ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

SAFETY & TOLERABILITY OF CLASCOTERONE (CORTEXOLONE 17α PROPIONATE, CB-03-01), CREAM FOR THE TREATMENT OF ACNE VULGARIS

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Introduction: Clascoterone cream, 1% is a topical anti-androgen intended for the treatment of acne; its safety and tolerability has been investigated in 26 non-clinical studies, 5 Phase I-, 3 Phase II-, and 2 Phase III studies.

Objective: To provide a comprehensive review of the safety and tolerability of clascoterone cream.

Materials and Methods: Pharmacokinetic, safety and tolerability results were gleaned from 10 clinical studies:
Phase 1 Single dose pharmacokinetics (PK); Repeat dose PK; Steady state PK; Three-week cumulative skin irritation; and a Repeat insult patch test in healthy subjects;
Phase 2 Hypothalamic-Pituitary-Adrenal (HPA)/PK, 14-day repeat-dose; Proof-of-Concept, randomized, double-blind, vehicle-controlled, active-comparator, tretinoin 0.05% cream; Dose-escalating. multi-center, randomized, double-blind, vehicle controlled, 12-week repeat-dose; Phase 3: Two randomized, double-blind vehicle control 12-week-studies
PK blood samples and/or safety assessments including adverse events (AEs), laboratory parameters, and vital signs were collected at predetermined time points specific to each study.

Results: Approximately 2200 subjects have been exposed to clascoterone cream, revealing minimal and mostly mild side effects with no reported severe systemic adverse events. Phase I studies affirmed tolerability with no measurable systemic side effects. Clascoterone permeates to dermal levels, with active ingredient and metabolites quantifiable at very low plasma levels. The patch test revealed no significant irritation; 9.6% (n=24) experienced an Adverse Event (AE), 1 probably related, 2 possibly related; 23 subjects experienced a mild AE. Phase II studies revealed minimal systemic clascoterone absorption with local activity within the hair follicle. Clinical evidence of adrenal suppression under maximal use

conditions was absent. Local side effects were mostly mild. In the Phase III clinical trials, there were no clinically meaningful changes in laboratory or vital sign parameters. Clascoterone cream, 1% was well tolerated with 12/1440 subjects experiencing 14 AE, 12 of which were mild.

Conclusions: Clascoterone topical cream, 1% is well tolerated with minimal systemic exposure.