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Health Technology Briefing
October 2023

Budesonide suspension for treating eosinophilic oesophagitis in children and adolescents

Company/Developer	Dr Falk Pharma UK Ltd

☐New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 29954	NICE TSID: N/A	UKPS ID: 656290

Licensing and Market Availability Plans

Currently in phase 2/3 clinical trials.

Summary

Budesonide suspension is currently in clinical development for treating eosinophilic oesophagitis in children and adolescents. Eosinophilic oesophagitis is inflammation of the oesophagus (the passage that leads from the mouth to the stomach), which causes symptoms such as dysphagia (difficulty swallowing) and blockage of the oesophagus. It is caused by a large build-up of white blood cells called eosinophils in the lining of the oesophagus. The oesophagus transmits food from the mouth to the stomach, so the inflammation makes swallowing difficult as the oesophagus becomes narrower than usual leading to restrictions. Eosinophilic oesophagitis has been identified only since the early 1990s but is now considered the second most common oesophageal disease/dysphagia. There is currently an unmet need for appropriate treatment options for paediatric populations.

The active substance in Jorveza, budesonide, is a corticosteroid. Corticosteroids attach to targets (receptors) on immune cells and reduce the release of substances that lead to inflammation. After Jorveza dissolves in the mouth, the saliva carries it to the oesophagus where it reduces the inflammation and relieves the symptoms of eosinophilic oesophagitis. Whichever way budesonide is administered orally, it coats the oesophagus to reduce inflammation and the suspension will offer a new treatment formulation option to children aged 2 to 18 with eosinophilic oesophagitis, if licensed.

Proposed Indication

Children and adolescents ages 2 to 18 years with active eosinophilic oesophagitis and maintenance of remission.[1]

Technology

Description

Budesonide (Jorveza) is a non-halogenated glucocorticosteroid, which acts primarily as an anti-inflammatory via binding to the glucocorticoid receptor. In the treatment of eosinophilic oesophagitis, budesonide inhibits antigen-stimulated secretion of many pro-inflammatory signal molecules such as thymic stromal lymphopoeitin, interleukin-13 and eotaxin-3 in the oesophageal epithelium, which results in a significant reduction of the oesophageal eosinophilic inflammatory infiltrate.[2] This medicine will be available as a viscous (thick) suspension to be taken by mouth in children. This formulation is expected to release budesonide in the oesophagus mainly due to its viscous characteristic, reducing the inflammation and relieving the symptoms of eosinophilic oesophagitis.[3]

Budesonide is in phase 2/3 clinical development for the treatment of children and adolescents aged 2 to 18 years with eosinophilic oesophagitis. The budesonide will be administered orally in the dosage 0.2mg/ml.[1]

Key Innovation

There are no satisfactory methods authorised in the EU for the treatment of eosinophilic oesophagitis in children. As allergy was thought to be one of the possible causes of the disease, allergens were excluded from the diet. Oesophageal dilation (widening) was performed in some patients, although it carries the risk of complication such as perforation of the oesophagus.[3] So far, there have been only a few studies on swallowed topical corticosteroids formulations developed specifically for oesophageal administration. The orodispersible budesonide tablet with effervescent properties was the first drug to be developed for oesophageal targeting in adults.[4] If licensed, budesonide oral suspension will give a new treatment option to paediatric patients with eosinophilic oesophagitis who have no effective therapies available.

Regulatory & Development Status

Budesonide (oral solution) does not currently have Marketing Authorisation in the EU/UK for any indication. However, for the budesonide orodispersible tablet has market authorisation in the EU/UK for the treatment of eosinophilic oesophagitis in adults aged 18+.[2]

Budesonide orodispersible is currently in clinical development for Oesophageal squamous cell carcinoma, Oesophageal adenocarcinoma and Barrett's oesophagus.[5]

Budesonide orodispersible has the following regulatory designations/awards:

- An orphan drug in the EU in 2013 for the treatment of eosinophilic oesophagitis.[3]

Patient Group

Disease Area and Clinical Need

Eosinophilic oesophagitis is a chronic immune system disease in which eosinophils build up in the oesophagus. It is a progressive type 2 inflammatory disease that damages the oesophagus and prevents it from working properly. This build-up, which is a reaction to foods, allergens or acid reflux, can inflame or injure the oesophageal tissue. Damaged oesophageal tissue can lead to difficulty swallowing or cause food to get stuck when swallowing.[6] The production and accumulation of eosinophils may be caused by many factors such as immune hypersensitivity responses to particular foods or allergens in some affected individuals.[7] Eosinophilic diseases are often found in those with a family history of allergic diseases such as rhinitis, asthma and/or eczema. A personal history of atopy (a predisposition to develop allergic diseases) is found prior to eosinophilic oesophagitis diagnosis in 50-60% of cases.[8] The symptoms of eosinophilic oesophagitis can vary from one person to another and depend on age. In children, symptoms can include: failure to thrive (poor growth, malnutrition and weight loss), regurgitation, difficulty eating, vomiting after eating and food refusal. Children may be labelled as picky eaters.[6]

A large meta-analysis, estimated eosinophilic oesophagitis incidence and prevalence rates in children of 3.7 cases/100,000 persons/year and 22.7 cases/100,000 persons, respectively.[9] Eosinophilic oesophagitis is diagnosed in 2–6.5% of patients undergoing esophagogastroduodenoscopy (EGD) for any indication and this increases to 12–22% if dysphagia is the indication. While eosinophilic oesophagitis can affect patients of all age groups, it has bimodal peak with most cases in either the paediatric age group or the third decade of life. Eosinophilic oesophagitis is more common in Caucasian males and has a strong association with concomitant atopic conditions such as asthma, eczema, rhinitis, and food allergies.[10] In 2022-23, in England, there were 21,442 finished consultant episodes (FCE) and 18,702 admissions of which primary diagnosis was oesophagitis (children and adults) (ICD10 K20), this resulted in 13,165 FCE bed days and 16,674 day cases. [11]

Recommended Treatment Options

There are currently no approved pharmacological treatment options for eosinophilic oesophagitis in Children.

Clinical Trial Information

Trial	EUdraCT2017-003737-29; Double-blind, randomized, placebo-controlled, Phase II/III trial on the efficacy and tolerability of treatment with budesonide oral suspension vs. placebo in children and adolescents with eosinophilic oesophagitis. **Phase 2/3:** Ongoing **Locations:** Five EU countries and UK
Trial Design	Double blind, randomised, placebo-controlled
Population	N=75; Males or females aged 2 to 18 years with confirmed clinic-pathological diagnosis of eosinophilic oesophagitis
Intervention(s)	Budesonide oral suspension (0.2mg/ml)
Comparator(s)	Matched placebo
Outcome(s)	Primary end points: • Rate of patients with pathological remission and clinical response at Double Blind week 12 See trial record for full list of outcomes

Results (efficacy)	-
Results (safety)	-

Estimated Cost

Budesonide orodispersible tablet is already marketed in the UK for the treatment of eosinophilic oesophagitis in adults; 90 x 1mg tablets currently costs £323 and 60 x 0.5mg tablets costs £214.80.[12]

Relevant Guidance

NICE Guidance

- NICE Technology Appraisal. Dupilumab for treating eosinophilic oesophagitis in people 12 years and over [ID5107]. Expected date of issue to be confirmed.
- NICE Technology Appraisal. Benralizumab for treating eosinophilic oesophagitis in people aged 12 to 65 [ID5093]. Expected date of issue to be confirmed.
- NICE Technology Appraisal. Budesonide orodispersible tablet for inducing remission of eosinophilic oesophagitis (TA708). June 2021.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract Paediatric Medicine: Specialised allergy services. E03/S/j

Other Guidance

- American Gastroenterological Association. AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. 2020.[13]
- United European Gastroenterology, European Academy of Allergy and Clinical Immunology, European Society for Paediatric Gastroenterology Hepatology and Nutrition, and EUREOS European Consortium for Eosinophilic Diseases of the GI Tract. Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. 2017.[14]

Additional Information

References

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