Health Technology Briefing
April 2025

Tildrakizumab for psoriatic arthritis in adults

Company/Developer	Almirall Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 27454	NICE ID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Tildrakizumab is in clinical development for the treatment of active psoriatic arthritis (PsA). PsA is a long-term condition that causes stiff, inflamed, or painful joints, especially in the hands and feet. PsA is caused when the immune system attacks healthy tissue in the body. People with PsA can have symptoms such as swollen toes or fingers, damaged nails, and joint pain. If not treated, PsA can lead to bone and tissue damage. There is an unmet need for therapies that address all the different types of PsA and that can improve patient quality of life.

Tildrakizumab is a medication that is injected beneath the skin. It is a type of protein known as a monoclonal antibody and works by blocking the activity of other proteins in the body that are thought to cause inflammation in people with PsA. By doing this, tildrakizumab reduces inflammation and other symptoms associated with PsA. If licensed, tildrakizumab could offer an additional treatment option for active PsA in adults.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

Treatment of active psoriatic arthritis (PsA).[1]

Technology

Description

Tildrakizumab (Ilumetri) is a humanised IgG1/k monoclonal antibody that specifically binds to the p19 protein subunit of the interleukin-23 (IL-23) cytokine without binding to IL-12 and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Tildrakizumab inhibits the release of proinflammatory cytokines and chemokines.[2] IL-23 is a key regulatory cytokine in the pathogenesis of PsA, and the p19 subunit of IL-23 is an effective therapeutic target for PsA in clinical studies.[3] By blocking the action of IL-23, tildrakizumab reduces inflammation and symptoms associated with the disease.[4]

Tildrakizumab is in phase III/II clinical development for the treatment of active PsA in adults. In the completed phase IIb clinical trial (NCT02980692), adults with PsA were randomised to receive either subcutaneous (SC) tildrakizumab 200 mg every 4 weeks, or tildrakizumab 200 mg, 100 mg or 20 mg every 12 weeks.[3]

Key Innovation

Chronic joint inflammation and potential joint damage from PsA can impose considerable economic burden. There is an unmet need for therapies that address all clinical manifestations of PsA and improve patient quality of life.[3] Treating PsA is generally regarded as challenging by clinicians because of its heterogeneity and varying clinical phenotypes. Some patients fail or are intolerant of currently available therapies.[5] The differences in disease phenotypes and response to treatment indicate an unmet need in the development of precision medicine to tailor personalised treatments for patients based on disease phenotype.[6] Tildrakizumab is already licensed for moderate to severe plaque psoriasis and has shown improvement in symptoms and quality of life.[7] If licensed, tildrakizumab could offer an additional treatment option for active PsA in adults.

Regulatory & Development Status

Tildrakizumab is currently marketed in the UK for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy.[2]

Tildrakizumab is in phase III/II clinical development for:[8]

- nail psoriasis; and
- moderate to severe genital psoriasis.

Patient Group

Disease Area and Clinical Need

PsA is an inflammatory joint condition associated with psoriasis that affects joints (such as the knees or those in the hands and feet), as well as areas where tendons join to bone (such as the heel and lower back).[9] Like psoriasis, PsA is caused by the immune system attacking healthy tissue.[10] Most people who have PsA find it occurs after developing skin psoriasis, but some develop the arthritis before they notice any psoriasis on their skin.[9] Symptoms of PsA include: pain; stiffness and swelling in one or more joints; swollen fingers

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or toes; nails changing from their usual colour, or tiny dents or pits in the nails; and feeling drained of energy. Some people also get symptoms of psoriasis such as dry, scaly skin at the same time. Symptoms can be worse in the morning and can improve with exercise. PsA can develop in people who have had psoriasis for many years. It is unclear why some people with psoriasis get PsA but others do not.[10] Active PsA means that there are three or more tender joints and three or more swollen joints.[11] PsA can cause long-term damage to joints, bones and other tissue in the body, especially if it is not treated.[12]

It is thought that around 1 in 5 people with psoriasis develop psoriatic arthritis. Men and women are equally likely to develop psoriatic arthritis and, although it can occur at any age, it is most common in the first decade of being diagnosed with psoriasis.[9] The standardised incidence of PsA per 100,000 person years increased from 8.97 in 1991 to 15.08 in 2020.[13] In England, in 2023-24, there were 3944 finished consultant episodes (FCE) and 3756 admissions for PsA (ICD-10 code L40.5), which resulted in 2522 FCE bed days and 3393 day cases.[14]

Recommended Treatment Options
The National Institute for Health and Care Excellence (NICE) recommends the disease-modifying antirheumatic drugs (DMARDs), apremilast, etanercept, infliximab, adalimumab, golimumab and ustekinumab to treat active PsA.[15] If there is an inadequate response to DMARDs, NICE also recommends the following treatment options: bimekizumab;[11] upadacitinib;[16] guselkumab;[17] risankizumab;[18] ixekizumab;[19] and certolizumab pegol in combination with secukinumab.[20]

Clinical Trial Information

Trial	**INSPIRE 2, NCT04314531, EudraCT2020-000956-37;** A Phase III, Randomized, Double-Blind, Placebo-Controlled Study to Demonstrate the Efficacy and Safety of Tildrakizumab in Anti- Tumor Necrosis Factor (TNF) Naïve Subjects with Active Psoriatic Arthritis **Phase III** - Active, not recruiting **Locations:** Four EU countries, USA, and other countries **Estimated primary completion date:** September 2024
Trial Design	Randomised, placebo-controlled, parallel assignment, single masking
Population	N= 296 (actual); adults aged 18 and over with active PsA for at least six months before administration of the study agent with no prior exposure to anti-TNF agents for the treatment of psoriasis or PsA
Intervention(s)	Tildrakizumab, 1mL injection
Comparator(s)	Matching placebo, 1 mL injection
Outcome(s)	Primary outcome measure: The proportion of subjects achieving a 20% reduction from baseline in response criteria [Time frame: At week 24] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

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Trial	**INSPIRE 1,** NCT04314544, EudraCT2020-000955-11; A Phase III, Randomized, Double-Blind, Single-Dose, Placebo-Controlled Study to Demonstrate the Efficacy and Safety of tildrakizumab in Subjects with Active Psoriatic Arthritis **Phase III – Active, not** recruiting **Locations:** Seven EU countries, USA, Canada, and other countries **Estimated primary completion date:** May 2025
Trial Design	Randomised, placebo-controlled, parallel assignment, single masking
Population	N=510 (actual); adults aged 18 years and older with active PsA and prior exposure to anti-TNF agent(s) for treating psoriasis or PsA
Intervention(s)	Tildrakizumab, 1 mL injection
Comparator(s)	Matching placebo, 1 mL injection
Outcome(s)	Primary outcome measure: The proportion of subjects achieving a 20% reduction from baseline in response criteria [Time frame: At week 24] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Trial	**INSPIRE LTE,** NCT04991116; An Open-Label Extension Study to Evaluate Long Term Safety and Efficacy of Tildrakizumab in Patients with Psoriatic Arthritis **Phase III** - Recruiting **Locations:** Seven EU countries, USA, Canada, and other countries **Estimated primary completion date:** December 2028
Trial Design	Single group assignment, open label
Population	N= 650 (estimated); participants with PsA who have met all eligibility criteria for the INSPIRE I or INSPIRE II, had completed the parent study treatment period and has not developed any parent protocol criteria for premature discontinuation of treatment or withdrawal from the study
Intervention(s)	Tildrakizumab 1 mL SC injection every 12 weeks
Comparator(s)	No comparator
Outcome(s)	Primary outcome measures: • Incidence and intensity of adverse events recorded through the study period [Time frame: week 124] • Proportion of subjects who reached ACR20 (American College of Rheumatology Score of 20) [Time frame: week 124] • Proportion of subjects who reached ACR50 [Time frame: week 124] • Proportion of subjects who reached ACR70 [Time frame: week 124]
Results (efficacy)	-

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Results (safety)	-

Trial	NCT02980692; A Randomized, Double-Blind, Placebo-Controlled, Multiple-Dose, Phase 2b study to Demonstrate the Safety and Efficacy of Tildrakizumab in Subjects with Active Psoriatic Arthritis **Phase II** - Completed **Location:** USA **Study completion date:** September 2019	NCT03552276; A Long-Term Extension Study to Demonstrate Safety of Tildrakizumab in Subjects with Psoriatic Arthritis Who Have Previously Completed Study with Tildrakizumab **Phase II/III** - Completed **Locations:** Three EU countries, USA, and other countries **Study completion date:** September 2023
Trial Design	Randomised, placebo-controlled, parallel assignment, quadruple masking	Non-randomised, sequential assignment, open-label
Population	N=391 (actual); adults aged 18 and over at the time of screening, diagnosed with PsA, on a stable dose of NSAID and a negative evaluation of TB	N=281 (actual); participants with PsA who met the inclusion criteria of the parent study and completed the parent study treatment period
Intervention(s)	In weeks 0-24 (part 1), and weeks 25-52 (part 2), patients were randomised 1: 1: 1: 1 to receive: • tildrakizumab 200 mg injection every 4 weeks; or • tildrakizumab 200 mg, 100 mg, or 20 mg injection every 12 weeks At week 24, patients receiving tildrakizumab 20 mg or placebo switched to tildrakizumab 200 mg injection every 12 weeks.[3]	• Tildrakizumab 200 mg injection for four weeks • Tildrakizumab 200 mg injection for 12 weeks • Tildrakizumab 100 mg injection for 12 weeks • Tildrakizumab 200 mg injection for 4 weeks, switched to 100 mg injection for 12 weeks • Tildrakizumab 200 mg injection for 12 weeks, switched to 100 mg for 12 weeks
Comparator(s)	Placebo injection every 4 weeks.[3]	No comparator
Outcome(s)	Primary outcome measure: Proportion of subjects who reached ACR20 [Time frame: week 24] See trial record for full list of other outcomes	Primary outcome measure: Number of participants with adverse events [Time frame: up to week 208]
Results (efficacy)	At week 24, 71.4%–79.5% of tildrakizumab-treated versus 50.6% of placebo-treated patients achieved ACR20 (all $p<0.01$).[3]	-

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Results (safety)	Treatment-emergent adverse events and serious treatment-emergent adverse events occurred in 64.5% and 3.3%, respectively, of all patients through week 52 and were comparable among treatment arms.[3]	-

Estimated Cost

Tildrakizumab is currently marketed in the UK for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy. A 100 mg/1 ml or 200mg/1 ml pre-filled disposable injection costs £3241.00.[21]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Deucravacitinib for treating active psoriatic arthritis (GID-TA11510). Expected date of issue to be confirmed.
- NICE technology appraisal. Bimekizumab for treating active psoriatic arthritis (TA916). October 2023.
- NICE technology appraisal. Guselkumab for treating active psoriatic arthritis after inadequate response to DMARDs (TA815). August 2022.
- NICE technology appraisal. Risankizumab for treating active psoriatic arthritis after inadequate response to DMARDs (TA803). July 2022.
- NICE technology appraisal. Upadacitinib for treating active psoriatic arthritis after inadequate response to DMARDs (TA768). February 2022.
- NICE technology appraisal. Tofacitinib for treating active psoriatic arthritis after inadequate response to DMARDs (TA543). October 2018.
- NICE technology appraisal. Ixekizumab for treating active psoriatic arthritis after inadequate response to DMARDs (TA537). August 2018.
- NICE technology appraisal. Certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs (TA445). May 2017.
- NICE technology appraisal. Ustekinumab for treating active psoriatic arthritis (TA340). June 2015. Last updated: March 2017
- NICE technology appraisal. Apremilast for treating active psoriatic arthritis (TA433). February 2017.
- NICE technology appraisal. Golimumab for the treatment of psoriatic arthritis (TA220). April 2011.
- NICE technology appraisal. Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (TA199). August 2010.
- NICE guideline. Spondyloarthritis in over 16s: diagnosis and management (NG65). June 2017.
- NICE quality standard. Spondyloarthritis (QS170). June 2018.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Specialised Rheumatology Services (Adult). A13/S/a.
- NHS England. 2013/14 NHS Standard Contract for Specialised Dermatology Services (All Ages). A12/S/a

Other Guidance

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- Tucker L, Allen A, Chandler D, Ciurtin C, Dick A, Foulkes A, et al. The 2022 British Society for Rheumatology guideline for the treatment of psoriatic arthritis with biologic and targeted synthetic DMARDs. September 2022.[23]
- Coates LC, Soriano ER, Corp N, Bertheussen H, Callis Duffin K, Campanholo CB, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. June 2022.[24]

Additional Information

Almirall 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.

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8 ClinicalTrials.gov. *Tildrakizumab | Not yet recruiting, Recruiting, Active, not recruiting, Enrolling by invitation studies | Adult (18 - 64), Older adult (65+) | Phase: 2, 3*. 2019. Available from: https://clinicaltrials.gov/search?intr=Tildrakizumab&aggFilters=ages:adult%20older,phase:2%203,status:not%20rec%20act%20enr [Accessed 4 February 2025].

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