Health Technology Briefing
July 2024

Cendakimab for eosinophilic oesophagitis in people aged 12 years and over

Company/Developer	Bristol-Myers Squibb Pharmaceuticals Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 31276	NICE ID: Not Available	UKPS ID: 673953

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Eosinophilic oesophagitis (EoE) is a chronic disorder of the digestive system in which large numbers of white blood cells called eosinophils are present in the tube that carries food from the mouth to the stomach (oesophagus). Eosinophils play a role in immune regulation. The production and accumulation of eosinophils seen in EoE may be caused by many factors such as immune hypersensitivity responses to foods or environmental allergens. Common symptoms include difficulty swallowing, food getting stuck in the throat, nausea, vomiting, poor growth, weight loss, stomach pain, poor appetite and malnutrition. The available treatment option is limited by side effects and there is evidence to suggest it is only partially effective. This demonstrates an unmet treatment need for patients with EoE.

Cendakimab is a humanised monoclonal antibody, which are man-made proteins that mimic protective immune system proteins called antibodies. Cendakimab is selective and can recognise a small protein called interleukin 13 (IL13) which is involved in cell signalling and is key in the development of EoE. Cendakimab prevents IL13 from binding to the surface of cells and inducing eosinophilic inflammation, therefore reducing EoE disease activity. Cendakimab is administered by subcutaneous (under the skin) injection and, if licensed, will offer a novel treatment for EoE.

Proposed Indication

Treatment of eosinophilic oesophagitis (EO) in adults and adolescents aged 12 to 75 years.[1,2]

Technology

Description

Cendakimab (CC-93538, RPC4046) is a selective, high-affinity, humanised immunoglobulin G1 monoclonal antibody that recognises wild-type and variant human interleukin 13 (IL13) and prevents it from binding to the cell surface receptor subunits IL13Rα1 and IL13Rα2.[3-5] IL13 has been implicated as a key cytokine in the pathogenesis of EO.[3]

Cendakimab is currently in phase III clinical development for the treatment of adult and adolescent patients with EO.[2,6] In these trials, cendakimab is administered subcutaneously.[2,6] Trial NCT04753697 specifies a dose of 360mg; in one treatment arm it is given once weekly for induction followed by once every other week for maintenance; and in the other arm it is given once weekly for both induction and maintenance.[2]

Key Innovation

Currently, a topical steroid in orodispersible tablet form is approved for EoE treatment in Europe. However, the use of corticosteroids is limited by side effects, including candidal esophagitis, oral candidiasis and atrophy of the oesophageal mucosa, and there are limited long-term safety data.[7] Moreover, evidence suggests that prolonged topical corticosteroid use may be only partially effective in maintaining disease remission and is associated with resistance.[7] This demonstrates an unmet need for non-steroidal treatment options for patients with EO.

Cendakimab, a monoclonal antibody against IL13, has been shown to be effective in a phase II trial where patients with both non–steroid-refractory and steroid-refractory EoE experienced disease improvement.[7] Therefore, if licensed, cendakimab will offer a novel treatment for people with EoE, especially for patients whose disease is unresponsive to steroid treatment who currently have no pharmacologic treatment options.[7]

Regulatory & Development Status

Cendakimab does not currently have marketing authorisation in the EU/UK for any indication.

Patient Group

Disease Area and Clinical Need

EoE is a chronic disorder of the digestive system in which large numbers of eosinophils are present in the oesophagus. The production and accumulation of eosinophils may be caused by factors such as immune hypersensitivity responses to particular foods or environmental allergens. It is now appreciated that pathological features of EoE such as oesophageal eosinophilia are driven by a strong response of the adaptive immune system, primarily orchestrated by type 2 helper T cells. These cells, along with oesophageal mast cells, produce high levels of the cytokine IL-13, which elicits multiple pathological processes in the oesophagus. Common symptoms include dysphagia, food getting stuck in the throat, nausea, vomiting, poor growth, weight loss, stomach pain, poor appetite and malnutrition.[10]

EoE affects about one in 3,000 people in the UK.{Digestive Health UK Gastroenterology Clinic, #240} In England, 2022-23, there were 21,442 finished consultant episodes (FCE) and 18,702 admissions for oesophagitis (ICD-10 code K20) which resulted in 13,165 FCE bed days and 16,674 day cases.[12] This is however, not specific to EoE and also accounts for non-eosinophilic oesophagitis.

Recommended Treatment Options

Many children and adults with EoE show improvement with proton pump inhibitor therapy, as well diet modification to remove allergenic food, most commonly milk, egg, soy, wheat, nuts and fish.[10] The National Institute for Health and Care Excellence (NICE) recommend budesonide orodispersible tablets for inducing remission of eosinophilic oesophagitis in adults.[13]

Clinical Trial Information

Trial	**CC-93538-EE-001**; NCT04753697, EudraCT-2020-004336-16; A Multi-Center, Multi-National, Randomized, Double-Blind, Placebo-Controlled Induction and Long-term Controlled Study to Evaluate the Efficacy and Safety of CC-93538 in Adult and Adolescent Subjects With Active Eosinophilic Esophagitis **Phase III** – Active, not recruiting **Locations:** Seven EU countries, UK, USA, Canada and other countries **Primary completion date (actual):** January 2024	**CC-93538-EE-002**; NCT04991935, EudraCT-2020-004335-24; A Phase 3, Multicenter, Multinational, Open-Label Extension Study to Evaluate the Long-Term Safety of CC-93538 in Adult and Adolescent Subjects With Eosinophilic Esophagitis **Phase III** - Recruiting **Locations:** Seven EU countries, UK, USA, Canada and other countries **Primary completion date (estimated):** June 2026
Trial Design	Randomised, parallel assignment, quadruple-blind, placebo-controlled	Uncontrolled, open label, single group assignment
Population	N=430 (actual); subjects with eosinophilic oesophagitis who have been unresponsive to proton pump inhibitors; aged 12 to 75 years	N=259 (estimated); subjects with eosinophilic oesophagitis who previously participated in CC-93538-EE-001 and CC-93538-DDI-001 trials; aged 12 to 75 years
Intervention(s)	- Cendakimab; 360g dose administered subcutaneously, once weekly for 24 weeks. - Cendakimab; 360g dose administered subcutaneously, once weekly for 24 weeks followed by a 360g dose administered subcutaneously, once every other week for 24 weeks	Cendakimab administered subcutaneously, once weekly.
Comparator(s)	Matched placebo	No comparator

Outcome(s)	**Primary outcomes:** - Mean change in dysphagia days, evaluated over the prior 14-day period using the modified daily symptom diary from baseline to week 24 - The proportion of participants with eosinophilic histologic response defined as a peak oesophageal eosinophil count ≤ 6/high-power field at week 24 See trial record for full list of other outcomes.	**Primary outcome:** incidence of adverse events for a minimum of 28 months. See trial record for full list of other outcomes.
Results (efficacy)	-	-
Results (safety)	-	-

Trial	NCT02098473; A Phase2, Multi-Center, Multi-national, Randomized, Double-blind, Placebo-controlled Parallel-group Clinical Trial to Evaluate the Efficacy and Safety of RPC4046 in Adult Subjects With Eosinophilic Esophagitis **Phase II** - Completed **Locations**: USA, Canada and Switzerland **Primary completion date (actual):** February 2016
Trial Design	Randomised, parallel assignment, quadruple-blind, placebo-controlled
Population	N=100 (actual); subjects with eosinophilic oesophagitis; aged 18 to 65 years
Intervention(s)	- Cendakimab administered by intravenous (IV) infusion at first dose followed by two subcutaneous (SC) injections weekly for 16 weeks, low dose (180mg)[3] - Cendakimab administered by IV infusion at first dose followed by two SC injections weekly for 16 weeks, high dose (360mg)[3]
Comparator(s)	Matched placebo
Outcome(s)	**Primary outcome:** mean eosinophil count in gastrointestinal biopsies from baseline to week 16
Results (efficacy)	At week 16, mean changes in oesophageal eosinophil count per high-power field were a reduction of 94.8 ± 67.3 in patients who received 180 mg cendakimab (P < .0001) and a reduction of 99.9 ± 79.5 in patients who received 360 mg cendakimab (P < .0001) compared with a reduction of 4.4 ± 59.9 in patients who received placebo.[3]
Results (safety)	The frequency of adverse events was numerically higher in the 360-mg cendakimab group. The most common treatment-emergent adverse events observed were headache, upper respiratory tract infection, arthralgia, nasopharyngitis, diarrhoea, and nausea. Overall, the frequency of treatment-

	emergent adverse events in the cendakimab treatment groups was low and similar to placebo.[3]

Estimated Cost

The cost of cendakimab is not yet known.

Relevant Guidance

NICE Guidance

- NICE Technology Appraisal In development. Benralizumab for treating eosinophilic oesophagitis in people aged 12 to 65 [GID-TA10995]]. Expected date of issue to be confirmed.
- NICE Technology Appraisal Guidance. 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

- British Society of Gastroenterology (BSG) and British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN). Joint consensus guidelines on the diagnosis and management of eosinophilic oesophagitis in children and adults. 2022.[11]
- American Gastroenterological Association. AGA Institute and the Joint Task Force on Allergy Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. 2020.[14]
- 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.[15]

Additional Information

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