NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
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Ustekinumab biosimilar for Plaque psoriasis

Company/Developer	Amgen Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30686	NICE TSID: 11790	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Ustekinumab biosimilar (ABP-654) is a biosimilar medicine of an approved monoclonal antibody (ustekinumab) and is proposed for the treatment of moderate to severe plaque psoriasis in adults. Plaque psoriasis is the most common type of psoriasis and is an inflammatory skin disease that typically follows a relapsing and remitting course. Plaque psoriasis is characterised by dry red skin lesions (called plaques) covered in silver scales which commonly appear on the elbows, knees, scalp and lower back. The plaques can be itchy and sore and in severe cases the skin may crack and bleed. Biosimilar medicines are biological therapies which have no clinically meaningful differences in efficacy, quality, and safety compared to the reference biologic product. Biosimilars are competitively priced to compete with the original medicinal product allowing them to be more widely available to the patients who need them.

Ustekinumab biosimilar is a type of monoclonal antibody, which is a type of protein that recognises and attaches to a specific target in the body. It is designed to attach to, and block, two messenger molecules in the immune system; interleukin 12 and interleukin 23 which are involved in inflammation and other processes that are important in psoriasis. Through the blocking of their activity, ustekinumab biosimilar reduces the activity of the immune system and the symptoms of plaque psoriasis. If licenced, ustekinumab biosimilar would offer clinicians and patients a potentially cheaper alternative to the reference medicine as a treatment option for patients with moderate to severe plaque psoriasis.

Proposed Indication

For the treatment of patients with moderate to severe plaque psoriasis who have had previous failure, inadequate response, intolerance, or contraindication to at least 1 conventional anti-psoriatic systemic therapy.[1,2]

Technology

Description

Ustekinumab (ABP-654) is a biosimilar of ustekinumab (Stelara), an approved human interleukin-12 and interleukin-23 antagonist indicated for the treatment of moderate to severe plaque psoriasis in adults and paediatric patients (6 years or older) who are candidates for phototherapy or systemic therapy. A biosimilar is a medicine which has no clinically meaningful differences compared to the reference medicine in terms of quality, safety and efficacy, with the same mechanism of action.[3]

Ustekinumab biosimilar has the same pharmaceutical form, dosage strength, route of administration and dosing regimen as United States-licensed and European Union (EU)-approved ustekinumab.[4] The active substance in ustekinumab, is a monoclonal antibody, a type of protein that has been designed to recognise and attach to a specific target in the body. Ustekinumab attaches to two messenger molecules in the immune system called interleukin 12 and interleukin 23 which are both involved in inflammation and other processes that are important in psoriasis. By blocking their activity, ustekinumab reduces the activity of the immune system and the symptoms of the disease.[5]

Ustekinumab biosimilar is currently in phase III clinical development for the treatment of adult patients with moderate to severe plaque psoriasis. In the phase III clinical trial (NCT04607980), ustekinumab biosimilar was administered subcutaneously (SC) to group 1 at a dose of 45mg or 90 mg (based on body weight at baseline) at weeks 0, 4, and 16. From week 28, participants received ustekinumab biosimilar (same dose) every 12 weeks (Q12W) at weeks 28 and 40, or may have received dose intensification every 8 weeks (Q8W) at weeks 28, 36, and 44, depending on psoriasis area and severity index (PASI) score. Group 2 received a SC injection of ustekinumab, at a dose of 45mg or 90 mg (based on body weight at baseline) at weeks 0, 4, and 16. At week 28, participants were re-randomised to continue on ustekinumab (treatment group B1), or to receive ustekinumab biosimilar (treatment group B2) on weeks 28 and 40. Depending on PASI score, some participants were not re-randomised and instead received dose intensification with ustekinumab Q8W at weeks 28, 36, and 44.[1] In the phase III clinical trial (NCT04761627), participants will receive SC injection of ustekinumab up to week 52 in the continued-use group whereas, in the switching group, participants will initially receive an injection of ustekinumab up to week 16. Thereafter, starting from week 28, participants will switch between ustekinumab biosimilar and ustekinumab Q12W up to week 52.[2]

Key Innovation

Initial data from a comparative trial assessing the safety and efficacy of ustekinumab biosimilar versus ustekinumab in adults with moderate to severe plaque psoriasis met the primary efficacy endpoint, showing no clinically meaningful differences between ustekinumab biosimilar and ustekinumab (Stelara).[6]

Biological medicines such as ustekinumab are currently the largest cost and cost growth areas in the NHS medicines budget but new commissioning framework by NHS England aims to drive an uptake in biosimilar medicines and ensure patients are given the choice of switching to a new product by their doctors; this

change to biosimilar products aims to save the NHS £300m each year, enabling more patients to have access to other life-saving and life-enhancing treatments.[3]

Regulatory & Development Status

Ustekinumab biosimilar does not currently have marketing authorisation in the EU/UK for any indication.

Ustekinumab biosimilar is not currently in phase II and/or III clinical development for any other indication.

Patient Group

Disease Area and Clinical Need

Psoriasis is an inflammatory skin disease that typically follows a relapsing and remitting course. Plaque psoriasis is the most common type of psoriasis, making up approximately 90% of cases. The disease is characterised by dry red skin lesions (called plaques) covered in silver scales which commonly appear on the elbows, knees, scalp and lower back. The plaques can be itchy and sore and in severe cases the skin may crack and bleed.[7] Plaque psoriasis is thought to occur when skin cells are replaced more quickly than usual, resulting in the build-up of immature skin cells on the surface of the skin (causing the development of plaques). The cause of this overproduction of skin cells is thought to have an autoimmune origin when T-cells attack healthy skin cells instead of pathogens, causing the deep skin layers to produce new skin cells more quickly than usual. This in turn further triggers the immune system to produce more T-cells and so perpetuates a cycle of inflammation.[8,9] The first triggers to the inflammatory process is currently unknown and is thought to be a complex mix of factors including: genetic susceptibility, skin injury, excessive alcohol consumption, smoking, stress, hormonal changes (e.g. puberty or menopause), certain medicines (e.g. lithium, antimalarial medicines, anti-inflammatory medicines, ACE inhibitors and beta blockers), throat inflections and other immune disorders.[9]

The prevalence of psoriasis is estimated to be around 1.3% to 2.2% in the UK. Psoriasis can occur at any age, although is uncommon in children (0.71%) and most cases occur before 35 years. Psoriasis is associated with joint disease in a significant proportion of patients (reported in one study at 13.8%).[7] The Hospital Episode Statistics for England 2020/21 recorded a total of 6,186 finished consultant episodes (FCE) and 5,564 hospital admissions for primary diagnosis of psoriasis (ICD-10 code L40) which resulted in 4,451 day cases and 4,829 FCE bed days.[10]

Recommended Treatment Options

For most people in the UK, psoriasis is managed in primary care, with specialist referral to a dermatologist being needed at some point for people with particularly severe symptoms.[11] According to NICE the treatment recommendations for psoriasis include non-biological and biological treatments:

Non-Biological medications include:[11,12]

- methotrexate
- ciclosporin
- acitretin
- apremilast
- dimethyl fumerate

Biological treatments include:

- etanercept
- adalimumab
- ustekinumab
- guselkumab
- brodalumab
- certolizumab pegol
- risankizumab
- tidrakizumab
- secukinumab

Clinical Trial Information	
Trial	NCT04607980; 2020-003184-25; A Phase 3, Multicenter, Randomized, Double-Blind Study Evaluating the Efficacy and Safety of ABP 654 Compared With Ustekinumab in Subjects With Moderate to Severe Plaque Psoriasis **Phase III –** Completed **Location(s):** 6 EU, USA and Canada **Study completion date:** June 2022
Trial Design	Randomised, quadruple masked, parallel assignment
Population	N=563 (actual); subjects aged 18 to 75 years with stable moderate to severe plaque psoriasis for at least 6 months
Intervention(s)	Participants will receive SC injections of ABP 654: • 45 mg, baseline bodyweight (BW) ⩽ 100 kg; • 90 mg if baseline BW ⩾ 100 kg at weeks 0, 4, and 16. After week 28 participants will receive ABP 654 (same dose) every 12 weeks at weeks 28 and 40 or may receive dose intensification every 8 weeks at weeks 28, 36, and 44, depending on psoriasis area and severity index (PASI) score.
Comparator(s)	Participants will receive SC injections of ustekinumab: • 45 mg, baseline BW ⩽ 100 kg; • 90 mg if baseline BW ⩾ 100 kg at weeks 0, 4, and 16. At week 28, participants will be re-randomised to continue ustekinumab (treatment group B1), or to receive ABP 654 (treatment group B2) on weeks 28 and 40. Depending on PASI score, some participants may not be re-randomised and may receive dose intensification with ustekinumab Q8W at weeks 28, 36, and 44.
Outcome(s)	Primary outcome measure: Percent Improvement in PASI from baseline to week 12 [time frame: baseline (day 1 [week 0]) until week 12] See trial record for full list of other outcomes
Results (efficacy)	-

Results (safety)	-

Trial	NCT04761627; 2020-005205-42; A Multicenter, Randomized, Double-blinded Study Evaluating the Pharmacokinetics, Efficacy and Safety of Multiple Switches Between Ustekinumab and ABP 654 Compared With Continued Use of Ustekinumab in Subjects With Moderate to Severe Plaque Psoriasis **Phase III** – Active, not recruiting **Location(s):** 6 EU, Georgia, USA and Canada **Primary completion date:** March 2023
Trial Design	Randomised, double blind, parallel assignment
Population	N=494 (actual); subjects aged 18 to 75 years with stable moderate to severe plaque psoriasis for at least 6 months
Intervention(s)	Participants will receive SC injection of ustekinumab up to week 52.
Comparator(s)	Participants will initially receive SC injection of ustekinumab up to week 16. Thereafter, starting from week 28, participants will switch between ABP 654 and ustekinumab every 12 weeks up to Week 52.
Outcome(s)	Primary outcome measures: • Area under the curve from time 0 over the dosing interval (AUCtau) [time frame: week 52 (pre-dose and post-dose) until week 64] • Maximum concentration (Cmax) [time frame: week 52 (pre-dose and post-dose) until week 64] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of ustekinumab biosimilar is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Deucravacitinib for treating moderate to severe plaque psoriasis (GID-TA10855). Expected January 2023.
- NICE technology appraisal. Bimekizumab for treating moderate to severe plaque psoriasis (TA723). September 2021.
- NICE technology appraisal. Risankizumab for treating moderate to severe plaque psoriasis (TA596). August 2019.
- NICE technology appraisal. Certolizumab pegol for treating moderate to severe plaque psoriasis (TA574). April 2019.

- NICE technology appraisal. Tildrakizumab for treating moderate to severe plaque psoriasis (TA575). April 2019.
- NICE technology appraisal. Guselkumab for treating moderate to severe plaque psoriasis (TA521). June 2018.
- NICE technology appraisal. Brodalumab for treating moderate to severe plaque psoriasis (TA511). March 2018.
- NICE technology appraisal. Dimethyl fumarate for treating moderate to severe plaque psoriasis (TA475). September 2017.
- NICE technology appraisal. Ixekizumab for treating moderate to severe plaque psoriasis (TA442). April 2017.
- NICE technology appraisal. Ustekinumab for the treatment of adults with moderate to severe psoriasis (TA180). March 2017.
- NICE technology appraisal. Apremilast for treating moderate to severe plaque psoriasis (TA419). November 2016.
- NICE technology appraisal. Secukinumab for treating moderate to severe plaque psoriasis (TA350). July 2015.
- NICE clinical guideline. Psoriasis: assessment and management (CG153). September 2017.
- NICE interventional procedures guidance. Grenz rays therapy for inflammatory skin conditions (IPG236). November 2007.
- NICE quality standards. Psoriasis (QS40). August 2013.

NHS England (Policy/Commissioning) Guidance

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

Other Guidance

- Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. 2020.[13]
- British Association of Dermatologists. Guidelines for biologic therapy for psoriasis. April
- 2017.[14]
- American Academy of Dermatology Association. Psoriasis Clinical Guideline. April 2019.[15]

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 to Investigate ABP 654 for the Treatment of Participants With Moderate to Severe Plaque Psoriasis*. *Trial ID: NCT04607980*. 2020. Status: Completed. Available from: https://clinicaltrials.gov/ct2/show/NCT04607980 [Accessed 14 July 2022].

2 ClinicalTrials.gov. *A Study to Investigate Interchangeability of ABP 654 for the Treatment of Participants With Moderate to Severe Plaque Psoriasis*. *Trial ID: NCT04761627*. 2021. Status: Active, not recruiting. Available from: https://clinicaltrials.gov/ct2/show/NCT04761627 [Accessed 14 July 2022].

3 National Health Service (NHS). *Biosimilar medicines*. Available from: https://www.england.nhs.uk/medicines-2/biosimilar-medicines/ [Accessed 14 July 2022].

4 AMGEN. *Amgen announces positive topline results from phase 3 study of abp 654, biosimilar candidate to Stelara (Ustekinumab).* 2020. Available from: https://www.amgen.com/newsroom/press-releases/2022/04/amgen-announces-positive-topline-results-from-phase-3-study-of-abp-654-biosimilar-candidate-to-stelara-ustekinumab [Accessed 14 July 2022].

5 European Medicines Agency (EMA). *Stelara Ustekinumab*. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/stelara [Accessed 14 July 2022].

6 Clinical Trials Arena. *Amgen's Phase III trial of ABP 654 meets primary efficacy endpoint*. 2022. Available from: https://www.clinicaltrialsarena.com/news/amgen-trial-primary-endpoint/ [Accessed 14 July 2022].

7 National Institute for Health and Care Excellence (NICE). *Psoriasis: assessment and management*. 2012. Available from: https://www.nice.org.uk/guidance/cg153/chapter/Introduction [Accessed 15 July 2022].

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9 National Health Service (NHS). *Causes-Psoriasis*. Available from: https://www.nhs.uk/conditions/psoriasis/causes/ [Accessed 15 July 2022].

10 NHS Digital. *Hospital Admitted Patient Care Activity 2020-21*. 2021. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2020-21 [Accessed 15 July 2022].

11 National Health Service (NHS). *Treatment-Psoriasis*. Available from: https://www.nhs.uk/conditions/psoriasis/treatment/ [Accessed 15 July 2022].

12 National Institute for Health and Care Excellence (NICE). *Psoriasis Products*. Available from: https://www.nice.org.uk/guidance/conditions-and-diseases/skin-conditions/psoriasis/products?ProductType=Guidance&Status=Published [Accessed 10 August 2022].

13 Menter A, Gelfand JM, Connor C, Armstrong AW, Cordoro KM, Davis DM, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *Journal of the American Academy of Dermatology*. 2020;82(6):1445-86. https://doi.org/10.1016/j.jaad.2020.02.044.

14 British Association of Dermatologists. *Guidelines for biologic therapy for psoriasis*. 2017. Available from: https://www.bad.org.uk/guidelines-and-standards/clinical-guidelines/ [Accessed 15 July 2022].

15 Menter A, Strober BE, Kaplan DH, Kivelevitch D, Prater EF, Stoff B, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *Journal of the American Academy of Dermatology*. 2019;80(4):1029-72. https://doi.org/10.1016/j.jaad.2018.11.057.

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