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Newcastle University

Health Technology Briefing
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Baricitinib for treating atopic dermatitis in children and adolescents

Company/Developer	Eli Lilly and Company Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 27427	NICE ID: 10639	UKPS ID: 661730

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Baricitinib is currently in clinical development for the treatment of moderate-to-severe atopic dermatitis (AD) in children and adolescents. 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.

Baricitinib is a type of immunosuppressant (a type of medicine that reduces the activity of the immune system). It is given to patients by oral administration and works by blocking the action of proteins known as Janus kinases (JAKs). These proteins play an important role in the processes of inflammation that contribute to the development of AD. By blocking these JAK proteins, baricitinib reduces skin inflammation and other symptoms of AD. Baricitinib is already approved for adults with moderate-to-severe AD. If licenced, baricitinib would offer an additional treatment option for children and adolescents with moderate-to-severe AD.

Proposed Indication

Children and adolescents (aged ≥2 to <18 years) with moderate-to-severe AD.[1]

Technology

Description

Baricitinib (Olumiant, LY3009104) is a selective and reversible inhibitor of Janus kinase (JAK)1 and JAK2. JAKs are enzymes that transduce intracellular signals from cell surface receptors for a number of cytokines and growth factors involved in haematopoiesis, inflammation and immune function. Within the intracellular signalling pathway, JAKs phosphorylate and activate signal transducers and activators of transcription (STATs), which activate gene expression within the cell. Baricitinib modulates these signalling pathways by partially inhibiting JAK1 and JAK2 enzymatic activity, thereby reducing the phosphorylation and activation of STATs.[2]

Baricitinib is currently in clinical development for the treatment of children and adolescents (aged 2 to 17 years) with moderate-to-severe AD. In the phase III clinical trial (BREEZE-AD-PEDS, NCT03952559), participants are given a low (1mg), mid (2mg) or high (4mg) dose of baricitinib by oral administration of a film-coated tablet.[1,3]

Key Innovation

Several studies have reported how AD burdens the quality of life for children with AD due to factors such as sleep loss, irritability, anxiety, lowered self-esteem and psychological impairment. Current treatment regimens including the frequent application of topical creams, can be complex, uncomfortable and stressful for children with AD and their caregivers. Therefore there is a need to develop additional treatment options to improve quality of life for children with AD.[4] Baricitinib offers a different mode of action to the currently available treatment options. It is the first medicine for moderate as well as severe atopic dermatitis that patients can take orally.[5]

Baricitinib has already received Marketing Authorisation by the EMA and recommendation from NICE for the treatment of adult patients with moderate-to-severe AD.[6,7] If licensed, baricitinib will offer an additional treatment option for children and adolescents aged 2 to 17 years with moderate-to-severe AD.

Regulatory & Development Status

Baricitinib currently has Marketing Authorisation in the EU/UK for the treatment of:[7]

- Moderate-to-severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs
- Moderate-to-severe AD in adult patients who are candidates for systemic therapy

Baricitinib is also currently in phase II and/or III development for other indications, including:[8]

- Aicardi Goutieres syndrome
- COVID-19
- Alopecia areata
- Juvenile idiopathic arthritis
- Pyoderma gangrenosum
- Systemic lupus erythematosus

Patient Group

Disease Area and Clinical Need

AD, also known as atopic eczema, is the most common form of eczema. It is a chronic disease that causes the skin to become itchy, red, dry and cracked. Any part of the body can be affected, however, the most commonly affected areas are: backs or fronts of the knees; outside or inside of the elbows; around the neck; hands; cheeks; and the scalp.[9] Moderate and severe cases of AD cover large areas of skin and are associated with a more intense itch than mild cases of AD.[10] Children with a family history of allergies, asthma and AD are more likely to develop AD, and mutations in skin barrier genes such as filaggrin are commonly associated with the disease.[11] People with AD usually have periods when symptoms are less noticeable, as well as periods when symptoms become more severe (flare-ups).[9] Triggers for AD flare-ups include: dry skin, irritants, stress, allergies, infection and heat/sweating.[11]

The UK has a high prevalence of AD, and whilst estimates vary, it is thought to affect 11-20% of children and 5-10% of adults.[12,13] Of the people who need treatment for AD, around 7% will have moderate-to-severe disease.[13] According to the Hospital Episode Statistics (HES) data for England in 2020-21, there were 371 finished consultant episodes (FCEs) amongst children aged 1 to 17 years where AD (ICD-10 code L20) was recorded as the primary diagnosis.[14]

Recommended Treatment Options

For managing moderate AD in children aged 12 years and under, NICE recommends a stepwise approach. Treatment can be tailored according to the severity of the disease, these treatments include: emollients, topical corticosteroids, topical calcineurin inhibitors, phototherapy and systemic therapy.[15]

Topical tacrolimus is recommended as a second-line treatment option for moderate-to-severe AD in adults and children aged 2 years and older whose disease has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.[16]

Pimecrolimus is recommended as a second-line treatment option for moderate AD on the face and neck in children aged 2 years to 16 years that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.[16]

Clinical Trial Information

Trial	**BREEZE-AD-PEDS**, NCT03952559, EudraCT 2018-000349; A phase 3, multi-centre, randomized, double-blind, placebo-controlled, parallel-group, outpatient study evaluating the pharmacokinetics, efficacy, and safety of baricitinib in paediatric patients with moderate to severe atopic dermatitis **Phase III** – Recruiting **Locations**: 7 EU countries, UK, and other countries. **Primary completion date:** July 2022
Trial Design	Randomised, double-blind, placebo-controlled, parallel-group
Population	N=465; aged 2 to 17 years; Subjects diagnosed with moderate-to-severe AD for at least 12 months (if 6 years old or older), or at least 6 months (if 2 up to 6 years

	old), with inadequate response or intolerance to existing topical medications within 6 months preceding screening
Intervention(s)	Baricitinib (oral) - low (1mg), mid (2mg) or high (4mg) dose
Comparator(s)	Placebo (oral)
Outcome(s)	Primary outcome measures: • Percentage of participants achieving investigator's global assessment (IGA) of 0 or 1 with a ≥2 point improvement [Time frame: 16 weeks] • Open label pharmacokinetics (PK): Maximum concentration (Cmax) of LY3009104 [Time frame: Baseline through 2 weeks] • Open label PK: Area under the concentration time curve (AUC) of LY3009104 [Time frame: baseline through 2 weeks] See trial record for full list of other outcome measures.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Baricitinib is already marketed in the UK; A pack of 28 x 2mg or 28 x 4mg tablets costs £805.56.[17]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Trakolimab for treating moderate to severe atopic dermatitis in people aged 12 and over (GID-TA10702). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Abrocitinib for treating moderate-to-severe atopic dermatitis in people aged 12 and over (GID-TA10764). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Tralokinumab for treating moderate to severe atopic dermatitis (GID-TA10596). Expected date of issue to be confirmed.
- NICE technology appraisal. Tacrolimus and pimecrolimus for atopic eczema (TA82). August 2004.
- NICE clinical guideline. Atopic eczema in under 12s: diagnosis and management (CG57). Last updated March 2021.
- NICE quality standard. Atopic eczema in under 12s (QS44). September 2013.

NHS England (Policy/Commissioning) Guidance

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

Other Guidance

- European Academy of Dermatology and Venereology. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis in adults and children: Part I. 2018[18]
- European Academy of Dermatology and Venereology. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis in adults and children: Part II. 2018.[19]
- Royal College of Paediatric and Child Health (RCPCH). Allergy Care Pathways for Children: Eczema. 2011.[20]

- Scottish Intercollegiate Guidelines Network (SIGN). Management of atopic eczema in primary care. 2011.[21]

Additional Information

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