Health Technology Briefing
March 2022

Dupilumab for treating eosinophilic oesophagitis in people aged 12 years and older

Company/Developer	Sanofi

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 26747	NICE ID: 10570	UKPS ID: 654882

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Dupilumab is in clinical development for the treatment of eosinophilic oesophagitis (EoE) in adults and adolescents. EoE is a condition that affects the gullet (oesophagus). There is a build-up of a particular type of immune cell (eosinophils) in the lining of the gullet causing inflammation or irritation. This affects how the gullet works, causing symptoms such as difficulty swallowing. EoE has been identified only since the early 1990s but is now considered a major cause of digestive system (gastrointestinal) illness. Research is ongoing and will likely lead to revisions in the diagnosis and treatment of EoE, as there is currently an unmet need for appropriate treatment options.

Dupilumab is a human monoclonal antibody, which is a manufactured version of an immune protein created by the body to fight infection. It is given as an injection under the skin. Dupilumab stops the action of two immune response mediators, interleukin-4 (IL-4) and interleukin-13 (IL-13). These proteins are responsible for inflammation in the body and blocking these decreases levels of inflammation. If licensed, dupilumab will provide a novel treatment option for adult and adolescent EoE patients.

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 unavailable to comment.

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Proposed Indication

Treatment of adult and adolescent patients with eosinophilic esophagitis (EoE)[1]

Technology

Description

Dupilumab (Dupixent) is a recombinant human IgG4 monoclonal antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signalling. Dupilumab inhibits IL-4 signalling through the Type I receptor (IL-4Rα/γc), and both IL-4 and IL-13 signalling through the Type II receptor (IL-4Rα/IL-13Rα). Blocking the IL-4/IL-13 pathway with dupilumab in patients decreases many of the mediators of type 2 inflammation.[2]

Dupilumab is currently in phase III clinical development for the treatment of adolescents and adults aged 12 years and older for the treatment of EoE. In the phase III clinical trial (NCT03633617), participants received a 300 mg solution of dupilumab via subcutaneous (SC) injection weekly for 24 weeks.[1-3]

Key Innovation

There are currently no standard treatment options available in the NHS for treating EoE.[4,5] IL-4 and IL-13 are type 2 cytokines targeted by dupilumab. They are involved in the pathogenesis of EoE and therefore, dupilumab has been hypothesized as a potential treatment for EoE.[6]

In a phase 2 trial of patients with active EoE, dupilumab reduced dysphagia, histologic features of disease (including eosinophilic infiltration and a marker of type 2 inflammation), and abnormal endoscopic features compared with placebo. Dupilumab increased oesophageal distensibility and was generally well tolerated.[1,3] Dupilumab is the only biologic medicine to show positive, clinically meaningful phase 3 results in these patients.[3] If licensed, dupilumab will provide a novel treatment option for EoE patients aged 12 years and older.

Regulatory & Development Status

Dupilumab has a Marketing Authorisation in the UK for the following indications:[2]

- Treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy
- Treatment of severe atopic dermatitis in children 6 to 11 years old who are candidates for systemic therapy
- Add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised fraction of exhaled nitric oxide (FeNO), who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment

Dupilumab as a monotherapy and in addition to various other medicinal products is being developed for the following indications in phase II and III clinical trials:[7]

- Asthma
- Atopic dermatitis
- Chronic rhinosinusitis phenotype with nasal polyps (CRSwNP)
- Chronicrhinosinusitis without nasalpolyps
- Allergic fungal rhinosinusitis
- Chronic obstructive pulmonary disease
- Cold urticaria

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- Chronic spontaneous urticaria
- Neurodermatitis
- Bronchopulmonary aspergillosis
- Moderate to severe atopic hand and foot dermatitis

Dupilumab has the following designations:

- US FDA Orphan designation for EoE in May 2017.[8]
- US FDA Breakthrough therapy designation for EoE in September 2020.[9]

Patient Group

Disease Area and Clinical Need

EoE is a chronic immune system disease in which eosinophils builds 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.[10] 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.[11] 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 EoE diagnosis in 50-60% of cases.[12] People with EoE may have poor quality of life and are more likely to experience depression, especially as they age.[3]

A large meta-analysis, which included studies from North America, Europe and Australia, estimated EoE incidence and prevalence rates of 3.7 cases/100,000 persons/year and 22.7 cases/100,000 persons, respectively.[13] In England (2020-21), there were 15,766 finished consultant episodes (FCE) and 13,052 admissions for oesophagitis (ICD-10 code K20) which resulted in 10,604 FCE bed days and 11,174 day cases.[14]

Recommended Treatment Options

NICE currently recommends budesonide orodispersable tablet (ODT) for the treatment of EO.[15]

Clinical Trial Information

Trial	NCT03633617, EudraCT 2018-000844-25; A Phase 3, Randomized, 3-Part Study to Investigate the Efficacy and Safety of Dupilumab in Adult and Adolescent Patients With Eosinophilic Esophagitis (EoE) **Phase III:** Active, not recruiting **Locations:** 7 EU countries, UK, USA, Canada and other countries
Trial Design	Randomized, parallel assignment, quadruple masking
Population	N=321; children, adolescents and adults aged 12 and older, documented diagnosis of EoE by endoscopic biopsy, history (by patient report) of an average of at least 2 episodes of dysphagia (with intake of solids) per week in the 4 weeks prior to screening.
Intervention(s)	Dupilumab - solution for injection administered via SC injection

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Comparator(s)	Matching placebo
Outcome(s)	Primary outcomes: • Proportion of patients achieving peak esophageal intraepithelial eosinophil count of ≤6 eosinophils per high-power field (eos/hpf) [Time Frame: At week 24] • Absolute change in Dysphagia Symptom Questionnaire (DSQ) score [Time Frame: At week 24] See trial record for full list of other outcomes.
Results (efficacy)	Preliminary results:[3] • 64% reduction in disease symptoms from baseline compared to 41% for placebo (p=0.0008). Dupixent patients experienced a 23.78 point improvement on the 0-84 DSQ scale, compared to a 13.86 point improvement for placebo (p<0.0001); baseline DSQ scores were approximately 38 and 36 points, respectively. • Nearly 10 times as many Dupixent patients achieved histological disease remission: 59% of patients achieved histological disease remission compared to 6% of placebo patients (p<0.0001). This was measured by the proportion of patients who achieved a peak esophageal intraepithelial eosinophil count of ≤6 eos/hpf; mean baseline peak levels were 89 and 84 eos/hpf, respectively.
Results (safety)	-

Estimated Cost

Dupilumab is already marketed in the UK for various indications; a 150mg/1ml pre-filled pen/syringe and a 175mg/1ml pre-filled pen/syringe cost £1,264.89.[16]

Relevant Guidance

NICE Guidance

- 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

- 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.[17]

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Additional Information

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NB: 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.

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