Farmacam

Comprar AGORA!

www.farmacam.com.br

Clascoterona

Nova alternativa terapêutica para acne e alopecia

DESCRIÇÃO

A **clascoterona** é um antagonista do receptor androgênico usado para o tratamento tópico da acne vulgar. Mais recentemente vem sendo investigada para o tratamento de alopecia androgenética.

MECANISMO DE AÇÃO

A clascoterona é um potente antagonista nos receptores androgênicos e compete com a testosterona e a diidrotestosterona na ligação ao receptor, inibindo, assim, a sinalização que promove o aumento da oleosidade da pele e o aumento da produção de citocinas inflamatórias que culminam com a acne. A alopecia androgenética também é uma condição andrógeno-dependente e altamente genética. A diidrotestosterona (DHT) se liga aos receptores expressos nas células da papila dérmica (DPC) no couro cabeludo para induzir genes que estão associados à alopecia. Ao bloquear essa interação, a clascoterona inibe a transcrição genética e a síntese de IL-6 induzida por DHT, reduzindo a queda capilar.

INDICAÇÕES

- Acne
- Adjuvante no tratamento da alopecia androgenética

DOSE USUAL

A recomendação de uso tópico da **clascoterona** para o tratamento de acne é de 1% e para o tratamento da alopecia androgenética é de 2,5% a 7,5%.

Obs. 1: Baseado em estudos.

Obs. 2: Estudo clínico relata que doses mais baixas de 0,1% e 0,5%, duas vezes ao dia, promoveram mudanças significativas em lesões inflamatórias e não inflamatórias de acne.

Sugestões de Fórmulas

Clascoterona 1%
Creme qsp ..... 30 g
Modo de uso: aplicar nas regiões afetadas, duas vezes ao dia.
Indicação: acne vulgar.

Clascoterona 5%
Solução capilar alcoólica ..... 100 ml
Modo de uso: aplicar nas regiões afetadas, duas vezes ao dia.
Indicação: alopecia androgenética.

Clascoterona

ESTUDOS

Efficacy and Safety of Topical Clascoterone Cream, 1%, for Treatment in Patients With Facial Acne: Two Phase 3 Randomized Clinical Trials.

Acne is a common, multifactorial skin condition, and treatments with novel mechanisms have been elusive. To assess the safety and efficacy of clascoterone cream, 1%, a novel topical androgen receptor inhibitor, in 2 phase 3 randomized clinical trials (CB-03-01/25 and CB-03-01/26). Two identical, multicenter, randomized, vehicle-controlled, double-blind, phase 3 studies conducted from November 2015 to April 2018 evaluated the efficacy and safety of use of clascoterone cream, 1%, in males and nonpregnant females 9 years and older with moderate or severe facial acne as scored on the Investigator's Global Assessment scale. Participants were enrolled if they had 30 to 75 inflammatory lesions and 30 to 100 noninflammatory lesions. Patients were randomized to treatment with clascoterone cream, 1%, or vehicle cream and applied approximately 1 g to the whole face twice daily for 12 weeks. Treatment success was defined as an Investigator's Global Assessment score of 0 (clear) or 1 (almost clear), and a 2-grade or greater improvement from baseline and absolute change from baseline in noninflammatory and inflammatory lesion counts at week 12. Safety measures included adverse event frequency and severity. A total of 1440 patients were randomzied in 2 studies. In CB-03-01/25, 353 participants were randomized to treatment with clascoterone cream, 1% (median [range] age, 18.0 [10-58] years; 221 [62.6%] female), and 355 participants were randomized to treatment with vehicle cream (median [range] age, 18.0 [9-50] years; 215 (60.6%) female); in CB-03-01/26, 369 participants were randomized to treatment with clascoterone cream, 1% (median [range] age, 18.0 [10-50] years; 243 [65.9%] female), and 363 participants were randomized to treatment with vehicle cream (median [range] age, 18.0 [range, 11-42] years; 221 [60.9%] female). At week 12, treatment success rates in CB-03-01/25 and CB-03-01/26 with clascoterone cream, 1%, were 18.4% (point estimate, 2.3; 95% CI, 1.4-3.8; P < .001) and 20.3% (point estimate, 3.7; 95% CI, 2.2-6.3; P < .001) vs 9.0% and 6.5% with vehicle, respectively. At week 12, in both CB-03-01/25 and CB-03-01/26, treatment with clascoterone cream, 1%, resulted in a significant reduction in absolute noninflammatory lesions from baseline to -19.4 (point estimate difference, -6.4; 95% CI, -10.3 to -2.6; P < .001) and -19.4 (point estimate difference, -8.6; 95% CI, -12.3 to -4.9; P < .001) vs -13.0 and -10.8 with vehicle, respectively, as well as a reduction in inflammatory lesions from baseline to -19.3 (point estimate difference, -3.8; 95% CI, -6.4 to -1.3; P < .001) and -20.0 (point estimate difference, -7.4; 95% CI, -9.8 to -5.1; P < .001) vs -15.5 and -12.6 with vehicle, respectively. Adverse events rates were low and mostly mild; the predominant local skin reaction was trace or mild erythema.

Cortexolone 17α-Propionate (Clascoterone) is an Androgen Receptor Antagonist in Dermal Papilla Cells In Vitro.

Cortexolone 17α-propionate (clascoterone) is a novel androgen antagonist that is currently being analyzed in a large phase 2 clinical trial for the topical treatment of androgenetic alopecia (AGA). While the pathogenesis of AGA is still debated, the consensus is that AGA is an androgen-dependent hair disorder with strong genetic links, and that the testosterone metabolite, dihydrotestosterone (DHT), plays a causal role in its development. DHT binds to the androgen receptor (AR) in scalp dermal papilla cells (DPC) to induce AR-mediated transcription of genes that contribute to AGA in genetically predisposed individuals. Several studies have established that clascoterone is a potent antiandrogen that is well tolerated and has selective topical activity. The study described herein elucidates a potential mechanism of clascoterone in AGA. Clascoterone was found to inhibit AR-regulated transcription in a reporter cell line with similar efficacy to the 5α-reductase inhibitor, finasteride. More importantly, when compared with another direct AR antagonist, enzalutamide, clascoterone was significantly better at inhibiting IL-6 synthesis from DHT-stimulated primary cultures of human scalp DPC. Therefore, clascoterone may be an excellent candidate to be the first topical antiandrogen for treating AGA. J Drugs Dermatol. 2019;18(2):197-201.

A Phase 2b, Randomized, Double-Blind Vehicle Controlled, Dose Escalation Study Evaluating Clascoterone 0.1%, 0.5%, and 1% Topical Cream in Subjects With Facial Acne.

Androgens play a key role in acne pathogenesis in both males and females. Clascoterone (CB-03-01, Cortexolone 17α propionate) cream is a topical anti-androgen under investigation for the treatment of acne. The results from a phase 2b dose escalating study are discussed. Methods: Primary objective: to compare the safety and efficacy of topical creams containing clascoterone 0.1% (twice daily [BID]), 0.5% (BID), or 1% (daily [QD] or BID) versus vehicle (QD or BID) in male and female subjects ≥12 years with facial acne vulgaris. Efficacy was assessed by: Investigator's Global Assessment (IGA)--the overall severity of acne using a five-point scale (from 0=clear to 4=severe); inflammatory and non-inflammatory acne lesion counts (ALC); and subject satisfaction with treatment--subjects assessed overall treatment satisfaction using a 4-point scale. Safety assessments: local and systemic adverse events (AEs), physical examination/vital signs, laboratory tests, local skin reactions (LSRs), and electrocardiograms (ECGs). Treatment success required a score of "clear" or "almost clear" (IGA score of 0 or 1) and a two or more-grade improvement from baseline. 363 subjects (N=72, 0.1% BID; N=76, 0.5% BID; N=70, 1% QD; N=70, 1% BID; and N=75, vehicle QD or BID) enrolled. 304 subjects (83.7%) completed the study. Intention to Treat (ITT) population: 196/363 (54.0%) females; 167/363 46.0%) males; (257/363 (70.2%) were white; average age=19.7 years. Demographic and baseline characteristics were similar across all groups. Treatment success at week 12 were highest for the 1% BID (6/70, 8.6%) and 0.1% BID (6/72, 8.3%) groups versus vehicle (2/75, 2.7%). Absolute change in inflammatory

Clascoterona

ESTUDOS

(P=0.0431) and non-inflammatory (P=0.0303) lesions was statistically significant among the treatment groups. The median change from baseline at week 12 in inflammatory and non-inflammatory lesions was greatest in the 1% BID group -13.5 and -17.5, respectively. Similar results were observed for the secondary efficacy endpoints whereby the highest success rate and greatest reduction in lesion counts from baseline to week 12 occurred with 1% BID. 93/363 subjects (25.6%) reported ≥1 AEs; total number of AEs=123 with 2 probably/possibly related to treatment (N=1, 1% QD group). Subjects with ≥1AEs: 0.1% BID=25.0%, 0.5% BID=38.2%, 1% QD=22.9%, 1% BID=18.6%, and vehicle=22.7%. AEs were mostly mild in severity and similar across all groups. Most AEs (93/121 76.8%) resolved by the end of the study. Erythema was the most prevalent LSR; 36.8% had at least minimal erythema at some point during the study. Conclusions: All clascoterone cream concentrations were well tolerated with no clinically relevant safety issues noted. Clascoterone 1% BID treatment had the most favorable results and was selected as the best candidate for further clinical study and development. Two Phase 3 investigations of clascoterone topical cream, 1% for the treatment of moderate-to-severe acne vulgaris in individuals ≥9 years recently concluded. J Drugs Dermatol. 2019;18(6):570-575.

Clascoterone: First Approval.

Clascoterone (Winlevi®) is an androgen receptor inhibitor being developed as a topical cream and solution by Cassiopea (a spin-out company of Cosmo Pharmaceuticals) for the treatment of androgen-dependent skin disorders, including androgenetic alopecia and acne vulgaris. Although the exact mechanism of action of clascoterone for the topical treatment of acne vulgaris is unknown, the drug is believed to compete with the androgen dihydrotestosterone for binding to androgen receptors in the sebaceous gland and hair follicles to attenuate signalling necessary for acne pathogenesis. In August 2020, clascoterone cream 1% received its frst approval in the USA for the topical treatment of acne vulgaris in patients 12 years of age or older. Clinical studies of a diferent formulation of clascoterone (a solution containing a higher concentration of the drug) for the treatment of androgenetic alopecia are underway in Germany and the USA. This article summarizes the milestones in the development of clascoterone leading to this frst approval for the topical treatment of acne vulgaris.

REFERÊNCIAS

SUN, H. Y.; SEBARATNAM, D. F. Clascoterone as a novel treatment for androgenetic alopecia. **Clinical and Experimental Dermatology**, v. 45, n. 7, p. 913-914, 2020. *https://onlinelibrary.wiley.com/doi/10.1111/ced.14292*

HEBERT, Adelaide et al. Efficacy and safety of topical clascoterone cream, 1%, for treatment in patients with facial acne: two phase 3 randomized clinical trials. **JAMA dermatology**, v. 156, n. 6, p. 621-630, 2020. *https://pubmed.ncbi.nlm.nih.gov/32320027/*

NESTOR, Mark S. et al. Treatment options for androgenetic alopecia: Efficacy, side effects, compliance, financial considerations, and ethics. **Journal of cosmetic dermatology**, v. 20, n. 12, p. 3759-3781, 2021. *https://onlinelibrary.wiley.com/doi/epdf/10.1111/jocd.14537*

CARTWRIGHT, Martina et al. A summary of in vitro, phase I, and phase II studies evaluating the mechanism of action, safety, and efficacy of clascoterone (cortexolone 17a propionate, CB-03-01) in androgenetic alopecia. In: **JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY**. 360 PARK AVENUE SOUTH, NEW YORK, NY 10010-1710 USA: MOSBY-ELSEVIER, 2019. p. AB13-AB13.

KIRCIK, Leon H. Androgens and acne: perspectives on clascoterone, the first topical androgen receptor antagonist. **Expert opinion on pharmacotherapy**, v. 22, n. 13, p. 1801-1806, 2021. *https://pubmed.ncbi.nlm.nih.gov/33906537/*

Cassiopea. Cassiopea announces very positive phase II twelve months results for Breezula® (clascoterone) in treating androgenetic alopecia [media release]. 16 Apr 2019. *https://www.cassiopea.com/.*

Cassiopea. Cassiopea announces first patient to be enrolled in phase II trial for the treatment of androgenetic alopecia in females with clascoterone solution [media release]. 13 Nov 2019. *https://www.cosmopharma.com/pipeline/copy-of-breezula.*

DHILLON, Sohita. Clascoterone: first approval. **Drugs,** v. 80, n. 16, p. 1745-1750, 2020. *https://link.springer.com/article/10.1007/s40265-020-01417-6*