

Health Technology Briefing

July 2024

Eptinezumab for cluster headache

Company/Developer

Lundbeck Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID:30974

NICE ID: Not available

UKPS ID: 669027

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Eptinezumab is in clinical development for cluster headache. Cluster headaches are excruciating attacks of pain in one side of the head, often felt around the eye. The most common presentation the majority of patients with cluster headache have is the episodic form, in which attacks appear daily lasting for weeks or months, followed by a complete remission for months or years. Cluster headache comes on very quickly, often without warning. Some other symptoms include red or watering eye, drooping, or swelling of the eyelid, a smaller pupil, sweaty face and blocked or runny nose. Attacks usually last between 15 minutes and three hours. Some people may have multiple attacks a day, up to eight times in some cases. Prevention of episodic cluster headache has been challenged by the limited number of available medicinal products and the side effects associated with currently available ones.

Eptinezumab is a medicinal product administered intravenously. It is a monoclonal antibody (a type of protein) that binds to a substance in the body called calcitonin gene-related peptide (CGRP). CGRP is a type of protein which contributes to the development of cluster headache. Eptinezumab attaches to CGRP and prevents it from binding to its target on the body's cells, thereby helping to prevent cluster headaches from occurring. If licensed, eptinezumab will offer an additional treatment option for patients with cluster headache.

Proposed Indication

For cluster headache.¹

Technology

Description

Eptinezumab (Vyepiti) is a recombinant humanised immunoglobulin G1 (IgG1) antibody that binds to α - and β - forms of human calcitonin gene-related peptide (CGRP) ligand with low picomolar affinity (4 and 3 pM Kd, respectively).² CGRP is a signalling molecule in the pathophysiology of migraine and cluster headache.³ CGRP induces potent vasodilatory effects on cerebral arteries, modulate the sensitivity of nociceptive trigeminal neurons and subsequently trigger migraine and cluster headache attacks.⁴ Eptinezumab prevents the activation of the CGRP receptors and hence the downstream cascade of physiological events linked to initiation of migraine attacks. Eptinezumab inhibits α and β - CGRP-mediated neurogenic inflammation and vasodilation.²

Eptinezumab is in clinical development for cluster headache. In the phase III clinical trial (ALLEVIATE, NCT04688775), patients receive 400mg eptinezumab intravenous (IV) infusion.^{1,5} In another phase III trial (CHRONICLE, NCT05064397), patients receive four IV infusions with eptinezumab (400mg) at baseline and at the end of Weeks 12, 24, and 36.^{6,7}

Key Innovation

Several medicines are effective in reducing the frequency of attacks in patients with episodic or chronic cluster headache. Current treatment options may require regular multiple dosing and/or periodic monitoring due to adverse effects on the body, such as arrhythmia and impact on kidney function.^{8,9}

In contrast to other CGRP antibodies, eptinezumab is in late-phase development as an IV formulation designed to produce a more immediate therapeutic response and is administered quarterly.^{1,10} Eptinezumab has also been proven to significantly reduce migraine frequency when used for the preventive treatment of migraine in adults with episodic migraine and is well tolerated with acceptable safety profile.¹¹

If licensed, eptinezumab will offer an additional treatment option for adult patients with cluster headaches.

Regulatory & Development Status

In the UK, eptinezumab has Marketing Authorisation for migraine prophylaxis in adults who have at least 4 migraine days per month.²

Eptinezumab is also in phase III clinical development for chronic or episodic migraine (paediatric, adolescent and adult patients), and migraine and medication overuse headache.¹²

Patient Group

Disease Area and Clinical Need

Cluster headache is a trigeminal autonomic cephalalgia characterised by extremely painful, strictly unilateral, short-lasting headache attacks accompanied by ipsilateral autonomic symptoms or the sense of restlessness and agitation, or both. The severity of the disorder has major effects on the patient's quality of life and, in some cases, might lead to suicidal ideation. The attacks are accompanied by at least one autonomic symptom (e.g., eyelid oedema, or forehead and facial sweating) that occurs ipsilateral to the pain side. Attack frequency ranges between one attack every other day and eight attacks a day.⁸ Some other symptoms include a red and watering eye, a smaller pupil in one eye and a blocked or runny nostril. These attacks generally last between 15 minutes and 3 hours.¹³ In addition, the fear of pain leads to anxiety and depression in patients with cluster headache.¹⁴ 85–90% of patients with cluster headache commonly present with the episodic form, in which attacks appear as a series of daily attacks lasting for weeks or months, followed by a complete remission for months or years. Typically, patients report one or two episodes a year.⁸ Cluster headache commonly starts when people are in their 30s and 40s, and is more common in men than women.¹⁵

Cluster headache accounts for 20% of headaches which always occur on the same side of the head (side-locked headache). The pooled lifetime prevalence of cluster headache is 0.12%.¹⁶ It affects approximately 1 in 1,000 people, which equates to about 67,000 people in the UK.^{15,17} In England 2022-23, there were 1,682 finished consultant episodes (FCE) and 1,537 admissions for cluster headache syndrome (ICD-10 code G44.0), which resulted in 1,011 FCE bed days and 772 day cases.¹⁸

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends the following pharmacological treatments for acute cluster headaches:

- Subcutaneous injection of sumatriptan initially 6mg for 1 dose, followed by 6mg after at least 1 hour if required, to be taken only if headache recurs; maximum 12mg per day.^{9,19}
- Intranasal administration of sumatriptan initially 10-20mg dose to be administered into one nostril, followed by 10-20mg after at least 2 hours if required; maximum 40mg per day.^{9,19}

NICE recommends the following off-label pharmacological treatments for cluster headaches:

- Zolmitriptan intranasal spray 5mg dose to be administered as soon as possible after onset into one nostril only, followed by 5mg after at least 2 hours only if symptoms recur; maximum 10mg per day.^{9,20}
- Verapamil for preventative treatment. Alternative prophylactic drugs such as lithium or topiramate may be recommended by a specialist if verapamil is not tolerated or is contraindicated. In addition, a short-term oral corticosteroid may be used as a “transition therapy” by a specialist at the onset of treatment to achieve a rapid response while prophylactic drug doses are being up-titrated. NICE indicates that this recommendation is based on expert opinion in review articles on cluster headache.⁹

Clinical Trial Information

Trial

ALLEVIATE, [NCT04688775](#), [EudraCT- 2020-001969-37](#); Interventional, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Delayed-Start Study to Evaluate the Efficacy and Safety of Eptinezumab in Patients With Episodic Cluster Headache
Phase III – Completed
Locations: 13 EU countries, UK, USA, and other countries

	Primary completion date: October 2023
Trial Design	Randomised, parallel assignment, double-blind
Population	N=232 (actual); Subjects with episodic cluster headache or has a prior history of cluster period(s) lasting 6 weeks or longer, when untreated; aged 18 to 75 years
Intervention(s)	Eptinezumab (400mg) IV infusion
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: Change From Baseline in the Number of Weekly Attacks, Averaged Over Weeks 1-2 [Time Frame: Baseline, Weeks 1-2] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Trial	CHRONICLE , NCT05064397 , EudraCT-2020-001968-28 ; Interventional, Open-label, Fixed-dose Multiple Administration Study to Evaluate Long-term Treatment With Eptinezumab in Patients With Chronic Cluster Headache Phase III- completed Locations: 7 EU countries, UK, and USA Primary completion date: June 2023
Trial Design	Single group assignment, open label
Population	N=131 (actual); Participants with a medical history/diagnosis of chronic cluster headache; aged 18 to 75 years
Intervention(s)	Eptinezumab (400mg); 4 intravenous (IV) infusions at Baseline (Day 0) and at the end of Weeks 12, 24, and 36
Comparator(s)	-
Outcome(s)	Primary outcome measure: Number of Participants with adverse events [Time Frame: From the day of first dose of study drug (Baseline [Week 0]) up to Week 56] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Cost of eptinezumab was confidential at the time of producing this briefing.

Relevant Guidance

NICE Guidance

- NICE Clinical Guideline. Headaches in over 12s: diagnosis and management (CG150). December 2021.
- NICE Quality Standard. Headaches in over 12s (QS42). August 2013.
- NICE Interventional Procedure Guidance. Transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine (IPG552). March 2016.
- NICE Interventional Procedure Guidance. Implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache (IPG527). June 2015.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Occipital Nerve Stimulation for Adults with Intractable Chronic Migraines and Medically Refractory Chronic Cluster Headaches. D08/P/c.
- NHS England. Clinical Commissioning Policy Statement: Sphenopalatine Ganglion Stimulation for Refractory Chronic Cluster Headache (Adults). 170083P

Other Guidance

- London Clinical Oxygen Network. Advice on oxygen treatment for cluster headache in adults: Information for GPs and neurologists. 2021.²¹
- British Association for the Study of Headache (BASH). National headache management system for adults. 2019.²²
- BASH. Guidelines for all Healthcare Professionals in the diagnosis and management of migraine, tension-type headache, cluster headache, medication-overuse headache. 2010.²³

Additional Information

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