Health Technology Briefing
February 2023

Galcanezumab for preventing migraine in children

Company/Developer	Eli Lilly and Company Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 30801	NICE ID: 10663	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Galcanezumab is in clinical development for the preventative treatment of paediatric patients with episodic or chronic migraine. Migraine is one of the most common neurological conditions in the paediatric population with unique clinical characteristics that can evolve with age. These characteristics can include shorter attacks, different location of pain (bilateral in younger children), and light and sound sensitivity are best inferred by changes in behaviour. Migraine can occur with or without aura. Migraine with aura consists of visual, sensory or other central nervous system symptoms that usually develop gradually lasting for 5 to 20 minutes, and are usually followed by headache. There remains an unmet need for additional preventative treatments that have proven efficacy and safety in children.

A neuropeptide called calcitonin gene-related peptide (CGRP) is believed to play an important role in development of migraine. Elevated levels of CGRP can lead to cascade of events including vasodilation (widening of blood vessels in the brain) and pain associated in migraine attacks. Galcanezumab is a monoclonal antibody (a type of protein), designed to bind to CGRP, preventing its biological activity and thus preventing a migraine attack. If licenced, galcanezumab will provide an additional preventative treatment option for children with chronic or episodic migraines.

Proposed Indication

The preventative treatment of episodic or chronic migraine in children.[1,2]

Technology

Description

Galcanezumab (Emgality, LY2951742) is a humanised IgG4 monoclonal antibody that binds calcitonin gene-related peptide (CGRP) thus preventing its biological activity. Galcanezumab binds to CGRP with high affinity and high specificity.[1,3] Although the pathophysiology of migraine is still under evaluation, many data indicate a crucial role of CGRP. CGRP is a 37-amino acid neuropeptide and a member of the calcitonin family and it is expressed in both central and peripheral nervous systems. During a migraine attack, CGRP concentrations increase with rapid turnover of effect.[4]

Galcanezumab is currently in clinical development for the preventative treatment of episodic or chronic migraine in children. In the phase III clinical trials (REBUILD-1, NCT03432286; REBUILD-2, NCT04616326) patients are given galcanezumab administered subcutaneously (SC).[1,2]

Key Innovation

There are currently few medications licenced for the preventative treatment of migraine in children.[5] Some treatments with proven efficacy in adults, such as valproate for episodic migraine prevention and onabotulinumtoxinA for chronic migraine, have not shown the same efficacy in children and adolescents, and a higher paediatric placebo response rate is observed.[6] In recent years, new acute and preventative treatments for migraine have been introduced, considerably increasing the possibility to achieve clinically significant responses to treatments, even in severe patients with chronic migraine and drug resistance. However, up until now, these promising results have been limited to adults.[7] There is therefore a need for additional preventative treatment options with proven efficacy and safety in paediatric populations.

If licenced, galcanezumab will provide an additional preventative treatment option for children with chronic or episodic migraines.

Regulatory & Development Status

Galcanezumab has Marketing Authorisation in the EU/UK for the prophylaxis of migraine in adults who have at least 4 migraine days per month.[8]

Galcanezumab is also in phase II clinical development for vestibular migraine and cluster headaches.[9]

Patient Group

Disease Area and Clinical Need

Migraine is the most common acute and recurrent headache syndrome in children. Migraine in children tend to be reported of shorter duration, with a lower limit of 2 hours, are more likely to be bilateral before adolescence, and light and sound sensitivity are best inferred by changes in behaviour.[10] Migraine can occur with or without aura. Migraine with aura consists of recurrent attacks, lasting for 5 to 20 minutes, of unilateral fully-reversible visual, sensory or other central nervous system symptoms that usually develop gradually and are usually followed by headache and associated migraine symptoms.[10,11] Migraines without aura are the most common type, where the migraine happens without warning signs such as seeing flashing lights.[12] This type of migraine manifests in attacks lasting 2-72 hours. Typical characteristics of the headache are unilateral location but bilateral in younger children, lack of physical activity and association

with nausea and vomiting.[10] The exact cause of migraines is unknown, but they are thought to be the result of abnormal brain activity temporarily affecting nerve signals, chemicals and blood vessels in the brain. It is not clear what causes this change in brain activity, but it is possible that a patient's genes make them more likely to experience migraines as a result of a specific trigger. There are many possible migraine triggers including: hormonal changes; emotional triggers such as stress or anxiety; physical triggers such as tiredness and shoulder tension; dietary triggers; and environmental triggers such as bright lights and certain medicines.[13]

Migraine occurs in 3% to 10% of children, and currently affects 50/1000 school-age children in the UK.[14] This is around 1.2 million children in the UK and has implications for younger sufferers in terms of loss of learning, impact on exam performance, and the knock-on from this with potential future jobs.[15]

Recommended Treatment Options
Expert sources advise that prophylactic treatment can be considered when migraine attacks are frequent and severe, and interfere with school and social life. However, there is limited evidence of benefit for prophylactic treatment in children and specialist advice should be sought. Propranolol hydrochloride and topiramate (unlicensed use) can be used for migraine prophylaxis. Pizotifen is licensed for prophylaxis of migraine, but its efficacy in children has not been clearly established.[5]

Clinical Trial Information

Trial	**REBUILD-1**, NCT03432286, 2017-004351-23; A Randomized, Double-Blind, Placebo-Controlled Study of Galcanezumab in Patients 6 to 17 Years of Age With Episodic Migraine **Phase III** – Recruiting **Locations:** 5 EU countries, USA and other countries **Study completion date:** January 2024
Trial Design	Randomised, parallel assignment, double-blind, placebo-controlled
Population	N=325 (estimated); have a diagnosis of migraine with or without aura as defined by the IHS ICHD-3 guidelines with a history of migraine headaches of at least 6 months prior to screening; aged 6 years to 17 years
Intervention(s)	Galcanezumab (SC)
Comparator(s)	Matched placebo
Outcome(s)	**Primary outcome measure:** Change from baseline in the number of monthly migraine headache days [Time frame: baseline, 3 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information

Trial	**REBUILD-2,** NCT04616326, 2018-004622-28; A Randomized, Double-Blind, Placebo-Controlled Study of Galcanezumab in Adolescent Patients 12 to 17 Years of Age With Chronic Migraine **Phase III** – Recruiting **Locations:** 6 EU countries, USA and other countries **Primary completion date:** February 2023
Trial Design	Randomised, parallel assignment, double-blind, placebo-controlled
Population	N=300 (estimated); have a diagnosis of chronic migraine as defined by the IHS ICHD-3 guidelines, that is, a headache occurring on 15 or more days per month for at least the last 3 months, which has the features of migraine headache on at least 8 days per month; aged 12 years to 17 years
Intervention(s)	Galcanezumab (SC)
Comparator(s)	Matched placebo
Outcome(s)	**Primary outcome measure:** Change from baseline in the number of monthly migraine headache days [Time frame: baseline, 3 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Galcanezumab is already marketed in the UK; a 120mg/1ml solution for injection pre-filled pen costs £450.00.[16]

Relevant Guidance

NICE Guidance

- NICE clinical guideline. Headaches in over 12s: diagnosis and management (CG150). September 2012. Last updated: December 2021.

NHS England (Policy/Commissioning) Guidance

No relevant guidance identified

Other Guidance

- Brighton and Sussex University Hospitals NHS Trust. Paediatric Clinical Practice Guideline: Management of acute headache. 2022.[17]

Additional Information

Eli Lilly and Company Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in

development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

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