## STUDY SYNOPSIS

**Title of Study:** A MULTI-CENTER, DOUBLE-BLIND, RANDOMIZED, PLACEBO CONTROLLED, PARALLEL-GROUP STUDY, COMPARING TEST TOPICAL PRODUCT TO BRAND TOPICAL PRODUCT AND BOTH ACTIVE TREATMENTS TO A PLACEBO CONTROL IN THE TREATMENT OF PLAQUE PSORIASIS

**Treatment Duration**: The study treatment period will last for 84 days (12 weeks). A window ± 4 days will be considered acceptable for each scheduled visit following the first visit. Expected study duration is 6 to 9 months.

**Test Product**: Test topical product

**Reference Product**: Brand topical product

**Placebo Control**: Vehicle of the test topical product

**Dose and Mode of Administration**: The assigned investigational product (IP) will be self-applied topically once daily, in the evening, to psoriatic lesions for 84 days (12 weeks). Subjects will apply enough cream (2 mg/cm2) to cover only the psoriasis lesions with a thin film of investigational product.

**Objectives**: To evaluate the therapeutic equivalence and safety of Test topical product and Brand topical product in the treatment of plaque psoriasis

To demonstrate the superiority of the efficacy of the test and reference products over that of the placebo control in the treatment of plaque psoriasis.

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**Design**: Subjects in this randomized, double-blind, placebo controlled, parallel-group, multiple-center study will be randomly assigned in a 1:1:1 ratio to treatment with the test product, reference product or placebo control, respectively.

**Clinical Evaluations will be performed at**:

Visit 1: Screening/Baseline Visit (Day 0);

Visit 2: First Interim Visit (Week 4 / Day 28 ± 4 Days);

Visit 3: Second Interim Visit (Week 8 / Day 56 ± 4 Days);

Visit 4: End of Treatment Visit (Week 12 / Day 84 ± 4 Days)

A window ± 4 days will be considered acceptable for each scheduled visit following the first visit. An Unscheduled Visit is allowed at any time, for any reason, if in the Principal Investigator's opinion it is warranted. If a Subject is discontinued from the study during an Unscheduled Visit, the Unscheduled Visit will be referred to as an Early Discontinuation Visit and all procedures scheduled for Visit 4 will be performed. If the Unscheduled Visit is not an Early Discontinuation Visit (i.e., the Subject will

continue to take part in the study), then all procedures will be performed and treated as an interim visit, with the exception of the collection of Investigational Product and Subject diaries from Subjects.

Subjects will be admitted into the study after informed consent has been obtained, a medical history and physical examination (with vital signs) have been performed and inclusion/exclusion criteria have been met. Subjects must have a clinical diagnosis of rosacea to qualify for inclusion in this study.

At the screening/baseline visit, a facial rosacea grade will be assigned to the subject using the Investigator Global Assessment (IGA) and a baseline lesion count will be performed. The subject will be evaluated for signs and/or symptoms of local irritation and telangiectasia.

At each subsequent visit the signs and/or symptoms of local irritation will be evaluated for the subject and the subject's facial rosacea will be assessed using the IGA, the subject's lesions will be counted and these results will be documented.

Safety will be assessed by the monitoring of all adverse events.

**Evaluations:**

- Investigator's Global Assessment (IGA).
- PASI
- Application site reactions such as erythema, dryness, burning/stinging, erosion, edema, pain and itching will be recorded at each visit to allow a comparison between treatment groups.

**Study Population**:

**Key Inclusion Criteria**

1. Male and non-pregnant females aged ≥18 years with a clinical diagnosis of stable (at least 6 months) plaque psoriasis involving at least 2% and no more than 20% body surface area (BSA), not including the scalp and intertriginous areas.
2. An Investigator's Global Assessment (IGA) of disease severity of at least moderate severity (score ≥ 3) as an overall assessment of all plaque psoriasis lesions to be treated.
3. A minimum plaque elevation of at least moderate severity per the PASI scoring (grade ≥ 3) at the target lesion site. The most severe lesion at baseline will be identified as the target lesion.

**Criteria for Evaluation:**

**Primary Endpoints**:
The proportion of Subjects with treatment success (defined as "absent", "very mild", or "mild disease", a score of 0, 1 or 2, within the treatment area") on the IGA at the week 12 visit (study day 84).

**Secondary Endpoint**:
1. The proportion of Subjects with disease severity at the week 12 visit (study day 84) consistent with "absent" or "very mild", a score of 0 or 1, within the treatment area" on the IGA, and
2. The proportion of Subjects with target site plaque elevation, scaling, and erythema scores of ≤ 1 on the PASI at the week 12 visit (study day 84).

**Statistical Methods**:

**Demonstration of Bioequivalence**
Bioequivalence will be established if the 90% continuity-corrected confidence interval of the test - reference difference for the primary endpoint (success proportion) is contained within the interval [-0.20, +0.20] in the PP population.

**Demonstration of Superiority**
The test product and reference product will be compared to the placebo group using a continuity-corrected Chi-square tests for statistical superiority at $p<0.05$ with regard to the primary endpoint using the modified intent-to-treat (mITT) study population and Last Observation Carried Forward (LOCF).

**Analysis of Primary Endpoint**
The evaluation of the primary endpoint will be based on the proportion of Subjects at week 12 with treatment success, defined as “absent”, “very mild”, or “mild disease”, a score of 0, 1 or 2, within the treatment area on the IGA.

**Analysis of Secondary Endpoints**
The following secondary endpoints will be evaluated for Bioequivalence and Superiority:

1. The proportion of Subjects with disease severity at the week 12 visit (study day 84) consistent with “absent” or “very mild disease”, a score of 0 or 1, within the treatment area on the IGA,

2. The proportion of Subjects with target site plaque elevation, scaling, and erythema scores of ≤ 1 on the PASI at the week 12 visit (study day 84).

**Analysis of Application Site Reactions**
A descriptive analysis comparing the application site reactions for each treatment group will be conducted to ensure that the test product is not worse than the reference product with regard to the expected and unexpected application site reactions.

**Summary of Subjects who Terminate Prematurely.**
Reasons for premature termination will be summarized by treatment group.

**Concomitant Medication**
The start and stop date of concomitant medication use during the study will be provided in the data set in addition to the reason for the medication use.

**Safety Analyses**
Safety analyses will be conducted on the safety population. Incidence of all adverse events reported during the study will be summarized using the MedDRA dictionary by treatment group, body system, severity and relationship to study drug.

The report of AEs will include date of onset, description of the AE, date of resolution, and suspected relationship to the study treatment. Formal statistical evaluation(s) of the comparability of the two active treatment groups will be conducted with regard to the frequency and severity of any AE that occurs in at least 5% of the Subjects in either active treatment group.

## STUDY VISIT SCHEDULE

| Visit Number | Visit 1 | Visit 2 | Visit 3 | Visit 4 |
|---|---|---|---|---|
| Visit Day | Day 0 | Day 28±4 | Day 56±4 | Day 84±4 |
| Visit Name | Baseline | Interim | Interim | EOT / UV / ED [1] |
| Informed Consent | X | | | |
| Demographics | X | | | |
| Medical History | X | | | |
| Concomitant Medication | X | X | X | X |
| Physical Exam including Vital Signs | X | | | |
| % BSA assesment | X | | | |
| Urine Pregnancy Test [2] | X | X | X | X |
| Inclusion/Exclusion Criteria | X | | | |
| Local Irritation Assessment | X | X | X | X |
| Target Lesion Assessments (PASI) | X | X | X | X |
| Investigator's Global Assessment | X | X | X | X |
| Randomization | X | | | |
| Adverse Event Reporting | | X | X | X |
| Drug Dispensing / Diary Dispensing | X | X | X | |
| Drug Return / Diary Collection | | X | X | X [3] |
| Diary Review | | X | X | X |
| Drug Accountability | X | X | X | X |
| Review of Instructions with Subjects (including Diary Completion Instructions) | X | X | X | |
| Review of Subject Compliance | | X | X | X |

[1] EOT - End of Treatment, UV - Unscheduled Visit, ED - Early Discontinuation Visit
[2] The urine pregnancy test is to be conducted for women of child-bearing potential.
[3] Investigational product and Subject diaries will be collected from Subjects during Visit 4 (End of Treatment Visit) or the Early Discontinuation Visit.