Health Technology Briefing
October 2024

Lebrikizumab for treating atopic dermatitis in children aged 6 Months to <18 Years

Company/Developer	Almirall Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 35992	NICE ID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Lebrikizumab is being developed for paediatric patients with atopic dermatitis (AD). AD is a common, long-term (chronic) inflammatory skin condition that results in patches of redness, itchiness, and scaling of the skin. In moderate to-severe cases of AD, the patches cover a large area of the skin and can be associated with intense itch. The quality of life for children with AD has been shown to be reduced due to sleep disturbances, anxiety, depression and low self-esteem. Flare-up of the disease, where the symptoms are more severe can be triggered by factors such as stress, allergies, skin irritants and heat. Current treatment regimens including the frequent application of topical creams, can be complex, uncomfortable, and stressful for children with AD and their caregivers. There is a need for additional treatment options for children and adolescents with AD to reduce the severity of symptoms associated with the disease and improve their quality of life.

Lebrikizumab is a People with AD produce high levels of a protein called interleukin 13 (IL-13), which can cause inflammation of the skin leading to the symptoms of the disease such as itching, dryness and redness. The active substance in lebrikizumab, is a monoclonal antibody (a type of protein) designed to neutralise IL-13. By doing so, lebrikizumab prevents IL-13 from causing skin inflammation and relieves disease symptoms. If licensed, lebrikizumab will offer an additional treatment option for paediatric patients with AD.

Proposed Indication

Treatment of moderate – to – severe Atopic Dermatitis in participants 6 months to <18 years.[1]

Technology

Description

Lebrikizumab (Ebglyss) is an immunoglobulin (IgG4) monoclonal antibody that binds with high affinity (<10 pM) to interleukin (IL)-13 and selectively inhibits IL-13 signalling through the IL-4 receptor alpha (IL-4Rα)/ IL-13 receptor alpha 1 (IL-13Rα 1) heterodimer, thereby inhibiting the downstream effects of IL-13. Inhibition of IL-13 signalling is expected to be of benefit in diseases in which IL-13 is a key contributor to the disease pathogenesis. Lebrikizumab does not prevent the binding of IL-13 to the IL-13 receptor alpha 2 (IL-13Rα 2 or decoy receptor), which allows the internalisation of IL-13 into the cell.[2]

Lebrikizumab is currently in phase III clinical development (NCT05559359, ADorable-1; NCT05735483, ADorable-2) for the treatment of moderate-to-severe AD. The lebrikizumab is administered subcutaneously using weight-based dosing and is being tested against a matched placebo.[1,3]

Key Innovation

AD is a heterogenous disease with signs and symptoms varying greatly between patients, underscoring the need for additional treatment options with different mechanisms of action.[4] Efficacy of topical therapies can be limited, and their frequent use is cumbersome and carries the risk for side effects. Standard systemic treatments used for moderate-to-severe disease also carry significant risks.[5] IL-13 cytokines and inflammatory pathways have been identified as important for the pathophysiology of AD. Lebrikizumab binds specifically to IL-13 and it has been theorised that targeting the most central pathologic mediators of AD, such as IL-13, can maximize efficacy and limit toxicity for patients.[5,6] Evidence supports the hypothesis that selective antagonism of IL-13 is sufficient to control AD, providing an improvement in the patient's quality of life. If approved, lebrikizumab would be an additional therapy that specifically targets IL-13, part of a new phase in the management of AD.[7]

Regulatory & Development Status

Lebrikizumab currently has Marketing Authorisation in the EU/UK for the treatment of moderate-to-severe AD in adults and adolescents 12 years of age and older with a body weight of at least 40 kg who are candidates for systemic therapy.[8]

Lebrikizumab is currently in phase III/II clinical development for the following indications:[9]

- Asthma
- Chronic obstructive pulmonary disease
- Idiopathic pulmonary fibrosis
- Perennial allergic rhinitis
- Chronic rhinosinusitis and nasal polyps

Patient Group

Disease Area and Clinical Need

Atopic dermatitis (AD), also known as atopic eczema, is one of the most common forms of eczema, a condition that causes the skin to become itchy, dry and cracked. AD is the most common type of eczema

in children, often developing before their first birthday, but it may also develop for the first time in adults. It is usually a long-term (chronic) condition, although it can improve significantly, or even clear completely, in some children as they get older.[10] Approximately 18% of all cases of childhood AD in the UK are moderate. The odds of having severe AD are twice as great for children with AD onset during the first year of life. Moderate-to-severe AD can not only impact a child's physical development but can also have psychological sequelae, placing a substantial burden on parents and carers.[11] AD can occur all over the body, but is most common on the insides of the elbows or backs of the knees, and the face and scalp in children. The severity of AD can vary a lot from person to person.[12] Severity of AD can be assessed objectively in a standardised manner using the SCORing AD (SCORAD) index. Higher numbers indicate greater severity, and the scale ranges from 0 to 103.[11] People with mild AD may only have small areas of dry skin that are occasionally itchy. In more severe cases, AD can cause widespread inflamed skin all over the body and constant itching.[12] AD is likely to be caused by a combination of things. People with AD often have very dry skin because their skin is unable to retain much moisture. This dryness may make the skin more likely to react to certain triggers, causing it to become itchy and sore. Common triggers include: irritants (soaps, detergents, shampoos etc), environmental factors or allergens (cold or dry weather, dampness, dust etc), food allergies (especially in young children with severe eczema),[13] certain materials worn next to skin, and skin infections.[14]

The United Kingdom (UK) has a high prevalence of AD, affecting 11–20% of children, approximately 2% of all cases of childhood AD in the UK are severe.[11] In England in 2022-23 there were 1,231 admissions and 1,366 finished consultant episode (ICD10 code L20) for atopic dermatitis, which resulted in 743 day cases and 1,198 FCE bed days. [15]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends a stepped treatment options depending on severity of AD in children under 12s. For moderate AD: emollients, moderate-potency topical corticosteroids, topical calcineurin inhibitors and bandages. For severe AD: the same recommendations as well as phototherapy and systemic therapy.[16]

Clinical Trial Information

Trial	**ADorable-2,** NCT05735483, EUCTIS2022-501478-21-00, A Phase 3, Multicenter, Long-Term Extension Study to Assess the Safety and Efficacy of Lebrikizumab in Participants 6 Months to <18 Years of Age With Moderate-to-Severe Atopic Dermatitis. **Phase III:** Recruiting **Locations:** US, Canada, Australia and 5 EU countries. **Primary completion date:** June 2026
Trial Design	Single group assessment, open label.
Population	N=250 (estimated). Received treatment in Study KGBI (ADorable-1) and have adequately completed the study treatments and last visit of study KGBI. ADorable-1 inclusion criteria: patients aged 6 months - <18 years moderate to severe diagnosed with AD prior to screening.
Intervention(s)	Lebrikizumab (subcutaneously administered)
Comparator(s)	Placebo (subcutaneously administered)

Outcome(s)	Primary outcome measures: • Percentage of participants discontinued from study treatment due to adverse events (AEs) [Time frame: Baseline through week 52] See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	**ADorable-1,** NCT05559359, A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Assess the Efficacy, Safety and Pharmacokinetics of Lebrikizumab Compared to Placebo in Participants 6 Months to <18 Years of Age With Moderate-to-Severe Atopic Dermatitis **Phase III:** Recruiting **Locations:** US, Canada, Australia and 5 EU countries **Primary completion date:** May 2025
Trial Design	Randomised, Parallel assignment, double masking.
Population	N=300 (estimated). Patients aged 6 months to 17 years with a diagnosis of AD.
Intervention(s)	Lebrikizumab (subcutaneously administered)
Comparator(s)	Placebo (subcutaneously administered)
Outcome(s)	Primary outcome measures: • Percentage of participants with an Investigator Global Assessment (IGA) score 0 or 1 and a reduction ≥2 points from baseline [Time frame: baseline to week 16] • Percentage of participants achieving Eczema Area and Severity Index-75 (EASI-75) ≥75% reduction from baseline in EASI Score [Time frame: baseline to week 16] See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of lebrikizumab is not yet known.[17]

Relevant Guidance

NICE Guidance

- NICE clinical guideline. Atopic eczema in under 12s: diagnosis and management. [C657]. Published December 2007. Updated June 2023.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Specialised Dermatology Services (All Ages). A12/S/a/.

Other Guidance

- Journal of the American Academy of Dermatology. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. 2024.[18]
- American Academy of Allergy, Asthma and Immunology/American college of Allergy, Asthma and Immunology Joint task force. Atopic dermatitis (eczema) guidelines. 2023.[19]
- Journal of the European Academy of Dermatology and Venereology. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. 2018.[20]
- Journal of the European Academy of Dermatology and Venereology. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II. 2018.[21]

Additional Information

Almirall 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

1 ClinicalTrials.gov. *A Phase 3, Multicenter, Long-Term Extension Study to Assess the Safety and Efficacy of Lebrikizumab in Participants 6 Months to <18 Years of Age With Moderate-to-Severe Atopic Dermatitis*. *Trial ID: NCT05735483*. 2023. Status: Recruiting. Available from: https://clinicaltrials.gov/study/NCT05735483 [Accessed 21 August 2024].

2 Electronic Medicines Compendium (EMC). *Ebglyss 250 mg solution for injection in pre-filled pen*. 2024. Available from: https://www.medicines.org.uk/emc/product/15366/smpc [Accessed 21 August 2024].

3 ClinicalTrials.gov. *A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Assess the Efficacy, Safety and Pharmacokinetics of Lebrikizumab Compared to Placebo in Participants 6 Months to <18 Years of Age With Moderate-to-Severe Atopic Dermatitis*. *Trial ID: NCT05559359*. 2022. Status: Recruiting. Available from: https://clinicaltrials.gov/study/NCT05559359 [Accessed 21 August 2024].

4 Eli Lilly and Company. *Lilly's lebrikizumab significantly improved skin clearance and itch in people with moderate-to-severe atopic dermatitis in two Phase 3 trials*. 2021. Available from: https://investor.lilly.com/news-releases/news-release-details/lillys-lebrikizumab-significantly-improved-skin-clearance-and [Accessed 22 October 2024].

5 Simpson EL, Flohr C, Eichenfield LF, Bieber T, Sofen H, Taïeb A, et al. Efficacy and safety of lebrikizumab (an anti-IL-13 monoclonal antibody) in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical corticosteroids: A randomized, placebo-controlled phase II trial (TREBLE). *Journal of the American Academy of Dermatology*.

2018;78(5):863-71.e11. https://www.sciencedirect.com/science/article/pii/S0190962218301026.

6 Hamann CR, Thyssen JP. Monoclonal antibodies against interleukin 13 and interleukin 31RA in development for atopic dermatitis. *Journal of the American Academy of Dermatology*. 2018;78(3, Supplement 1):S37-S42. https://www.sciencedirect.com/science/article/pii/S0190962217328190.

7 Gonçalves F, Freitas E, Torres T. Selective IL-13 inhibitors for the treatment of atopic dermatitis. *Drugs in Context* 2021;10. https://www.drugsincontext.com/selective-il-13-inhibitors-for-the-treatment-of-atopic-dermatitis/.

8 Electronic Medicines Compendium (EMC). *Ebglyss 250 mg solution for injection in pre-filled pen*. 2023. Available from: https://www.medicines.org.uk/emc/product/15366/smpc [Accessed 09 July 2024].

9 ClinicalTrials.gov. *Search results - Lebrikizumab*. 2014. Available from: https://clinicaltrials.gov/search?intr=Lebrikizumab%20&aggFilters=phase:2%203&page=1 [Accessed 09 July 2024].

10 National Health Service (NHS). *Overview- Atopic eczema*. 2023. Available from: https://www.nhs.uk/conditions/atopic-eczema/ [Accessed 09 July 2024].

11 Cork MJ, Danby SG, Ogg GS. Atopic dermatitis epidemiology and unmet need in the United Kingdom. *Journal of Dermatological Treatment*. 2020;31(8):801-9. Available from: https://doi.org/10.1080/09546634.2019.1655137.

12 National Health Service (NHS). *Symptoms- Atopic eczema*. 2023. Available from: https://www.nhs.uk/conditions/atopic-eczema/symptoms/ [Accessed 09 July 2024].

13 National Health Service (NHS). *Atopic eczema*. 2024. Available from: https://www.nhs.uk/conditions/atopic-eczema/ [Accessed 12 September 2024].

14 National Health Service (NHS). *Causes -Atopic eczema*. 2023. Available from: https://www.nhs.uk/conditions/atopic-eczema/causes/ [Accessed 09 July 2024].

15 National Health Service. *Hospital Admitted Patient Care Activity, 2022-23*. 2023. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2022-23.

16 National Insitute for Health and Care Excellence (NICE). *Atopic eczema in under 12s: diagnosis and management* (*CG57)*. Available from: https://www.nice.org.uk/guidance/cg57/chapter/Recommendations#treatment [Accessed 21 August 2024].

17 British National Formulary (BNF). *Lebrikizumab - Medicinal forms*. 2024. Available from: https://bnf.nice.org.uk/drugs/lebrikizumab/medicinal-forms/ [Accessed 09 July 2024].

18 Davis DMR, Drucker AM, Alikhan A, Bercovitch L, Cohen DE, Darr JM, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *Journal of the American Academy of Dermatology*. 2024;90(2):e43-e56. https://doi.org/10.1016/j.jaad.2023.08.102.

19 Chu DK, Schneider L, Asiniwasis RN, Boguniewicz M, De Benedetto A, Ellison K, et al. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE and Institute of Medicine based recommendations. *Annals of Allergy, Asthma & Immunology*. 2024;132(3):274-312. https://doi.org/10.1016/j.anai.2023.11.009.

20 Wollenberg A, Barbarot S, Bieber T, Christen-Zaech S, Deleuran M, Fink-Wagner A, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *Journal of the European Academy of Dermatology and Venereology*. 2018;32(5):657-82. https://doi.org/10.1111/jdv.14891.

21 Wollenberg A, Barbarot S, Bieber T, Christen-Zaech S, Deleuran M, Fink-Wagner A, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in

adults and children: part II. *Journal of the European Academy of Dermatology and Venereology*. 2018;32(6):850-78. https://onlinelibrary.wiley.com/doi/abs/10.1111/jdv.14888.

NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.