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Health Technology Briefing
October 2022

Nemolizumab for treating atopic dermatitis and prurigo nodularis

Company/Developer	Galderma (UK) Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 29543	NICE TSID: 10515	UKPS ID: 658947, 658946

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Nemolizumab is currently in development for atopic dermatitis and prurigo nodularis. Atopic dermatitis is the most common form of eczema, a long-term (chronic) condition that causes patches of the skin to become itchy, dry and cracked. In moderate-to-severe cases, the patches cover a large area of the skin and can be associated with an intense itch. Prurigo nodularis is a chronic skin disorder characterised by the presence of hard, extremely itchy bumps known as nodules. Although the cause of the condition is unknown, the nodules are the result of persistent, intense scratching and rubbing of the skin. Current treatment options for atopic dermatitis and prurigo nodularis have varied effectiveness, and can cause side-effects. Therefore, there is a need to develop additional treatment options for these patients.

Nemolizumab is a first-in-class monoclonal antibody (a type of protein) that is administered to patients by subcutaneous (under the skin) injection. It attaches to, and blocks the activity of, the IL-31 receptor (a type of protein). By blocking this receptor, nemolizumab blocks the IL-31 signalling pathway which plays a key role in the development of both atopic dermatitis and prurigo nodularis. If licensed, nemolizumab will offer an additional treatment option for patients with atopic dermatitis and prurigo nodularis.

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

Atopic dermatitis and prurigo nodularis.[1]

Technology

Description

Nemolizumab (CD14152) is a humanised monoclonal antibody that binds to the interleukin-31 (IL-31) receptor A and inhibits IL-31 signalling in cells.[2] IL-31 signalling plays a key role in the pathways associated with heightened sensations of itching (pruritus), and affects inflammatory response and epidermal-barrier disruption in atopic dermatitis.[3,4]

Nemolizumab is being developed for the treatment of atopic dermatitis and prurigo nodularis.[5] Patients will receive a dose of nemolizumab by subcutaneous injection every 4 weeks.[1]

Key Innovation

Current treatment options for atopic dermatitis and prurigo nodularis target the signs and symptoms of disease. However, these agents have limited efficacy, and their use can be hampered by adverse effects and safety risks. There is an unmet need for the development of a safe and effective long-term therapy for moderate-to-severe atopic dermatitis and prurigo nodularis.[2,3] Nemolizumab targets the specific pathways involved in the pathophysiology of atopic dermatitis and prurigo nodularis.[2] Recent clinical data has demonstrated that nemolizumab has a rapid onset of action and provides significant relief of symptoms for people with prurigo nodularis and atopic dermatitis.[1]

Regulatory & Development Status

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

Nemolizumab was granted a breakthrough therapy designation by the US FDA in December 2019 for the treatment of prurigo nodularis.[6]

Nemolizumab is also in clinical development for chronic kidney disease associated with moderate to severe pruritus.[7]

Patient Group

Disease Area and Clinical Need

Prurigo nodularis is a chronic inflammatory skin disease where an extremely itchy, symmetrically distributed rash appears most commonly on the arms, legs, the upper back and/or the abdomen.[4] Though the cause of the condition is unknown, the nodules are the result of persistent, intense scratching and rubbing of the skin.[8] The itch associated with prurigo nodularis can significantly reduce a patient's quality of life due to difficulty sleeping, missing work, and higher rates of anxiety and depression.[8] Atopic dermatitis is the most common form of eczema, a condition that causes the skin to become itchy, dry and cracked. Atopic dermatitis can affect any part of the body, most often the hands, inside of the elbows, backs of the knees, and the face and scalp in children. People with atopic dermatitis usually have periods

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where symptoms are less noticeable and periods where symptoms are more severe (flare-ups).[9] The exact cause of atopic dermatitis is unknown, but is likely to be caused by a combination of things. Atopic disease often occurs in people who have allergies and in people with a family history of the disease.[10]

Prevalence estimates for atopic dermatitis in the UK vary considerably from 2.5% to 15%.[11] In England (2021-22), there were 1,188 finished consultant episodes (FCE) and 1,050 admissions for atopic dermatitis, unspecified (ICD-10 code L20.9) which resulted in 678 day cases and 848 FCE bed days. In England, the estimated prevalence of prurigo nodularis is 3.27 per 10,000 population, and the estimated incidence is 2.88 per 100,000 patient years.[12] There were 233 FCE and 217 admissions for prurigo nodularis (ICD-10 code L28.1), which resulted in 175 day cases and 332 FCE bed days.[13]

Recommended Treatment Options

Currently there are no treatments recommended by NICE, specifically for the treatment of prurigo nodularis. Treatments instead aim to stop the skin itching, these include:[14]

- Emollients
- Corticosteroid creams
- Ointments such as tacrolimus (a calcineurin inhibitor, off-label use)
- Antihistamines
- Oral steroids
- Ultraviolet light treatment
- Immunosuppressants such as azathioprine, ciclosporin or methotrexate (off-label use)

Currently available treatments for atopic dermatitis include:[15]

- Phototherapy including with ultraviolet (UVB) radiation or psoralen-ultraviolet A (PUVA)
- Immunosuppressive therapies such as azathioprine, ciclosproin, methotrexate, and mycophenolate mofetil
- Alitretinoin
- Dupilumab
- Baracitinib
- Abrocitinib, tralokinumab and upadacitinib
- Topical corticosteroids

Clinical Trial Information

Trial	NCT04204616, 2019-004294-13; A Prospective, Multicenter, Long-Term Study to Assess the Safety and Efficacy of Nemolizumab (CD14152) in Subjects With Prurigo Nodularis **Phase III** – Enrolling by invitation **Locations:** 12 EU countries, UK, US, Canada and Republic of Korea **Primary completion date:** January 2023
Trial Design	Single group assignment, open-label
Population	N=450 (approximated); adults aged 18 years and older; prurigo nodularis; previously completed the treatment period in a phase 3 pivotal study (NCT04501666 and NCT04501679); participants who were previously randomised in the nemolizumab phase 2a study (NCT03181503)

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Intervention(s)	Nemolizumab (subcutaneous injection)
Comparator(s)	No comparator
Outcome(s)	Primary outcome measure: • Incidence of adverse events (AEs) by severity [Time frame: Up to 192 weeks] See trial record for full list of outcome measures
Results (efficacy)	-
Results (safety)	-

Trial	NCT05052983; 2021-003928-32; A Double-Blind, Placebo-Controlled, Randomized Study to Assess the Durability of Effect and Safety of Nemolizumab for 24 Weeks in Subjects With Prurigo Nodularis **Phase III** – Recruiting **Locations:** Austria and US **Primary completion date:** December 2023
Trial Design	Parallel assignment, randomised, double masked, placebo-controlled
Population	N=60 (approximated); adults aged 18 years and older; participants who achieved a clinical response at week 52 of the LTE study RD.06.SPR.202699 (NCT04204616).
Intervention(s)	Nemolizumab (subcutaneous injection)
Comparator(s)	Placebo (subcutaneous injection)
Outcome(s)	Primary outcome measures: Time to relapse which is defined as meeting at least 1 of the following criteria: • Increase in weekly average of the Peak Pruritus Negative Response Score (PP-NRS) score ≥4 points from baseline [Time frame: Baseline up to week 24] • Increase in investigator global assessment (IGA) score ≥2 points from baseline [Time frame: Baseline up to week 24] See trial record for full list of outcome measures
Results (efficacy)	-
Results (safety)	-

Trial	NCT04501666, 2019-004293-25; A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Nemolizumab (CD14152) in Subjects With Prurigo Nodularis **Phase III** – Active, not recruiting **Locations:** 7 EU countries, UK, US, and Canada **Primary completion date**: February 2023

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Trial Design	Randomised, parallel assignment, double masked, placebo-controlled,
Population	N=270 (planned); adults aged 18 years and older; clinical diagnosis of prurigo nodularis for at least 6 months; severe pruritus as defined by the peak pruritus (PP) NRS score
Intervention(s)	Nemolizumab (subcutaneous injection)
Comparator(s)	Placebo (subcutaneous injection)
Outcome(s)	Primary outcome measures: • Proportion of participants with an improvement of ≥4 from baseline in PP NRS at week 16 [Time frame: Week 16] • Proportion of participants with an investigator global assessment (IGA) success (defined as an IGA of 0 [clear] or 1 [almost clear] and a ≥2 point improvement from baseline at week 16 [Time frame: Week 16] See trial record for full list of outcome measures
Results (efficacy)	-
Results (safety)	-

Trial	NCT04501679, 2019-004789-17; A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Nemolizumab (CD14152) in Subjects With Prurigo Nodularis **Phase III** – Completed **Locations:** 6 EU countries, US, Canada and other countries **Actual Primary completion date:** March 2022
Trial Design	Randomised, parallel assignment, double masked, placebo-controlled
Population	N=274; adults aged 18 years and older; clinical diagnosis of prurigo nodularis for at least 6 months; severe pruritus as defined by PP NRS score
Intervention(s)	Nemolizumab (subcutaneous injection)
Comparator(s)	Placebo (subcutaneous injection)
Outcome(s)	Primary outcome measures: • Proportion of participants with an improvement ≥4 from baseline in PP NRS at week 16 [Time frame: Week 16] • Proportion of participants with an IGA of 0 [clear] or 1 [almost clear] and a ≥2 point improvement from baseline at week 16 [Time frame: Week 16] See trial record for full list of outcome measures
Results (efficacy)	-
Results (safety)	-

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Trial	NCT03181503; 2017-001715-36; A Study to Assess the Safety and Efficacy of Nemolizumab (CD14152) in Subjects With Prurigo Nodularis (PN) **Phase II** – Completed **Locations:** 4 EU countries **Actual primary completion date**: September 2018
Trial Design	Randomised, parallel assignment, quadruple masked
Population	N=70; adults aged 18 years and older; clinical diagnoses of prurigo nodularis for at least 6 months; severe pruritus
Intervention(s)	Nemolizumab (subcutaneous injection)
Comparator(s)	Placebo (subcutaneous injection)
Outcome(s)	Primary outcome measures: • Percentage change from baseline in weekly average of the peak pruritus numeric rating scale (NRS) score at week 4 using last observation carried forward (LOCF) approach [Time frame: Baseline, Week 4] • Percentage change from baseline in weekly average of the peak pruritus numeric rating scale (NRS) score at week 4 using multiple imputation (MI) method [Time frame: Baseline, Week 4] • Percentage change from baseline in weekly average of the peak pruritus numeric rating scale (NRS) score at week 4 using observed data [Time frame: Baseline, Week 4] See trial record for full list of outcome measures
Results (efficacy)	A total of 70 patients were randomly assigned in a 1:1 ratio to receive nemolizumab (34 patients) or placebo (36). The initial pruritus score on the numerical rating scale was 8.4 in each group. At week 4, the peak pruritus score on the numerical rating scale was reduced from baseline by 4.5 points (change, -53.0%) in the nemolizumab group, as compared with a reduction of 1.7 points (change, -20.2%) in the placebo group (difference, -32.8 percentage points; 95% confidence interval, -46.8 to -18.8; P<0.001).[16]
Results (safety)	Nemolizumab was associated with gastrointestinal symptoms (abdominal pain and diarrhoea) and musculoskeletal symptoms.[16]

Trial	NCT03989349; A Randomised, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Nemolizumab in Subjects With Moderate-to-Severe Atopic Dermatitis **Phase III** – Active, not recruiting **Locations:** 8 EU countries, US, Georgia and Singapore **Primary completion date:** December 2022
Trial Design	Randomised, double-blind, quadruple-masked, placebo-controlled
Population	N=750; aged 12 years and older; chronic atopic dermatitis for at least 2 years
Intervention(s)	Nemolizumab (subcutaneous injection)

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Comparator(s)	Placebo (subcutaneous injection)
Outcome(s)	Primary outcome measure: • Proportion of subjects with IGA success (IGA of 0 or 1) and a ≥2 point reduction. [Time frame: Baseline to week 16] See trial record for full list of outcome measures.
Results (efficacy)	-
Results (safety)	-

Trial	NCT03985943; A Randomised, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Nemolizumab in Subjects With Moderate-to-Severe Atopic Dermatitis **Phase III** – Active, not recruiting **Locations:** 8 EU countries, UK, US and other countries **Primary completion date:** October 2022
Trial Design	Randomised, double-blind, quadruple-masked, placebo-controlled
Population	N=750; aged 12 years and older; chronic atopic dermatitis for at least 2 years
Intervention(s)	Nemolizumab (subcutaneous injection)
Comparator(s)	Placebo (subcutaneous injection)
Outcome(s)	Primary outcome measure: • Proportion of subjects with IGA success (IGA of 0 or 1) and a ≥2 point reduction. [Time frame: Baseline to week 16] See trial record for full list of outcome measures.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The estimated cost of nemolizumab is not known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Dupilumab for treating prurigo nodularis (GID-TA11801). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Tralokinumab for treating moderate to severe atopic dermatitis (GID-TA10596). Expected date of issue to be confirmed.

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- NICE technology appraisal in development. Upadacitinib for treating moderate to severe atopic dermatitis in people aged 12 and over (TA10597). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Abrocitinib for treating moderate to severe atopic dermatitis in people aged 12 and over (GID-TA10764). Expected date of issue to be confirmed.
- NICE technology appraisal guidance. Abrocitinib, tralokinumab or upadacitinib for treating moderate to severe atopic dermatitis. August 2022.
- NICE technology appraisal guidance. Baricitinib for treating moderate to severe atopic dermatitis (TA681). March 2021.
- NICE technology appraisal guidance. Dupilumab for treating moderate to severe atopic dermatitis (TA534). August 2018
- NICE technology appraisal guidance. Tacrolimus and pimecrolimus for atopic eczema (TA82). August 2004.
- NICE clinical guidance in development. Atopic dermatitis (eczema) (GID-NG10289). Expected date of issue to be confirmed.

NHS England (Policy/Commissioning) Guidance

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

Other Guidance

- International Forum for the Study of Itch (IFSI). IFSI guideline on chronic prurigo including prurigo nodularis. December 2020.[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]
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