Health Technology Briefing
December 2023

Delgocitinib for treating moderate to severe chronic hand eczema after 1 previous therapy

Company/Developer	LEO Pharma UK

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 36137	NICE ID: Not available	UKPS ID: 672897

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Delgocitinib is currently in clinical development for the treatment of adults with moderate to severe chronic hand eczema. Hand eczema is one of the most common types of eczema. It mainly affects the palms but can also affect other parts of the hand. Chronic hand eczema is hand eczema that lasts for more than three months or relapses twice or more within a year. It is characterised by dry, itchy, and painful skin that is red or darker than the surrounding skin. In severe cases, the hands can become very painful, making it difficult to carry out day-to-day tasks. Chronic hand eczema is a significant disease burden and traditionally has had limited treatment options beyond topical and short-term systemic medicines.

Delgocitinib is a Janus kinase (JAK) inhibitor that is administered topically (to the body surface, e.g., skin). Delgocitinib works by blocking the action of enzymes known as JAK to reduce inflammation and skin dysfunction. Previous studies indicate that delgocitinib demonstrated a rapid and sustained clinical improvement among patients with chronic hand eczema. If licensed, delgocitinib will offer an additional treatment option for adults with moderate to severe chronic hand eczema.

Proposed Indication

Adults with moderate to severe chronic hand eczema who have had an inadequate response to, or for whom topical corticosteroids are not advisable.[a]

Technology

Description

Delgocitinib (LEO124249) is a topical Janus kinase (JAK) inhibitor that targets the proteins JAK1, JAK2, JAK3, and tyrosine kinase 2 (TYK2) to reduce inflammation and skin dysfunction. These tyrosine kinases decrease the activity of effector T-cells, which release inflammatory cytokines such as interleukins 4 and 16 (IL-4, IL-16) and interferon-gamma (IFN-γ).[1]

Delgocitinib is in clinical development for the treatment of adults with moderate to severe chronic hand eczema. In the phase III clinical trial (DELTA FORCE; NCT05259722), patients were administered delgocitinib 20 milligrams (mg)/gram (g) cream twice daily topical application for up to 24 weeks.[2]

Key Innovation

Chronic hand eczema is a common condition with significant disease burden and traditionally has had limited treatment options beyond topical and short-term systemic corticosteroids.[1] Pan-JAK inhibitors such as delgocitinib prevent the activation of the JAK-STAT (signal transducer and activator of transcription protein) signalling pathway, which plays a key role in the pathogenesis of chronic hand eczema.[3] In a previous clinical study, delgocitinib demonstrated a rapid (within 1 week of initiation of therapy) and dose-dependent clinical improvement as well as a sustained reduction in itch and pain among patients with chronic hand eczema.[3,4] Delgocitinib cream is expected to provide the benefits observed for other JAK inhibitors but without the safety concerns inherent to systemic administration due to the topical application to limited skin areas and limited systemic exposure.[3]

If licensed, delgocitinib will offer an additional treatment option for adults with moderate to severe chronic hand eczema who have had an inadequate response to, or for whom topical corticosteroids are not advisable.

Regulatory & Development Status

Delgocitinib does not currently have Marketing Authorisation in the EU/UK for any indication.

Delgocitinib is currently in phase II clinical development for the following indication:[5]

- Frontal fibrosing alopecia

Patient Group

Disease Area and Clinical Need

Hand eczema (dermatitis) is one of the most common types of eczema. It mainly affects the palms but can also affect other parts of the hand.[6] Chronic hand eczema is defined as the presence of hand eczema for more than 3 months, or the recurrence of symptoms more than two times within a year.[7] The main symptoms of hand eczema are dry, itchy skin that is red or darker than the surrounding skin. Other

[a] Information provided by LEO Pharma

symptoms include cracking, soreness, and bleeding, and in some cases, blisters may develop. The skin is generally dry, scaly, and thickened, and the fingers can become swollen when the eczema is flaring. If the eczema is severe over a long time, the hands can become very painful, making it difficult to carry out day-to-day tasks. In people with eczema, the immune system overreacts in the skin, making it inflamed and itchy.[6] Genetics, contact allergens and irritating substances play a role in triggering this form of eczema.[8] Hand eczema is more common in young women and affects 30% of those in high-risk occupations (such as health care workers, hairdressers, cleaners, cooks) or those working in manufacturing industries.[1]

Hand eczema affects up to 10% of the UK population.[9] In England, 2022-23, there were 15,599 finished consultant episodes (FCE) and 13,386 admissions for dermatitis and eczema (ICD-10 code L20-L30) which resulted in 18,769 FCE bed days and 4,547 day cases.[10]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends alitretinoin for the treatment of severe chronic hand eczema.[11]

Other treatment options include:[12]

- emollients
- topical steroids
- topical calcineurin inhibitors –pimecrolimus cream, tacrolimus ointment
- phototherapy
- oral steroids
- immunosuppressant drugs
- biologic drugs
- Janus kinase (JAK) inhibitors

Clinical Trial Information

Trial	**DELTA FORCE;** NCT05259722, EudraCT 2021-003543-16; A 24 Week, Randomised, Assessor Blinded, Active-controlled, Parallel Group, Phase 3, 2 Arm Trial to Compare the Efficacy and Safety of Delgocitinib Cream 20 mg/g Twice-daily With Alitretinoin Capsules Once-daily in Adult Participants With Severe Chronic Hand Eczema **Phase III -** Active, not recruiting **Locations:** 7 EU countries, UK, Norway, and Canada **Primary completion date:** October 2023
Trial Design	Randomised, parallel assignment, single masking
Population	N=513 (actual); aged 18 years and older; subjects with diagnosis of severe chronic hand eczema with documented recent history of inadequate response to treatment with topical corticosteroids (TCS) or for whom TCS are documented to be otherwise medically inadvisable
Intervention(s)	Delgocitinib 20mg/g cream twice daily topical application for up to 24 weeks
Comparator(s)	Alitretinoin 30 mg capsules; 1 capsule daily for up to 24 weeks
Outcome(s)	Primary outcome measure:

	• Change in Hand Eczema Severity Index score from baseline to Week 12 [Time Frame: 12 weeks] See trial record for full list of outcome measures
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information

Trial	**DELTA 1**; NCT04871711, EudraCT 2020-002960-30; A Phase 3 Clinical Trial to Confirm Efficacy and Evaluate Safety of Twice-daily Delgocitinib Cream 20 mg/g Compared With Cream Vehicle for a 16-week Treatment Period in Adult Subjects With Moderate to Severe Chronic Hand Eczema **Phase III** - Completed **Locations:** 4 EU countries, UK, and Canada **Study completion date:** October 2022	**DELTA 3**; NCT04949841, EudraCT 2020-002962-15; A Phase 3 Extension Trial of DELTA 1 and DELTA 2 to Evaluate the Long-term Safety of a Twice-daily Treatment With Delgocitinib Cream 20 mg/g as Needed for up to 36 Weeks in Adult Subjects With Chronic Hand Eczema **Phase III** - Enrolling by invitation **Locations:** 8 EU countries, UK, and Canada **Primary completion date:** September 2023
Trial Design	Randomised, parallel assignment, double masking	Randomised, parallel assignment, double masking
Population	N=487 (actual); aged 18 years and older; subjects with diagnosis of moderate to severe chronic hand eczema with documented recent history of inadequate response to treatment with TCS or for whom TCS are documented to be otherwise medically inadvisable	N=473 (actual); aged 18 years and older; subjects with diagnosis of moderate to severe chronic hand eczema with documented recent history of inadequate response to treatment with TCS or for whom TCS are documented to be otherwise medically inadvisable
Intervention(s)	Delgocitinib 20mg/g cream twice daily topical application for 16 weeks	Delgocitinib 20mg/g cream twice daily topical application for 16 weeks
Comparator(s)	Cream vehicle (placebo) twice daily topical application for 16 weeks	None
Outcome(s)	Primary outcome measure: • Investigator's Global Assessment for chronic hand eczema treatment success at Week 16 [Time Frame: 16 weeks] See trial record for full list of outcome measures	Primary outcome measure: • Number of treatment-emergent adverse events from baseline up to Week 38 [Time Frame: From baseline to Week 38] See trial record for full list of outcome measures

Results (efficacy)	The trial met its primary endpoint with a significantly larger proportion of delgocitinib-treated patients achieving treatment success compared with the vehicle arm. The study also met key secondary endpoints including a reduction of itch and pain scores of at least 4 points (as measured by the Hand Eczema Symptom Diary), as well as at least 75% improvement from baseline and at least 90% improvement from baseline on the Hand Eczema Severity Index at week 16.[13]	Patients who entered the DELTA 3 trial after receiving delgocitinib cream in the DELTA 1 and DELTA 2 trials maintained similar levels of symptom relief and treatment success over an additional 36-week treatment regimen.[14]
Results (safety)	Majority of adverse events were non-serious, mild, or moderate and not related to the treatment.[15]	An additional analysis concluded that twice-daily application of delgocitinib cream in adults with moderate to severe chronic hand eczema resulted in minimal systemic exposure over 16 weeks, further supporting its safety profile.[16]

Clinical Trial Information	
Trial	**DELTA 2**; NCT04872101, EudraCT 2020-002961-32; A Phase 3 Clinical Trial to Confirm Efficacy and Evaluate Safety of Twice-daily Delgocitinib Cream 20 mg/g Compared With Cream Vehicle for a 16-week Treatment Period in Adult Subjects With Moderate to Severe Chronic Hand Eczema **Phase III** - Completed **Locations:** 6 EU countries and Canada **Study completion date:** January 2023
Trial Design	Randomised, parallel assignment, double masking
Population	N=473 (actual); aged 18 years and older; subjects with diagnosis of moderate to severe chronic hand eczema with documented recent history of inadequate response to treatment with TCS or for whom TCS are documented to be otherwise medically inadvisable
Intervention(s)	Delgocitinib 20mg/g cream twice daily topical application for 16 weeks
Comparator(s)	Cream vehicle (placebo) twice daily topical application for 16 weeks
Outcome(s)	Primary outcome measure: • Investigator's Global Assessment for chronic hand eczema treatment success (IGA-CHE TS) at Week 16 [Time Frame: 16 weeks] See trial record for full list of outcome measures
Results (efficacy)	A significantly greater proportion of delgocitinib-treated patients, compared to cream vehicle, achieved this IGA-CHE improvement (29.1% vs. 6.9%; p<0.001).

	The trial also achieved its key secondary endpoints at Week 16, including a significantly greater proportion of delgocitinib-treated patients achieving a ≥75% improvement in the Hand Eczema Severity Index (HECSI-75) compared to cream vehicle (49.5% vs. 18.2%; p<0.001). All endpoints were consistent with those from the identically designed DELTA 1 study.[16]
Results (safety)	An additional analysis concluded that twice-daily application of delgocitinib cream in adults with moderate to severe chronic hand eczema resulted in minimal systemic exposure over 16 weeks, further supporting its safety profile.[16]

Estimated Cost

The cost of delgocitinib is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Alitretinoin for the treatment of severe chronic hand eczema (TA177). August 2009.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Specialised Dermatology Services (All Ages). A12/S/a.
- NHS England. 2013/14 NHS Standard Contract for Specialised Allergy Services (All Ages). B09/S/b.

Other Guidance

- European Society of Contact Dermatitis: Guidelines for Diagnosis, Prevention, and Treatment of Hand Eczema. April 2022.[7]
- European Dermatology Forum. Living EuroGuiDerm Guideline for the Systemic Treatment of Atopic Eczema. June 2022.[17]
- European Academy of Dermatology and Venereology. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis in adults and children): Part I. 2018.[18]
- European Academy of Dermatology and Venereology. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis in adults and children): Part II. 2018.[19]

Additional Information

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