Health Technology Briefing
March 2024

Depemokimab for treating chronic rhinosinusitis with nasal polyps

Company/Developer	GlaxoSmithKline UK Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 34870	NICE ID: Not Available	UKPS ID: 672609

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Depemokimab is in clinical development for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adults. CRSwNP is a combination of two conditions: chronic rhinosinusitis and nasal polyps. Chronic rhinosinusitis is a condition in which the sinuses (air-filled spaces in the bones around the nose) are inflamed causing difficulty in breathing due to nasal blockage. Nasal polyps are painless soft growths inside the nose. Symptoms of CRSwNP include congestion, nasal discharge, reduced or loss of smell and facial pain or pressure. The exact cause of CRSwNP is unknown, but allergy, asthma, infection, and aspirin sensitivity have been shown to be associated with the disease. After treatment with standard of care therapy, many patients still experience symptoms and sometimes a reoccurrence of nasal polyps thereby posing a therapeutic challenge.

Depemokimab is administered subcutaneously. It is a type of medicine called a monoclonal antibody, that works by reducing the number of eosinophils (a type of white blood cell) in the body. Eosinophils are involved in nasal polyp creation and patients with nasal polyps have comparatively higher levels of eosinophils in their blood. Depemokimab has a long half-life (time required for the drug to reduce to half of its initial value) and is being developed to be administered once every 6 months, with a potential of an efficacy and safety profile similar to current therapies at a reduced dosing frequency. If licensed, depemokimab will offer an additional add-on therapy option for patients with CRSwNP.

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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Proposed Indication

Treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adults.[1]

Technology

Description

Depemokimab (GSK3511294) is a monoclonal antibody that works by blocking interleukin 5 (IL-5) from binding to its cognate receptor. IL-5 mediates the growth and differentiation of eosinophils in the bone marrow, and their recruitment and activation within tissues.[2,3] Therefore, inhibiting IL-5 removes a key eosinophil growth factor, and given the short half-life of eosinophils, causes a rapid reduction in the circulating population.[4] Eosinophils are the main inflammatory cells in the substantial proportion of nasal polyp tissues.[5] It is a long acting, humanised anti-interleukin 5 (anti-IL-5) monoclonal antibody engineered for extended half-life and improved IL-5 affinity versus other anti-IL-5 monoclonal antibodies.[3]

Depemokimab is in clinical development as an add on therapy for the treatment of CRSwNP in adults. In the phase III clinical trial (NCT05274750), participants receive depemokimab subcutaneously.[6]

Key Innovation

CRSwNP is usually treated with topical corticosteroids. Oral corticosteroids can be used in severe cases, but benefits are short lived, and side-effects restrict long term use.[7] Multiple studies have proven the effectiveness of using monoclonal antibodies as a form of precision medicine in sinusitis with polyps.[8] Biological drug therapies are aimed at specific immune cells or inflammatory cells in the disease development and progression and therefore have been shown to improve drug efficacy and reduce the incidence of complications.[9] Depemokimab is being developed as a long-acting subcutaneous injectable anti-IL-5 therapy and is expected to deliver an efficacy and safety profile similar to the current anti-IL-5 therapies with a reduced dosing frequency.[10] Depemokimab has the potential to be the first biologic to deliver long-acting suppression of IL-5 from one subcutaneous injection every six months.[11]

If licensed, depemokimab will offer an additional add-on therapy option for patients with CRSwNP.

Regulatory & Development Status

Depemokimab does not currently have Marketing Authorisation in the EU/UK for any indication.

Depemokimab is in phase III clinical development for the treatment of:[12]

- Hypereosinophilic syndrome
- Severe eosinophilic asthma
- Eosinophilic granulomatosis with polyangiitis

Patient Group

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Disease Area and Clinical Need

Rhinosinusitis is defined as inflammation of the nose and paranasal sinuses. Nasal polyps are abnormal inflammatory and oedematous tissue growths that grow inside the nasal passages and sinuses.[13] Chronic rhinosinusitis (CRS) is a chronic inflammatory condition of the upper airways, often associated with the formation of nasal polyps (CRSwNP). CRSwNP is an important clinical entity diagnosed by the presence of both subjective and objective evidence of chronic sinonasal inflammation.[14,15] Symptoms of CRSwNP include anterior or posterior rhinorrhea, nasal congestion, hyposmia and/or facial pressure or pain that last for greater than 12 weeks duration.[15] CRSwNP is frequently associated with asthma and allergic rhinitis but the cellular and molecular mechanisms that contribute to the clinical symptoms are not fully understood.[15] The exact cause of CRSwNP is unknown. Symptoms can be triggered by anything that irritates the nasal passages. The irritation causes the nasal polyps to swell, leading to nasal congestion. Common triggers include tobacco smoke, chemicals and other irritants, allergens (pollen, mould, or dust), strong smells, and use of aspirin or other non-steroidal anti-inflammatory drugs.[16]

Chronic rhinosinusitis is a highly prevalent condition affecting 10% of the UK adult population.[13] In England 2018, prevalence of CRSwNP was 476 cases per 100,000 persons.[17] In England (2022-23), there were 4,850 finished consultant episodes (FCEs) and 4,351 admissions for chronic sinusitis, unspecified (ICD-10 code J32.9), which resulted in 1,442 day cases and 3,031 FCE bed days. In England (2022-23), there were 2,463 finished consultant episodes (FCEs) and 2,440 admissions for nasal polyp, unspecified (ICD-10 code J33.9), which resulted in 1,968 day cases and 459 FCE bed days.[18]

Recommended Treatment Options

There are no National Institute for Health and Care Excellence (NICE) recommended treatments for CRSwNP.
Current treatment options focus on controlling tissue inflammation and include nasal saline irrigation, topical corticosteroids, antibiotics, short-course oral corticosteroids and sinus surgery.[19] Betamethasone nasal drop is recommended for the treatment of smaller polyps and medical polypectomy (oral prednisolone with betamethasone nasal drops) for larger polyps. Maintenance therapy with fluticasone (drops, spray) or mometasone (spray) is also recommended.[20]

Clinical Trial Information

Trial	**ANCHOR-2**, NCT05281523, EudraCT 2021-005055-36; A Randomised, Double-blind, Parallel Group Phase III Study to Assess the Efficacy and Safety of 100 mg SC Depemokimab in Patients With Chronic Rhinosinusitis With Nasal Polyps (CRSwNP) - ANCHOR-2 (depemokimAb iN CHrOnic Rhinosinusitis) **Phase III** - Recruiting **Locations:** 5 EU countries, USA, and other countries **Primary completion date:** November 2024
Trial Design	Randomised, parallel assignment, double-blind, placebo-controlled
Population	N=250 (planned); subjects with chronic rhinosinusitis with nasal polyps, aged 18 years and older
Intervention(s)	Depemokimab administered subcutaneously
Comparator(s)	Matched placebo
Outcome(s)	Primary outcomes:

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	• Change from Baseline in total endoscopic nasal polyps score at Week 52 (scores on a scale) [Time frame: Baseline and at Week 52] • Change from Baseline in mean nasal obstruction score using verbal response scale from Weeks 49 to 52 (scores on a scale) [Time frame: Baseline and from Week 49 to Week 52] See trial record for full list of all outcomes
Results (efficacy)	-
Results (safety)	-

Trial	**ANCHOR-1, NCT05274750;** A Randomised, Double-blind, Parallel Group Phase III Study to Assess the Efficacy and Safety of 100 mg SC Depemokimab in Patients With Chronic Rhinosinusitis With Nasal Polyps (CRSwNP) - ANCHOR-1 (depemokimAb iN CHrOnic Rhinosinusitis) **Phase III** - Active, not recruiting **Locations:** 5 EU countries, UK, USA, Canada, and other countries **Primary completion date:** August 2024
Trial Design	Randomised, parallel assignment, double-blind, placebo-controlled
Population	N=276 (actual); subjects with CRSwNP, aged 18 years and older
Intervention(s)	Depemokimab administered subcutaneously
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: • Change from Baseline in total endoscopic nasal polyps score at Week 52 (Scores on a scale) [Time frame: Baseline and at Week 52] • Change from Baseline in mean nasal obstruction score using verbal response scale (VRS) from Weeks 49 to 52 (Scores on a scale) [Time frame: Baseline and from Week 49 to Week 52] See trial record for full list of all outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of depemokimab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Tezepelumab for treating severe chronic rhinosinusitis with nasal polyps (GID-TA11429). Expected date of issue to be confirmed.

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NHS England (Policy/Commissioning) Guidance
No relevant guidance identified.
Other Guidance
• British Rhinological Society (BRS). BRC Consensus Guidance on the use of biological therapies for chronic rhinosinusitis with nasal polyps. 2021.[21] • European Forum for Research and Education in Allergy and Airway Diseases (EUFOREA). EUFOREA Consensus on biologics for CRSwNP with or without asthma. 2019.[22]

Additional Information

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