

Health Technology Briefing December 2022

Dupilumab for treating Chronic obstructive pulmonary disease (COPD)

Company/Developer

Sanofi

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 27118

NICE TSID: 10741

UKPS ID: 666467

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Dupilumab is in clinical development for the treatment of chronic obstructive pulmonary disease (COPD) in adults aged 40 years and older. COPD is the name for a group of lung conditions that cause breathing difficulties. It is a disease that causes obstructed airflow from the lungs. It is typically caused by long-term exposure to irritating gasses or matter, most often from cigarette smoke. Symptoms include difficulty breathing, coughing, mucus production and wheezing. People with COPD are at increased risk of developing heart disease, lung cancer and a variety of other conditions. There is currently an unmet need for appropriate treatment options for COPD.

Dupilumab is a human monoclonal antibody (a type of protein that is made in the laboratory), 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 them decreases levels of inflammation. If licensed, dupilumab would provide a new treatment option for patients with COPD.

Proposed Indication

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.

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Treatment adults aged 40 to 85 years old with moderate to severe Chronic Obstructive Pulmonary Disease (COPD).^{1,2}

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 (IL4Ra/γc), and both IL-4 and IL-13 signalling through the Type II receptor (IL-4Ra/IL-13Ra). Blocking the IL4/IL-13 pathway with dupilumab in patients decreases many of the mediators of type 2 inflammation.³

Dupilumab is currently in phase III clinical development for the treatment of adults ages 40 to 85 years for the treatment of moderate to severe chronic obstructive pulmonary disease (COPD). In the phase III clinical trials (NCT04456673, NCT03930732), participants received a solution of dupilumab via subcutaneous (SC) injection every 2 weeks.^{1,2}

Key Innovation

One of the most studied subtypes of COPD is type 2 (T2), for which there are an increasing number of biologic agents developed. IL-4 and IL-13 Th2 cytokines are responsible for many functions and are involved in COPD development. Allergic eosinophilic inflammation is partially driven by cytokines such as IL-4, IL-5 and IL-13. IL-13 binding to the IL-13 receptor alpha 1 (IL-13Ra1) induces recruitment of IL-4 receptor alpha 1 (IL-4Ra1), in turn forming a heterodimeric receptor complex responsible for the activation of signalling pathways. IL-13 is produced by T cells, mast cells, basophils and dendritic cells. It is involved in regulation of inflammatory and immune responses as well as mucous hypersecretion. Dupilumab is a human monoclonal antibody targeting IL-4Ra leading to inhibition of IL-13 and IL-4 signalling and hence, inhibiting eosinophilic inflammation. Targeting IL-4Ra has shown significant improvement in patient lung function.⁴ If licensed, dupilumab will offer a novel treatment option for patients with COPD.

Regulatory & Development Status

Dupilumab currently has Marketing Authorisation in the UK for the following indications:³

- moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy
- severe atopic dermatitis in children 6 to 11 years old who are candidates for systemic therapy
- severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised fraction of exhaled nitric oxide (FeNO) in adults and adolescents 12 years and older as add-on maintenance treatment
- severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised fraction of exhaled nitric oxide (FeNO) in children 6 to 11 years old as add-on maintenance treatment
- severe chronic rhinosinusitis with nasal polyposis (CRSwNP) in adults for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control

Dupilumab is also in phase II/III clinical development for the following indications:⁵

- Bullous Pemphigoid
- Pruritus
- Chronic Cold/Spontaneous Urticaria
- Cholinergic urticaria

- Hand Eczema
- Peanut Allergy
- Cow's milk allergy
- Keloids
- Atopic Keratoconjunctivitis
- Alopecia areata (AA)
- Allergic rhinitis
- Allergic bronchopulmonary aspergillosis
- Eosinophilic Oesophagitis
- Allergic fungal rhinosinusitis
- Prurigo nodularis (PN)
- Aspirin-exacerbated respiratory disease (AERD)
- Eosinophilic Gastritis

Patient Group

Disease Area and Clinical Need

Chronic obstructive pulmonary disease (COPD) is the name for a group of lung conditions that cause breathing difficulties. It includes emphysema (damage to the air sacs in the lungs) and chronic bronchitis (long-term inflammation of the airways). It is a common condition that mainly affects middle-aged or older adults who smoke. The main symptoms of COPD are increasing breathlessness, a persistent chesty cough with phlegm, frequent chest infections, and persistent wheezing. Without treatment, the symptoms usually get progressively worse. There may also be periods when they get suddenly worse, known as a flare-up or exacerbation.⁶

An estimated 1.2 million people in the UK are living with diagnosed COPD. In terms of diagnosed cases, this makes COPD the second most common lung disease in the UK, after asthma. Around 2% of the whole population – 4.5% of all people aged over 40 – live with diagnosed COPD. The number of people who have ever had a diagnosis of COPD has increased by 27% in the last decade, from under 1,600 to nearly 2,000 per 100,000.⁷ In England (2021-22), there were 195,957 finished consultant episodes (FCE) and 102,561 admissions for other COPD (ICD-10 code J44) which resulted in 546,728 FCE bed days and 1,309 day cases.⁸

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends Roflumilast for treating chronic obstructive pulmonary disease.⁹

Other potential pharmacological treatment options can include:¹⁰

- Inhalers:
 - o short-acting bronchodilator inhalers, long-acting bronchodilator inhalers, steroid inhalers
- Tablets:
 - o theophylline tablets, mucolytics, steroid tablets, antibiotics

Clinical Trial Information

Trial	<p>BOREAS; NCT03930732; 2018-001953-28; A Randomized, Double-blind, Placebo-controlled, Parallel-group, 52-week Pivotal Study to Assess the Efficacy, Safety and Tolerability of Dupilumab in Patients With Moderate-to-severe Chronic Obstructive Pulmonary Disease (COPD) With Type 2 Inflammation</p> <p>Phase III: Active, not recruiting</p> <p>Location(s): 12 EU countries, USA, Canada, and other countries</p> <p>Primary completion date: February 2023</p>
Trial Design	Randomised, parallel assignment, quadruple masking
Population	N=939 (actual); 40 years to 80 years old; participants with a physician diagnosis of COPD; current or former smokers with a smoking history of ≥ 10 pack-years, moderate-to-severe COPD; patient-reported history of signs and symptoms of chronic bronchitis; documented history of high exacerbation; evidence of Type 2 inflammation
Intervention(s)	Dupilumab SC injection every two weeks, 52-week treatment period.
Comparator(s)	Matched placebo
Outcome(s)	<p>Primary Outcome(s):</p> <ol style="list-style-type: none"> Annual rate of acute COPD exacerbation (AECOPD) [Time frame: baseline to Week 52] <p>See trial record for full list of outcomes.</p>
Results (efficacy)	-
Results (safety)	-
Clinical Trial Information	
Trial	<p>NOTUS; NCT04456673; 2018-001954-91; A Randomized, Double-blind, Placebo-controlled, Parallel-group, 52-week Pivotal Study to Assess the Efficacy, Safety, and Tolerability of Dupilumab in Patients With Moderate-to-severe Chronic Obstructive Pulmonary Disease (COPD) With Type 2 Inflammation</p> <p>Phase III: Recruiting</p> <p>Location(s): 15 EU countries, UK, USA, Canada other countries</p> <p>Primary completion date: July 2023</p>
Trial Design	Randomised, Parallel Assignment, Quadruple masking
Population	N=924 (estimated); ages 40 years to 85 years; participants with a physician diagnosis of COPD; current or former smokers with a smoking history of ≥ 10 pack-years; moderate-to-severe COPD; patient-reported history of signs and symptoms of chronic bronchitis; documented history of high exacerbation risk; evidence of Type 2 inflammation
Intervention(s)	Dupilumab SC injection every 2 weeks. 52-week treatment period.
Comparator(s)	Matched placebo.

Outcome(s)	<p>Primary Outcome(s):</p> <p>1. Annual rate of acute COPD exacerbation (AECOPD) [Time frame: baseline to Week 52]</p> <p>See trial record for full list of outcomes.</p>
Results (efficacy)	-
Results (safety)	-

Estimated Cost
Dupilumab is already marketed in the UK for various indications; a 300mg/2ml pre-filled pen/syringe and a 200mg/1.14ml pre-filled pen/syringe cost £1,264.89. ¹¹

Relevant Guidance
NICE Guidance
<ul style="list-style-type: none"> • NICE technology appraisal in development. Chronic obstructive pulmonary disease in adults (ID1237). Expected publication date to be confirmed. • NICE technology appraisal. NICE technology appraisal. Roflumilast for treating chronic obstructive pulmonary disease (TA461). July 2017. • NICE guideline. Chronic obstructive pulmonary disease in over 16s: diagnosis and management (NG115). July 2017. • NICE Quality Standard. Chronic obstructive pulmonary disease in adults (QS10). July 2011. •
NHS England (Policy/Commissioning) Guidance
<ul style="list-style-type: none"> • NHS England. 2013/14 NHS Standard Contract For Specialised Allergy Services (All Ages). B09/S/b.
Other Guidance

Additional Information

References

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