormality score (%)</th>
<th>Adverse effects (AEs)</th>
<th>Expected reporting date</th>
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<td></td>
<td>(p=0.0003), -98 (p=0.0020), -8</td>
<td>73.7, 57.9, 57.9, 57.9, 26.3.</td>
<td>No serious AEs reported. For budesonide 1mg, 2mg, suspension, and placebo respectively, proportions of patients with suspected treatment-emergent adverse drug reactions, 4/19, 5/19, 6/19, 0/19.</td>
<td>May 2017.</td>
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**ESTIMATED COST and IMPACT**

**COST**

The cost of budesonide orodispersible tablets is not yet known.

**IMPACT - SPECULATIVE**

**Impact on Patients and Carers**

- Reduced mortality/increased length of survival
- Other:

- Reduced symptoms or disability
- No impact identified

**Impact on Health and Social Care Services**

- Increased use of existing services
- Re-organisation of existing services
- Other:

- Decreased use of existing services
- Need for new services
- None identified

**Impact on Costs and Other Resource Use**

- Increased drug treatment costs
- Other increase in costs:

- Reduced drug treatment costs
- Other reduction in costs:

- None identified

**Other Issues**

- Clinical uncertainty or other research question identified:

- None identified
REFERENCES


