Health Technology Briefing
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Apremilast for the treatment of juvenile psoriatic arthritis

Company/Developer	Amgen Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 31431	NICE ID: N/A	UKPS ID: N/A

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Psoriatic arthritis is an inflammatory arthritis (a condition that causes pain and inflammation in a joint) associated with psoriasis. Psoriasis is a skin condition that causes flaky patches of skin which form scales. When this occurs in children it is referred to as juvenile psoriatic arthritis. Symptoms of juvenile psoriatic arthritis can include swelling of joints; swelling of fingers and toes; arthritis of the lower back and spine; inflammation of the eyes; morning stiffness; back pain or stiffness; pitting or peeling of the nails; red nail beds or cuticles. Juvenile psoriatic arthritis is a form of juvenile idiopathic arthritis. A few treatments are recommended for this wider indication, but options specifically for juvenile psoriatic arthritis are not recommended in children despite several treatments available for psoriatic arthritis in adults. Therefore, there is an unmet need for specific treatment options for children with juvenile psoriatic arthritis.

Apremilast blocks the action of an enzyme inside cells called phosphodiesterase 4 (PDE4). This enzyme plays a role in triggering the production of messenger molecules in the immune system (the body's natural defences) called cytokines, which are involved in the inflammation and other processes that cause psoriasis and psoriatic arthritis. By blocking PDE4, apremilast reduces the level of these cytokines in the body, and so reduces inflammation and other symptoms. Apremilast is administered orally and is currently licensed for use in adults with psoriatic arthritis, psoriasis and Behçet's disease. If licensed for use in children, apremilast will provide a specific, additional treatment option for children with juvenile psoriatic arthritis.

Proposed Indication

Treatment of juvenile psoriatic arthritis (JPsA) in patients aged 5 to 18 years who have displayed an inadequate response or intolerance to one or more disease-modifying anti-rheumatic drugs (DMARDs).[1,2]

Technology

Description

Apremilast (Otezla), an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4), works intracellularly to modulate a network of pro-inflammatory and anti-inflammatory mediators. PDE4 is a cyclic adenosine monophosphate (cAMP)-specific phosphodiesterase (PDE) and the dominant PDE in inflammatory cells. PDE4 inhibition elevates intracellular cAMP levels, which in turn down-regulates the inflammatory response by modulating the expression of TNF-α, IL-23, IL-17 and other inflammatory cytokines. cAMP also modulates levels of anti-inflammatory cytokines such as IL-10. These pro- and anti-inflammatory mediators have been implicated in psoriatic arthritis and psoriasis.[3]

Apremilast is currently in phase III clinical development for the treatment of JPsA (NCT04804553, PEAPOD; NCT05767047).[1,2] Apremilast is administered orally twice daily (bd) by participant weight as follows:[1,2]

- Between 12 kg and 20 kg will receive apremilast 10 mg bd
- Greater than 20 kg and up to 50kg will receive 20 mg bd
- 50 kg and greater will receive 30 mg bd

Key Innovation

Although the National Institute for Health and Care Excellence (NICE) recommends a number of treatments for psoriatic arthritis in adults, there are no recommendations specifically for children with JPsA.[4] Some medications are recommended for the wider indication of juvenile idiopathic arthritis (JIA) under which JPsA is considered a subgroup.[5-7]Apremilast is recommended by NICE for use in adults with psoriatic arthritis.[8] A phase III clinical trial studying apremilast demonstrated clinically meaningful improvements in adults with psoriatic arthritis.[9] Thus, if licensed, apremilast could provide an additional treatment option for patients with JPsA who have had poor responses to DMARDs.

Regulatory & Development Status

Apremilast currently has Marketing Authorisation in the EU/UK for the treatment of adult patients with psoriatic arthritis, psoriasis and Behçet's disease.[3]

Apremilast is in phase III/II clinical development for:[10]

- Plaque psoriasis
- Atopic dermatitis
- Genital psoriasis
- Palmoplantar pustulosis
- Ulcerative colitis
- Rheumatoid arthritis
- Ankylosing spondylitis

Patient Group

Disease Area and Clinical Need

Psoriatic arthritis is an inflammatory arthritis associated with psoriasis. Psoriatic arthritis 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). Most people who have psoriatic arthritis find it occurs after developing skin psoriasis, but some do develop the arthritis before they notice any psoriasis on their skin. It is thought that around 1 in 5 people with psoriasis develop psoriatic arthritis.[11] In children, psoriatic arthritis is a form of JIA, accounting for ~6% of all cases of juvenile arthritis. Although the cause of psoriatic arthritis is unknown, factors such as immunity and the environment may play a role. Genetics also appear to be involved: 40-80% of children with psoriatic arthritis have an affected first- or second- degree family member, such as a sibling, parent, grandparent or aunt/uncle. Children with psoriatic arthritis may have any of the following symptoms: swelling of the small and large joints; inflammation where the tendons and ligaments attach to bone (enthesitis); swelling of an entire finger or toe (dactylitis); arthritis of the lower back (sacroiliitis); arthritis of the spine (spondylitis); inflammation of the eyes (uveitis); morning stiffness; back pain or stiffness; pitting or peeling of the nails; red nail beds or cuticles.[12]

Approximately 12,000 children and young people in the UK have JIA which represents 1 child in every 1,000 under the age of 16 years old.[13] JPsA is a relatively rare condition as it represents approximately 5% of the whole JIA population.[14] In England, 2022-23, there were 387 finished consultant episodes (FCE) and 387 admissions for people with a primary diagnosis of JIA (ICD-10 code M09.0) which resulted in 34 FCE bed days and 338 day cases.[15]

Recommended Treatment Options

The goal of treatment for psoriatic arthritis is to reduce pain and stiffness, prevent deformities, and help the patient maintain as normal and active a lifestyle as possible.[12] Currently, NICE recommends treatment for JIA including JPsA with methotrexate, etanercept and tofacitinib, but there is no guidance specific for JPsA alone.[5-7]

Clinical Trial Information

Trial	**PEAPOD**; NCT04804553, EudraCT-2019-002788-88; A Phase 3, Multicenter, Double-blind, Randomized, Placebo-controlled, Parallel Group Study to Evaluate the Efficacy, Safety and Pharmacokinetics of Apremilast in Children From 5 to Less Than 18 Years of Age With Active Juvenile Psoriatic Arthritis **Phase III** – Recruiting **Locations:** 12 EU countries, UK, South Africa and Turkey **Primary completion date (estimated):** March 2028	NCT05767047, EudraCT- 2022-003024-41; A Phase 3, Multicenter, Open-label, Long-term Extension Study of Apremilast in Children 2 Years of Age or Older With Oral Ulcers Associated With Behçet's Disease or 5 Years of Age or Older With [Active] Juvenile Psoriatic Arthritis **Phase III** – Recruiting **Locations:** 2 EU countries, Israel and Turkey **Primary completion date (estimated):** December 2032
Trial Design	Randomised, parallel assignment, quadruple blind, placebo controlled	Open-label, parallel assignment

Population	N=60 (estimated); paediatric patients with juvenile psoriatic arthritis who inadequately respond or are intolerant to one or more disease-modifying anti-rheumatic drugs; aged 5 to 17 years.	N=48 (estimated); paediatric patients who have completed Week 52 on treatment on core study; aged 5 to 18 years.
Intervention(s)	Apremilast administered orally in the double-blind 16-week treatment phase. Then the participants will continue to receive apremilast in the active 36 weeks treatment phase.	Apremilast administered orally as a tablet or liquid suspension twice daily; dose dependent on weight ranging from 10-30mg twice daily.
Comparator(s)	Participants will receive the matching placebo in the double-blind 16-week treatment phase. Then the participants will receive apremilast in the active 36 weeks treatment phase.	No comparator
Outcome(s)	**Primary outcome:** Number of Participants who Achieve American College of Rheumatology Pediatric (ACR) Pedi 30 Response at Week 16.	**Primary outcome measures** [Time Frame: Up to approximately 4 years]: • Number of Participants with Adverse Events • Columbia-Suicide Severity rating Scale • Tanner Staging • Change from Baseline in Body Weight • Change from Baseline in Body Mass Index • Number of Participants with Clinically Significant Changes in Vital Signs • Number of Participants with Clinically Significant Changes in Laboratory Parameters See trial record for full list of other outcomes
Results (efficacy)	-	-
Results (safety)	-	-

Estimated Cost

The NHS indicative cost of one pack of 56 apremilast 30mg tablets is £550.[16]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Sarilumab for treating polyarticular or oligoarticular juvenile idiopathic arthritis in people 2 to 17 years [GID-TA11328]. Expected date of issue to be confirmed.
- NICE technology appraisal guidance. Tofacitinib for treating juvenile idiopathic arthritis (TA735). October 2021.
- NICE technology appraisal guidance. Anakinra for treating Still's disease (TA685). March 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.[17]
- Ravelli A *et al.* Treating juvenile idiopathic arthritis to target: recommendations of an international task force. 2018.[18]
- British Society for Paediatric and Adolescent Rheumatology. Standards of care for children and young people with juvenile idiopathic arthritis. 2010.[19]

Additional Information

Amgen 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 Study of Apremilast in Children With Oral Ulcers Associated With Behçet's Disease or Juvenile Psoriatic Arthritis*. *Trial ID: NCT05767047*. 2023. Status: Recruiting. Available from: https://clinicaltrials.gov/study/NCT05767047 [Accessed 07 May 2024].

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