Health Technology Briefing
May 2022

Baricitinib for treating juvenile idiopathic arthritis in paediatric patients

Company/Developer	Eli Lilly and Company Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 28238	NICE ID: 10662	UKPS ID: 662305

Licensing and Market Availability Plans

Currently in phase III/II clinical trials.

Summary

Baricitinib is in clinical development for children aged 1 to 17 years with juvenile idiopathic arthritis (JIA). JIA is defined as arthritis of unknown causes that manifests itself before the age of 16 years and persists for at least 6 weeks, while excluding other known conditions. JIA occurs when the body's immune system attacks its own cells and tissues. The most common symptoms include joint swelling, pain and limited range of motion. Treatment for JIA focuses on controlling symptoms; reducing the possibility of joint damage, and helping the child maintain a normal level of physical and social activity. In cases where previous treatment has not worked well enough in improving symptoms, there is need for more effective therapies.

Baricitinib is an immunosuppressant (a medicine that reduces the activity of the immune system) that works by blocking the action of enzymes known as Janus kinases. These enzymes play an important role in the processes of inflammation and damage that occur in rheumatoid arthritis. By blocking the enzymes, baricitinib reduces joint and skin inflammation and other symptoms of these diseases. Baricitinib is administered orally. If licensed, baricitinib will offer an additional treatment option for children aged 1 to 17 years.

Proposed Indication

Treatment of juvenile idiopathic arthritis (JIA) in paediatric patients aged 1 to 17 years.[1,2]

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.[3]

Baricitinib is in clinical development for the treatment of JIA in paediatric patients aged 1 to 17 years. In the phase III clinical trials (NCT04088396, NCT03773978), baricitinib is administered orally at an unspecified dose.[1,2]

Key Innovation

Three studies in around 2,500 patients with rheumatoid arthritis showed that baricitinib improves symptoms, such as tenderness and joint swelling, in patients whose previous disease-modifying drugs have not worked well enough. In these studies, baricitinib (alone or with disease-modifying medicines such as methotrexate and adalimumab) resulted in more patients achieving an improvement of 20% or more in a standard symptom score (ACR 20) than comparator medicines and placebo.[4] In addition, baricitinib being administered orally offers potential advantages over conventional or biological disease-modifying anti-rheumatic drugs (DMARDs) that are administered by subcutaneous injections or intravenous infusions, thereby avoiding the need to train patients or carers to administer the dose, or for the patients to attend a clinic for treatment.[5]

If licensed, baricitinib will offer an additional treatment option for children aged 1 to 17.

Regulatory & Development Status

Baricitinib is already licensed in the UK/EU for:[3]

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

Baricitinib is in phase III/II clinical development for several indications, some of which include:[6]

- COVID-19
- Atopic Dermatitis
- Systemic Lupus Erythematosus
- Sjogren's Syndrome
- Uveitis
- Type 1 Diabetes

Patient Group

Disease Area and Clinical Need

Juvenile idiopathic arthritis (JIA) is a group of disorders that cause arthritis (stiff, swollen, painful joints) in children.[7] It typically causes joint pain and inflammation in the hands, knees, ankles, elbows and/or wrists, but it may affect other body parts too.[8] JIA occurs when the body's immune system attacks its own cells and tissues. It is not known why this happens, but both heredity and environment seem to play a role. Several serious complications can result from JIA. Some forms can cause eye inflammation, which if left untreated, may result in cataracts, glaucoma and even blindness. Eye inflammation frequently occurs without symptoms. Another complication includes growth problems which can interfere with the child's growth and bone development.[9]

JIA has an annual incidence of 1:10,000 children and an overall prevalence in childhood of 1:1000. At any one time, there are >12,000 children with JIA.[10] In England, in 2020-2021 were 9,638 admissions (of which 8,756 were day cases) for primary diagnosis of juvenile arthritis and juvenile arthritis in diseases classified elsewhere (ICD-10 code M08), which resulted in 9,705 finished consultant episodes (FCE) and 1,420 FCE bed days.[11]

Recommended Treatment Options

Drugs can not cure arthritis, but they can control the symptoms and help to reduce the possibility of joint damage.[12] Pharmacological treatments for people with JIA include:[12,13]

- Painkillers. These drugs help to control the pain of arthritis. Common painkillers include paracetamol, codeine or combinations.
- Non-steroidal anti-inflammatory drugs (NSAIDs). These drugs help to reduce pain, stiffness and swelling. Examples include ibuprofen, piroxicam, naproxen and diclofenac
- DMARDs which dampen down inflammation and can reduce the joint damage caused by arthritis. Methotrexate is the most commonly used DMARD in JIA
- Biological therapies. These drugs are prescribed for patients that do not respond to DMARDs such as methotrexate. The main biological therapies used for JIA are abatacept, adalimumab, etanercept, infliximab, and tocilizumab
- Systemic corticosteroids. These drugs are used to control inflammation, pain and stiffness

Clinical Trial Information

Trial	**JUVE-X;** NCT03773965; EudraCT 2017-004471-31; A Phase 3 Multicentre Study to Evaluate the Long-Term Safety and Efficacy of Baricitinib in Patients From 1 Year to <18 Years of Age With Juvenile Idiopathic Arthritis (JIA) **Phase III –** Recruiting **Location(s):** 9 EU countries, UK and other countries **Primary completion date:** December 2027
Trial Design	Single group assignment, open label
Population	N=190 (estimated); children (aged 1 to 18 years) who have completed a previous study of baricitinib for the treatment of JIA
Intervention(s)	Baricitinib administered orally
Comparator(s)	No comparator

Outcome(s)	Primary outcome measures: • Number of participants with one or more serious adverse event(s) (SAEs) [time frame: baseline through week 264] • Number of participants with permanent investigational product discontinuations [time frame: baseline through week 264] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Trial	NCT04088396; EudraCT 2017-004495-60; Randomized, Double-Blind, Placebo-Controlled, Withdrawal, Safety and Efficacy Study of Oral Baricitinib in Patients From 1 Year to Less Than 18 Years Old With Systemic Juvenile Idiopathic Arthritis **Phase III** - Recruiting **Location(s):** 8 EU countries, UK and other countries **Primary completion date:** August 2023
Trial Design	Randomised, parallel assignment, double-blinded, placebo-controlled
Population	N=103 (estimated); children (aged 1 to 17 years) who have a diagnosis of systemic Juvenile Idiopathic Arthritis (sJIA)
Intervention(s)	Baricitinib administered orally
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: time to disease flare [time frame: week 24 to end of double blind withdrawal (DBW) Period (Disease Flare or up to Week 56)] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Trial	**JUVE-BASIS**; NCT03773978; EudraCT 2017-004518-24; A Randomized, Double-Blind, Placebo-Controlled, Withdrawal, Safety and Efficacy Study of Oral Baricitinib in Patients From 2 Years to Less Than 18 Years Old With Juvenile Idiopathic Arthritis (JIA) **Phase III –** Completed **Location(s):** 9 EU countries, UK and other countries **Study completion date:** January 2022
Trial Design	Randomised, parallel assignment, triple-blinded, placebo-controlled
Population	N=220; children (aged 2 to 17 years) who have a diagnosis of active JIA (polyarticular, extended oligoarticular, or enthesitis-related juvenile idiopathic

	arthritis [ERA] including JPsA) and had an inadequate response to at least one conventional or biologic DMARD
Intervention(s)	Baricitinib administered orally
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: time to disease flare [time frame: week 12 to week 44] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Baricitinib is already marketed for moderate to severe rheumatoid arthritis (adults); a pack of 28 for 2mg and 4mg tablets cost £805.56.[14]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Tofacitinib for treating juvenile idiopathic arthritis (TA735). October 2021
- NICE technology appraisal guidance. Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis (TA373). December 2015.
- NICE technology appraisal guidance. Tocilizumab for the treatment of systemic juvenile idiopathic arthritis (TA238). December 2011.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy Statement: Biologic Therapies for the treatment of Juvenile Idiopathic Arthritis (JIA). NHS England E03X04. July 2015.
- 2013/14 NHS Standard Contract Paediatric Medicine: Rheumatology. E03/S/b.

Other Guidance

- American College of Rheumatology. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. 2019.[15]
- Ravelli A et al. Treating juvenile idiopathic arthritis to target: recommendations of an international task force. 2018.[16]
- British Society for Paediatric and Adolescent Rheumatology. Standards of care for children and young people with juvenile idiopathic arthritis. 2010.[17]

Additional Information

References

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4 European Medicines Agency (EMA). *Olumiant* Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/olumiant [Accessed 4 April 2022].

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