Health Technology Briefing
February 2025

Povorcitinib for treating hidradenitis suppurativa

Company/Developer	Incyte Corp

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 26619	NICE ID: Not available	UKPS ID: 675068

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Povorcitinib is in clinical development for the treatment of moderate to severe hidradenitis suppurativa (HS) in adults. HS is a painful, long-term skin condition that causes skin abscesses and scarring on the skin. As time goes by, more and more scarring appears. It can have a significant impact on a person's everyday life. The exact cause of HS is unknown, but it occurs near hair follicles where there are sweat glands, usually around the groin, bottom, breasts, and armpits. HS abscesses are usually painful and may make it uncomfortable to sit or move one's arms. Discharge of pus can be a problem and may require daily dressings. HS can have a severe psychological effect such as depression and can sometimes be associated with inflammation of the joints (arthritis). Many patients with HS may be unresponsive to current treatment options. Therefore, there is a high need for new treatments for this population.

Povorcitinib is an inhibitor of Janus kinase (JAK) (proteins that are involved in the immune response and inflammation). By blocking these, povorcitinib disrupts the signalling process involved in developing HS, which may alleviate inflammation, reduce disease activity, and hinder disease progression. If licensed, povorcitinib which is administered orally, will offer an additional treatment option for patients with moderate to severe HS.

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

For the treatment of moderate to severe hidradenitis suppurativa (HS) in adults.[1,2]

Technology

Description

Povorcitinib (INCB054707) is an oral, small-molecule, selective Janus kinase (JAK)1 inhibitor.[3] It works by targeting the JAK enzymes, which are pivotal in the signalling pathways of various cytokines and growth factors.[4,5] High proinflammatory cytokine levels contribute to HS pathogenesis by driving inflammation through multiple signalling pathways, including the JAK/signal transducer and activator of transcription pathway.[3] By inhibiting these JAK enzymes, povorcitinib disrupts the signalling process, which may alleviate inflammation, reduce disease activity, and hinder disease progression.[3,4]

Povorcitinib is in clinical development for the treatment of HS. In the phase III clinical trials (STOP-HS2; NCT05620836 and STOP-HS1; NCT05620823), povorcitinib was administered orally for 54 weeks.[1,2]

Key Innovation

Current HS medical treatments primarily consist of topical or oral antibiotics and, for moderate to severe disease, biologics. Early anti-inflammatory therapy is preferable to minimise risk of tissue destruction that may lead to surgical intervention. Many patients experience lack of initial response or loss of efficacy after a primary response with some of the current treatments. There is a need for novel treatments offering robust efficacy, quality of life improvements, a favourable risk-benefit profile, and convenient administration.[3] By specifically targeting JAK1, povorcitinib may reduce cytokine signalling involved in HS pathogenesis while limiting JAK2-mediated cytopenias (low blood cell counts).[6] Additionally, the oral formulation of povorcitinib addresses needle-phobic patients' needs.[7] If licensed, povorcitinib will offer an additional treatment option for adults with moderate to severe HS.

Regulatory & Development Status

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

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

- Prurigo nodularis
- Vitiligo
- Chronic spontaneous urticaria
- Asthma

Patient Group

Disease Area and Clinical Need

HS is a painful, long-term skin condition that causes skin abscesses and scarring on the skin. The exact cause of HS is unknown, but it occurs near hair follicles where there are sweat glands, usually around the groin, bottom, breasts, and armpits. The symptoms of HS range from mild to severe. HS usually starts around puberty, but it can occur at any age after puberty. Smoking and obesity are both strongly correlated with HS. HS is not infectious and runs in families in about 1 in 3 cases. It is more common in women and in people with skin of colour.[9,10] HS abscesses are usually painful. The pain may make it uncomfortable to sit or move one's arms. Discharge of pus can be a problem and may require daily dressings. HS can have a

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severe psychological effect such as depression and can sometimes be associated with inflammation of the joints (arthritis). In the early stages of HS, there are a mixture of blackheads, pus spots or abscesses. In the later stages of HS, tunnels may form under the skin that leak pus with wounds that may not heal easily. As time goes by, more and more scarring appears.[10]

In the UK, HS is estimated to affect 1 in 130 people.[11] In England (2023-24), there were 3,201 finished consultant episodes (FCEs) and 2,916 admissions for HS (ICD-10 code L73.2), which resulted in 3,849 FCE bed days and 1,740 day cases.[12]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends the following treatment options for treating active moderate to severe HS in adults:

- Adalimumab when the disease has not responded to conventional systemic therapy.[13]
- Secukinumab when the disease has not responded well enough to conventional systemic treatment, only if adalimumab is not suitable, did not work, or has stopped working.[14]

Clinical Trial Information

Trial	**STOP-HS2;** NCT05620836; A Phase 3, Double-Blind, Randomized, Placebo-Controlled, Efficacy and Safety Study of Povorcitinib (INCB054707) in Participants With Moderate to Severe Hidradenitis Suppurativa **Phase III –** Active, not recruiting **Location(s):** Seven EU countries, UK, USA, Canada and Australia **Primary completion date (estimated):** March 2025
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N=619 (actual); aged 18 years and older; diagnosis of moderate to severe HS for at least 3 months
Intervention(s)	• Povorcitinib (oral) dose A for 54 weeks • Povorcitinib (oral) dose B for 54 weeks
Comparator(s)	Placebo (oral) for 12 weeks, followed by povorcitinib (dose A or dose B) for 42 weeks
Outcome(s)	Primary outcome measure: • Proportion of participants who achieve HS clinical response [time frame: week 12] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information

Trial	**STOP-HS1;** NCT05620823; A Phase 3, Double-Blind, Randomized, Placebo-Controlled, Efficacy and Safety Study of Povorcitinib (INCB054707) in Participants With Moderate to Severe Hidradenitis Suppurativa **Phase III – Active, not** recruiting

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	Location(s): Nine EU countries, USA, Canada and Japan **Primary completion date (estimated):** March 2025
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N=609 (actual); aged 18 years and older; diagnosis of moderate to severe HS for at least 3 months
Intervention(s)	• Povorcitinib (oral) dose A for 54 weeks • Povorcitinib (oral) dose B for 54 weeks
Comparator(s)	Placebo (oral) for 12 weeks, followed by povorcitinib (dose A or dose B) for 42 weeks
Outcome(s)	Primary outcome measure: • Proportion of patients who achieve HS clinical response [time frame: week 12] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-
Clinical Trial Information	
Trial	**STOP-HS LTE;** NCT06212999**;** A Phase 3, Double-Blind Study to Evaluate the Long-Term Safety and Efficacy of Povorcitinib in Participants With Moderate to Severe Hidradenitis Suppurativa Phase III – Recruiting **Location(s):** Twelve EU countries, UK, USA, Canada, Australia and Japan **Primary completion date (estimated):** December 2026
Trial Design	Randomised, parallel assignment, quadruple-blinded (cohorts A and B) or open label (cohort C)
Population	N=960 (estimated); aged 18 years and older; completion of the study treatment period of the originating parent study (STOP-HS1, NCT05620823 or STOP-HS2, NCT05620836)
Intervention(s)	Povorcitinib (oral)
Comparator(s)	No comparator
Outcome(s)	Primary outcome measure: • Proportion of patients with treatment-emergent adverse events [time frame: up to approximately 56 weeks] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-
Clinical Trial Information	

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Trial	NCT04476043; EudraCT 2020-001981-13; A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of the Efficacy and Safety of INCB054707 in Participants With Hidradenitis Suppurativa **Phase II –** Completed **Location(s):** Four EU countries, USA and Canada **Study completion date:** August 2023
Trial Design	Randomised, parallel assignment, triple-blinded
Population	N=209 (actual); aged 18 to 75 years; HS duration of at least 3 months
Intervention(s)	• Povorcitinib (oral) 15mg for 16 weeks, followed by povorcitinib (oral) 75 mg for 36 weeks, with the option to continue for an additional 48 weeks • Povorcitinib (oral) 45mg for 16 weeks, followed by povorcitinib (oral) 75 mg for 36 weeks, with the option to continue for an additional 48 weeks • Povorcitinib (oral) 75mg for 52 weeks, with the option to continue for an additional 48 weeks
Comparator(s)	Placebo (oral) for 16 weeks, followed by povorcitinib (oral) 75 mg for 36 weeks, with the option to continue for an additional 48 weeks
Outcome(s)	Primary outcome measure: • Mean change from baseline in abscess an inflammatory nodule count [time frame: baseline; week 16] See trial record for full list of other outcomes.
Results (efficacy)	Of 209 patients randomised (15 mg, n = 52; 45 mg, n = 52; 75 mg, n = 53; placebo, n = 52), 83.3% completed the 16-week treatment. At week 16, povorcitinib significantly reduced abscess and inflammatory nodule count from baseline (least squares mean [SE] change: 15 mg, −5.2 [0.9], P = .0277; 45 mg, −6.9 [0.9], P = .0006; 75 mg, −6.3 [0.9], P = .0021) versus placebo (−2.5 [0.9]). More povorcitinib-treated patients achieved HS clinical response at week 16 (15 mg, 48.1%, P = .0445; 45 mg, 44.2%, P = .0998; 75 mg, 45.3%, P = .0829) versus placebo (28.8%).[3]
Results (safety)	In total, 60.0% of povorcitinib-treated (15 mg, 59.6%; 45 mg, 60.0%; 75 mg, 60.4%) and 65.4% of placebo-treated patients reported a treatment-emergent adverse event. Treatment-related adverse events occurred in 21.3% of patients receiving any povorcitinib dose (15 mg, 17.3%; 45 mg, 24.0%; 75 mg, 22.6%) and 23.1% with placebo. Povorcitinib was generally well tolerated at all doses tested, with no trends in treatment-emergent adverse event incidence or severity observed with increasing doses.[3]
Clinical Trial Information	
Trial	NCT03607487; EudraCT 2018-000827-15; A Phase 2, Dose-Escalation, Placebo-Controlled Study of the Safety of INCB054707 in Participants With Hidradenitis Suppurativa **Phase II –** Completed **Location(s):** Two EU countries and Canada **Study completion date:** August 2019

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Trial Design	Randomised, parallel assignment, triple-blinded
Population	N=35 (actual); aged 18 to 75 years; diagnosis of HS with a disease duration of at least 6 months
Intervention(s)	Povorcitinib administered orally once daily at a dose of 30 mg, 60 mg or 90 mg.[6]
Comparator(s)	Matched placebo (oral)
Outcome(s)	Primary outcome measure: • Number of treatment-emergent adverse events [time frame: up to 12 weeks] See trial record for full list of other outcomes.
Results (efficacy)	Patients were enrolled 3:1 experimental to placebo within each cohort. Among the evaluable patients, 17 (65% overall: 30 mg, 56%; 60 mg, 56%; 90 mg, 88%) receiving povorcitinib versus 4 patients (57%) receiving placebo achieved HS clinical response at week 8.[6]
Results (safety)	Overall, 81% of patients experienced at least one treatment-emergent adverse event; 42% of patients had at least one treatment-related adverse event. No serious treatment-emergent adverse events were observed.[6]
Clinical Trial Information	
Trial	NCT03569371; A Phase 2, Open-Label, Single-Arm Study of the Safety of INCB054707 in Participants With Hidradenitis Suppurativa **Phase II** – Completed **Location(s):** USA **Study completion date:** April 2019
Trial Design	Single group assignment, open label
Population	N=10 (actual); aged 18 to 75 years; diagnosis of HS with a disease duration of at least 6 months
Intervention(s)	Povorcitinib 15 mg (oral) once daily for 8 weeks.[6]
Comparator(s)	No comparator
Outcome(s)	Primary outcome measure: • Number of participants with treatment-emergent adverse events [time frame: up to approximately 12 weeks] See trial record for full list of other outcomes.
Results (efficacy)	Among the evaluable patients, 3 (43%) achieved HS clinical response at week 8.[6]
Results (safety)	Overall, 70% experienced at least one treatment-emergent adverse event; 30% of patients had at least one treatment-related adverse event. There were no serious treatment-emergent adverse events.[6]

Estimated Cost

The cost of povorcitinib is not yet known.

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Relevant Guidance

NICE Guidance

- NICE technology appraisal. Secukinumab for treating moderate to severe hidradenitis suppurativa (TA935). December 2023.
- NICE technology appraisal. Adalimumab for treating moderate to severe hidradenitis suppurativa (TA392). June 2016.

NHS England (Policy/Commissioning) Guidance

- NHS England. Service Specification: Specialised Dermatology Services (Adult and Children). A12 S/a. August 2024.
- NHS England. Clinical Commissioning Policy: Infliximab for the treatment of hidradenitis suppurativa. 16018/P. July 2016.

Other Guidance

- Journal of the American Academy of Dermatology. North American clinical management guidelines for hidradenitis suppurativa: A publication from the United States and Canadian Hidradenitis Suppurativa Foundations. 2019.[15]
- British Association of Dermatologists. British Association of Dermatologists guidelines for the management of hidradenitis suppurativa (acne inversa). 2018.[16]
- Zouboulis CC, Desai N, Emtestam L, Hunger RE, Ioannides D, Juhász I, et al. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. 2015.[17]

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