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HEALTH TECHNOLOGY BRIEFING
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Tralokinumab for adolescents with moderate to severe atopic dermatitis

NIHRIO ID	27152	**NICE ID**	10265
Developer/Company	Leo Pharma UK	**UKPS ID**	653217

Licensing and market availability plans	Currently in phase III clinical trials

SUMMARY

Tralokinumab is proposed for the treatment of moderate to severe atopic dermatitis (AD) in adolescent patients (12-17 years old). AD is a chronic inflammatory skin disease that affects both children and adults and is characterised by redness, itchiness, and scaling of the skin. Some people only have small patches of dry skin, but others may experience widespread red, inflamed skin all over the body. Patients with moderate to severe AD could experience sleep disturbances, anxiety, depression, and poor quality of life. Currently, the management of AD involves the removal or treatment of trigger factors that contribute to the development of the disease.

Tralokinumab is a human monoclonal antibody that binds and neutralises the effect of the protein, interleukin 13 (IL-13), which plays a key role in triggering immune system responses in patients leading to AD. Tralokinumab is administered subcutaneously and is currently licenced for the treatment of adults. Evidence from clinical trials suggests an improvement in disease symptoms. If licensed, tralokinumab will offer an additional treatment option for adolescents with moderate to severe AD.

PROPOSED INDICATION

Treatment of moderate-to-severe atopic dermatitis (AD) in adolescents.[1]

TECHNOLOGY

DESCRIPTION

Tralokinumab is a first-in-class fully human, immunoglobulin (Ig) G4 monoclonal antibody that works by specifically blocking the effects of the Type 2 cytokine interleukin-13 (IL-13). Tralokinumab specifically binds to circulating IL-13, thereby preventing interaction with the IL-13 receptor.[2] IL-13 is a crucial driver of the inflammation that plays a significant role in atopic dermatitis.[3]

INNOVATION AND/OR ADVANTAGES

There is an unmet clinical need for safe and efficacious long-term therapy for the management of moderate-severe AD, for whom management with topical corticosteroids is not effective.[3,4]

Evidence from clinical trials suggests that combining tralokinumab treatment with or without topical corticosteroids could result in improvements in patients whose symptoms cannot be effectively controlled by topical corticosteroids alone.[3] Topical corticosteroids are widely used in AD treatments; however, they are associated with multiple systematic and topical side effects, precluding long-term use on a large body surface area.[3,4]

In addition, tralokinumab has been investigated in phase III clinical trials in adults with moderate-to-severe AD (ECZTRA-1, ECZTRA-2 and ECZTRA-3). Tralokinumab met all primary and secondary endpoints and the overall adverse event rate was comparable between tralokinumab and placebo.[5] Therefore, agents such as tralokinumab could reduce the need for high-dose topical corticosteroids whilst reducing symptom severity.[3]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

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

PATIENT GROUP

DISEASE BACKGROUND

Atopic dermatitis, also known as eczema or atopic eczema, is a chronic inflammatory skin disease characterised by erythema, pruritus, and scaling of skin that affects both children and adults. AD has a complex and heterogeneous aetiology, characterised histologically by skin infiltration of inflammatory cells, predominantly lymphocytes, eosinophils, and mast cells [6]

Although the pathogenesis and aetiology of AD remain to be completely understood, this multifactorial disease likely results from complex crosstalk between genetic and environmental factors.[7,8] The symptoms of AD can have certain triggers, such as soaps, detergents, stress and the weather.[9] An exaggerated response from type 2 helper T-cells (Th2); disruption of the epidermal barrier functions; high level of serum Immunoglobulin E; decreased production of antimicrobial peptides (AMPs) are the key findings in AD. Some people only have

small patches of dry skin, but others may experience widespread red, inflamed skin all over the body. Although atopic dermatitis can affect any part of the body, it most often affects the hands, insides of the elbows, backs of the knees and the face and scalp in children. [7,8]

The appearance and location of AD changes with age. In infants it mainly affects the face and limb extensor surfaces. In adolescents and adults, it is most commonly localised and found on the flexural surfaces of the body, anterior and lateral neck, eyelids, forehead, scalp, face, wrists, dorsa of the feet, and hands.[10]

For patients with moderate to severe atopic dermatitis, skin lesions encompassing large surface areas are often associated with severe itching. These lesions can cause sleep disturbances and, in turn, symptoms of anxiety, depression, and poor quality of life.[11]

It has been reported that the quality of life of children with AD is often impaired, particularly in respect to clothing, holidays, staying with friends, owning pets, swimming or the ability to play or do sports. The impairment of quality of life caused by childhood AD has been shown to be greater than or equal to other common childhood diseases such as asthma and diabetes, emphasising the importance of eczema as a major chronic childhood disease. Restriction of normal family life, difficulties with complicated treatment regimens and increased work in caring for a child with AD lead to parental exhaustion and feelings of hopelessness, guilt, anger and depression. The hidden costs involved in AD management can be significant and have particular impact on lower income families.[12]

CLINICAL NEED AND BURDEN OF DISEASE

Although AD presents most frequently in childhood, it can present at any age.[13,14] Prevalence estimates vary due to the different populations examined; it is indicated that AD affects 1 in 5 children in the UK.[15] A 2019 publication suggests that AD affects about 11-20% of children and 5-10% of adults in the UK. Prevalence of AD decreases with age, with 30% of 4-year-olds, 11–20% of school-aged children, and 5–10% of adults diagnosed with AD.[16] AD affects both males and females equally.[17]

According to the 2018-19 Hospital Episodes Statistics data, for primary diagnosis, collectively there were 1,212 finished consultant episodes (FCE), 1,092 hospital admissions which resulted in 542 day cases and 1,132 FCE bed days for other atopic dermatitis and atopic dermatitis unspecified (ICD-10 codes: L20.8 and L20.9) in England.[18]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

Treatment of AD focuses on the alleviation of symptoms and limiting exposure to contributory factors that may trigger the development of the disease or worsen a flare. In addition, patients can use different therapies to ease symptoms.[19] There is no cure, but many children find their symptoms naturally improve as they get older. [20]

For the treatment of AD, NICE recommends a stepped approach. Treatment can be stepped up or down according to the severity of the condition and includes a range of therapies such as emollients, bandages, phototherapy topical and oral corticosteroids.[19]

CURRENT TREATMENT OPTIONS

The main treatments for atopic eczema include:[20]

- Emollients (moisturisers)
- Topical corticosteroids (glucocorticoids)
- Topical pimecrolimus or tacrolimus for eczema
- Antihistamines

In addition, for moderate-to-severe AD, the following treatment options have been recommended: [19]

- Potent topical corticosteroids
- Topical calcineurin inhibitors
- Oral corticosteroids
- Dupilumab[21]

PLACE OF TECHNOLOGY

If licensed, tralokinumab will offer an additional treatment option for adolescent patients who have moderate to severe AD.

CLINICAL TRIAL SUMMARY INFORMATION

Trial	**ECZTRA 6;** NCT03526861; EudaratCT 2017-005143-33; A Randomised, Double-blind, Placebo-controlled, Parallel-group, Multi-centre Trial to Evaluate the Efficacy, Safety, and Tolerability of Tralokinumab Monotherapy in Adolescent Subjects With Moderate-to-severe Atopic Dermatitis (AD) Who Are Candidates for Systemic Therapy; **Phase III** Locations: Europe (including UK), US, Canada and others
Trial design	Randomised, double-blind, placebo-controlled, parallel-group, multi-centre
Population	• Population N=294 (planned) • Diagnosis of moderate to severe atopic dermatitis for at least 1 year • History of topical corticosteroids and/or topical calcineurin inhibitor treatment failure (due to inadequate response or intolerance) or subjects whom these topical AD treatments are medically inadvisable • Adolescents (12-17 years old)
Intervention(s)	• Initial dose tralokinumab + maintenance dose tralokinumab • Placebo + maintenance tralokinumab • Placebo + placebo • Initial dose tralokinumab + maintenance dose tralokinumab + topical corticosteroids
Comparator(s)	• Matched placebo
Outcome(s)	• Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) at Week 16 • At least 75% reduction in Eczema Area and Severity Index (EASI75) at Week 16 See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

ESTIMATED COST

The cost of tralokinumab is not yet known.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE Technology Appraisal Guidance. Dupilumab for treating moderate to severe atopic dermatitis (TA534). August 2018.
- NICE technology Appraisal Guidance. Tacrolimus and pimecrolimus for atopic eczema (TA82). August 2004.
- NICE Technology Appraisal Guidance. Frequency of application of topical corticosteroids for atopic eczema (TA81). August 2004.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Specialised Allergy Services (All ages). B09/S/b.
- NHS England. 2013/14 NHS Standard Contract for Specialised Dermatology Services (All ages). A12/S/a.

OTHER GUIDANCE

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- Scottish Intercollegiate Guidelines Network (SIGN). Management of atopic eczema in primary care: A national clinical guideline (SIGN 125). March 2011.[26]

ADDITIONAL INFORMATION

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