Health Technology Briefing
October 2024

Clascoterone for acne vulgaris

Company/Developer	Glenmark Pharmaceuticals Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 7282	NICE ID: 9792	UKPS ID: 674907

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Acne vulgaris is a common skin condition where the skin pores become clogged with oil and dead skin cells. Pore blockages produce blackheads, whiteheads, and other types of pimples and possible scarring. Pimples are pus-filled, sometimes painful, bumps on the skin. It primarily affects the face, upper part of the chest, and back. The causes of acne vulgaris include increased sebum production (of which the androgen hormone can be the cause) and possible infection of the clogged pore among others. Acne occurs more in adolescents and appears to be heritable. Moderate severity acne is characterised by higher numbers of swollen bumps (papules and pustules), while severe acne occurs when painful bumps (nodules) are extensive on the face and body. Possible triggers of acne flare-ups include hormonal factors, stress, diet, smoking, cosmetics, and some medicines. Current treatment of moderate to severe acne is a combination of topical treatments, or antibiotic tablets combined with topical treatments.

Clascoterone works by minimising the effects of androgen-induced sebum production in the skin, thereby regulating sebum production and preventing infection. It is applied topically (to the skin). If licensed, clascoterone may offer an additional treatment option for treating acne vulgaris.

Proposed Indication

Treatment of moderate to severe acne vulgaris in adolescents and adults (9 years and above).[1-3]

Technology

Description

Clascoterone (Winlevi, Cortexolone 17α-Propionate, CB-03-01)[4] is an ester derivative of cortexolone and an androgen receptor inhibitor that shares a 4-ring backbone with the androgen dihydrotestosterone (DHT) and the androgen receptor inhibitor spironolactone.[5] Clascoterone counteracts the androgenic effects of DHT in the skin.[5,6] While the exact mechanism of action remains unknown, *in vitro* studies showed that clascoterone binds to androgen receptors with high affinity and inhibits DHT-stimulated signalling. Clascoterone dose-dependently inhibited DHT-induced lipid synthesis and inflammatory cytokine production in human primary sebocytes.[5,7]

Clascoterone is currently in clinical development for treating acne vulgaris in adolescents and adults. In the phase III clinical trial (NCT02682264), clascoterone, 1%, cream was applied twice daily to the whole face and affected areas of the trunk for up to an additional 9 months.[1]

Key Innovation

Topical clascoterone cream 1% is a novel solution to targeting the androgen component of acne. As the first topical androgen inhibitor potentially available to men and women, clascoterone would avoid the systemic adverse effects of other anti-androgen medications, such as combined oral contraceptive pills (OCP) and spironolactone. For example, OCP can only be used in a subset of women and carries an undesirable side effect profile, while spironolactone's off-label treatment of acne is often not tolerated in men because of its systemic side effects.[5,8] Additionally, increasing antibacterial resistance has made it inadvisable to prescribe topical or systemic antibiotics for acne vulgaris as monotherapy or longer than 3-6 months in patients with acne.[5]

If licensed, clascoterone may offer an additional treatment option in treating people with moderate to severe acne vulgaris in adolescents and adults.

Regulatory & Development Status

Clascoterone does not currently have Marketing Authorisation in the UK or EU for any indication.

Clascoterone is also in phase II clinical development for treating pilonidal sinus disease.[9]

Clascoterone received Marketing Authorisation from the FDA for the topical treatment of acne vulgaris in patients 12 years of age and older in August 2020.[10]

Patient Group

Disease Area and Clinical Need

Acne vulgaris is a chronic inflammatory skin condition affecting mainly areas with the greatest density of pilosebaceous units, including the face (99% of cases), back (60% of cases), and chest (15% of cases). Acne is characterised by blockage and inflammation of the pilosebaceous unit (the hair follicle, hair shaft, and sebaceous gland).[11] A spectrum of lesions may be present, including non-inflammatory open and closed comedones (blackheads and whiteheads, respectively) and inflammatory papules, pustules, nodules, and cysts.[12] The pathogenesis of acne is thought to involve several processes, including the formation of follicular plugs (comedones), androgen-induced seborrhoea (increased sebum production) within the sebaceous follicles, the proliferation of bacteria (such as *Cutibacterium acnes*) within sebum in hair follicles, and inflammation of the pilosebaceous unit.[11,13]

The severity of acne is often categorised as:[14,15]

- mild – mostly whiteheads and blackheads (<20), with a few papules and pustules (<15)
- moderate – more widespread whiteheads and blackheads (20-100), with many papules and pustules (15-50)
- severe –more widespread whiteheads and blackheads (>100), lots of large, painful papules, pustules, nodules (>50), or cysts (>5); might also have some scarring

Risk factors include genetic factors, endocrine disorders, stress, diet, smoking, insulin resistance, oil-based cosmetics, and certain medications.[14,16] The presence of acne can negatively affect quality of life, self-esteem, and mood in adolescents. Acne is associated with an increased incidence of anxiety, depression, and suicidal ideation.[17]

Acne is very common in adolescents and younger adults. About 95% of people aged 11 to 30 are affected by acne to some extent. Acne is most common in girls from the ages of 14 to 17 and in boys from the ages of 16 to 19. Acne often disappears when a person is in their mid-20s, but in some cases, can continue into adult life. About 3% of adults have acne over the age of 35 [14] In the United Kingdom, acne accounts for more than 3.5 million annual visits to general practitioners.[12]

Recommended Treatment Options

The National Institute of Health and Care Excellence (NICE) has the following recommendations for the treatment of acne vulgaris:[18,19]

- a fixed combination of topical adapalene with topical benzoyl peroxide for any acne severity
- a fixed combination of topical tretinoin with topical clindamycin for any acne severity
- fixed combination of topical adapalene with topical benzoyl peroxide, plus either oral lymecycline or oral doxycycline for moderate to severe acne
- topical azelaic acid, plus either oral lymecycline or oral doxycycline for moderate to severe acne
- trimethoprim or an oral macrolide, for people who cannot tolerate or have contraindications to oral lymecycline or oral doxycycline.

Clinical Trial Information	
Trial	NCT02682264; An open-label, long-term extension study to evaluate the safety of cortexolone 17α-Propionate (CB-03-01) cream, 1% applied twice daily in subjects with acne vulgaris **Phase III** - Completed **Location(s):** Three EU countries, USA and other countries **Actual study completion date:** August 2018
Trial Design	Single group assigned, open label
Population	N= 609 (actual); children (9 years and older) and adults, who completed participation in one of the phase III pivotal studies (CB-03-01/25 and CB-03-01/26)
Intervention(s)	Clascoterone topical cream, 1%, applied twice daily to the whole face (about 1 gram) and affected areas of the trunk (if applicable) for up to an additional 9 months.
Comparator(s)	None
Outcome(s)	**Primary outcome:** Number of participants with any local and systemic treatment emergent adverse events (TEAEs) in 52 weeks
Results (efficacy)	-
Results (safety)	72 participants (11.9%) experienced 110 TEAEs that were mild, 51 (8.4%) had 71 TEAEs that were moderate, and 7 (1.2%) had 10 severe TEAEs. The most frequent local skin reactions on the face and trunk were erythema, scaling/dryness, and pruritus, and most were trace/minimal or mild in severity. Nine participants experienced 9 TEAEs that led to study discontinuation. Systemic AEs, including reduced libido and feminization in male participants, were absent in this long-term safety study[20]

Clinical Trial Information	
Trial	NCT02608450; A phase 3, multicentre, randomised, double-blind, vehicle-controlled study to evaluate the safety and efficacy of cortexolone 17α-propionate (CB-03-01) cream, 1% applied twice daily for 12 weeks in subjects with facial acne vulgaris **Phase III** - Completed **Location(s):** USA, Georgia, and Ukraine **Actual study completion date:** April 2018
Trial Design	Randomised, double-blind, parallel assigned
Population	N=708 (actual); individuals aged 9 years or older; moderate to severe facial acne vulgaris with at least 30 to a maximum of 75 inflammatory lesions (papules, pustules, and nodules) and 30 to a maximum of 100 non-inflammatory lesions (open and closed comedones)

Intervention(s)	Clascoterone cream, 1%, applied twice daily for 12 weeks
Comparator(s)	Vehicle cream applied twice daily for 12 weeks
Outcome(s)	**Primary outcome(s):** • Percentage of subjects in each treatment group achieving "success" at week 12, with "success" defined as an Investigator's Global Assessment (IGA) score of "clear(score=0)" or "almost clear(score=1)" and at least a two-point reduction in IGA compared to baseline • Absolute change from baseline in non-inflammatory lesion counts in each treatment group at week 12 • Absolute change from baseline in inflammatory lesion counts in each treatment group at week 12 See trial record for full list of other outcomes.
Results (efficacy)	The trial met the primary efficacy endpoints, more patients receiving clascoterone cream, 1%, vs vehicle achieved treatment success at week 12, 18.4% vs 9.0% respectively.[21]
Results (safety)	Clascoterone cream was well tolerated and demonstrated a similar safety profile to that of the vehicle. 4 TEAES considered related to the use of clascoterone cream were application site pain, oropharyngeal pain, application site dryness, and application site hypersensitivity (all mild in severity).[21]

Clinical Trial Information	
Trial	NCT02608476; A phase 3, multicentre, randomised, double-blind, vehicle-controlled study to evaluate the safety and efficacy of cortexolone 17α-Propionate (CB-03-01) cream, 1% applied twice daily for 12 weeks in subjects with facial acne vulgaris **Phase III** - Completed **Location(s):** Three EU countries, Georgia and Serbia **Actual study completion date**: February 2018
Trial Design	Randomised, double-blind, parallel assigned
Population	N= 732 (actual); individuals aged 9 years or older; moderate to severe facial acne vulgaris with at least 30 to a maximum of 75 inflammatory lesions (papules, pustules, and nodules) and 30 to a maximum of 100 non-inflammatory lesions (open and closed comedones)
Intervention(s)	Clascoterone cream, 1% applied twice daily for 12 weeks
Comparator(s)	Vehicle cream applied twice daily for 12 weeks
Outcome(s)	**Primary outcome(s):**

	• Percentage of subjects in each treatment group achieving "success" at week 12, with "success" defined as an Investigator's Global Assessment (IGA) score of "clear(score=0)" or "almost clear(score=1)" and at least a two-point reduction in IGA compared to baseline • Absolute change from baseline in non-inflammatory lesion counts in each treatment group at week 12 • Absolute change from baseline in inflammatory lesion counts in each treatment group at week 12 See trial record for full list of other outcomes.
Results (efficacy)	The trial met the primary efficacy endpoints, more patients receiving clascoterone cream, 1%, vs vehicle achieved treatment success at week 12, 20.3% vs 6.5% respectively.[21]
Results (safety)	The TEAEs (n = 9) considered related to clascoterone cream were application site dryness, application site erythema, application site hypertrichosis, acne, dermatitis contact, hair colour changes, eye irritation, peritonsillar abscess, and headache. The majority of TEAEs were mild or moderate in severity.[21]

Estimated Cost

The cost of clascoterone is not yet known.

Relevant Guidance

NICE Guidance

- NICE guideline. Acne vulgaris: management [NG198]. June 2021. Last updated December 2023

NHS England (Policy/Commissioning) Guidance

- NHS England. Specialised Dermatology Services (Adults and Children). Service Specification (240501S). August 2024

Other Guidance

- Primary Care Dermatology Society. Guideline on acne vulgaris. 2024.[13]
- American Academy of Dermatology. Guidelines of care for the management of acne vulgaris. 2024.[22]
- NHS Dorset medicine advisory group guidelines. Acne Vulgaris - Primary Care Treatment Pathway. 2018.[23]

Additional Information

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