CLINICAL STUDY REPORT SYNOPSIS

Name of Sponsor/Company:	VERISFIELD (UK) Ltd, Greek branch
Name of Finished Product:	ERYBENZ® Benzoyl peroxide + Erythromycin gel (5+3)% w/w
Name of Active Ingredient(s):	Benzoyl peroxide and Erythromycin
ATC Code:	D10AF52
Title of Study: Multicenter, randomized, double-blind, comparative with the reference product clinical study to evaluate the efficacy and safety of the therapy with the combination of benzoyl peroxide-erythromycin/Verisfield, gel, (5+3)% w/w for the topical treatment of acne vulgaris	
Principal Investigators: • A' Clinic: A. Katsambas, MD, PhD • B' Clinic: N. Zakopoulou, MD • C' Clinic A. Petridis Venereal and Skin Diseases Hospital, Andreas Syggros, I. Dragoumi 5, 161 21, Athens, Greece	
Study centers: Venereal and Skin Diseases Hospital , Andreas Syggros, I. Dragoumi 5, 161 21, Athens, Greece, • First, A' Dermatological Clinic of University of Athens, Andreas Syggros Hospital • Second, B' Department of Dermatology, Andreas Syggros Hospital • Third, C' Department of Dermatology, Andreas Syggros Hospital	
Publication (reference): N/A	
Phase of Development	Therapeutic equivalence
Study period: ***(date of first enrollment)*** ***(date of last completed)***	 8/11/2010 (first patient enrolled) 3/8/2011 (last visit of last patient)
Objectives:	The purpose of this study was to provide evidence that the Verisfield formulation Benzoyl peroxide-Erythromycin/Verisfield, gel (5 +3) % is therapeutically equivalent to BENZADERMINE/Laboratoires Pharmaceutiques Trenker, gel, benzoyl peroxide-erythromycin (5 +3) %.
Methodology:	This was a randomized, double-blind, parallel group, therapeutic equivalence study.
Number of patients (planned and analyzed):	Planned: 90 Analyzed: 83 (Full analysis set), 78 (Per protocol set), 74 (Per protocol set, outliers excluded)
Diagnosis and main criteria for inclusion: Volunteers, aged 12 - 35 years old, diagnosed with mild or moderate acne, who had acne lesions, divided into regions (forehead, cheeks, jaw). Acne lesions consisting of inflammatory and non inflammatory acne characteristics, but not cysts and nodules. Patients that were willing, in good physical condition based on their medical history and were able to attend the scheduled study visits.	
Test product: ***Dose:*** ***Mode of administration:*** ***Batch Number:***	ERYBENZ® Benzoyl peroxide + Erythromycin gel (5+3)% w/w 0.5 g of gel (pea size) was spread to the affected skin surface with dimensions 10cm x 10cm' Topical application 450050/450040
Reference product: ***Dose:*** ***Mode of administration:*** ***Batch number:***	BENZADERMINE 30mg-50mg/g, gel Erythromycin – benzoyl peroxide (Reference), Laboratoires Pharmaceutiques Trenker 0.5 g of gel (pea size) was spread to the affected skin surface with dimensions 10cm x 10cm Topical application 09C30
Duration of treatment:	60 days ± 2 days

Criteria for evaluation:

Efficacy:

Difference in total number of inflammatory (papules, pustules) and non-inflammatory (comedones) acne lesions between 1st and 3rd visit.

Efficacy: Secondary parameters:

- Scale IGII (Investigator Global Improvement Index)
- Scale PGII (Patient Global Improvement Index)

Safety: Main Parameters:

- Topical reactions
- Adverse events

Statistical methods: The assessment of therapeutic equivalence of the two products was performed in comparing the difference in the total number of lesions of the first visit, minus the total number of lesions of the third visit (difference in lesions) between the two products. The rule of rejecting the null hypothesis was based on a 90% Confidence Interval (CI) and more specifically, the null hypothesis (no equivalent) was rejected if the 90% CI falls entirely within the prescribed limits.

Summary – Conclusions:

EFFICACY RESULTS:

Primary parameter – Therapeutic Equivalence

The point estimate of the difference between the reference and the test formulation, $\bar{x}_R - \bar{x}_T$, was almost zero in all sets analyzed (full analysis set, per protocol set with and without outliers). This indicates that the best estimate for the difference between the test and the reference formulations was zero.

The 90% CI lied within the pre-specified acceptance limits, (-0.43 μ_α, 0.43 μ_α), as well as narrower acceptance limits (-0.30 μ_α, 0.30 μ_α), in all sets analyzed (full analysis set, per protocol set with and without outliers).

As far as the per protocol analysis set is concerned, the point estimate of the difference between the reference and the test formulation was 0.454. The 90% CI for the difference between the mean reductions in the total lesions counts of the two treatment arms which lies within pre-specified acceptance limits (-6.778, 6.778), was (-3.626, 4.534). Moreover, it should be noted that the 90% CI (-3.626, 4.534) lied also within the narrower acceptance limits (-0.30 μ_α, 0.30 μ_α), which equals to (-4.729, 4.729).

Therefore, according to the statistical methodology of this study as described in the study protocol and expanded in the statistical analysis plan, the hypothesis of therapeutic equivalence of the two products was acceptable.

Secondary parameter – IGII

For the full analysis set, Mann Whitney test showed no statistically significant difference between the two treatment groups (Mann Whitney test p-value=0.266).

For the per protocol set, Mann Whitney test showed no statistically significant difference between the two treatment groups (Mann Whitney test p-value = 0.177).

Secondary parameter – PGII

For the full analysis set, Mann Whitney test showed no statistically significant difference between the two treatment groups (Mann Whitney test p-value=0.250).

For the per protocol set, Mann Whitney test showed no statistically significant difference between the two treatment groups (Mann Whitney test p-value = 0.138).

SAFETY RESULTS:

The two products are equivalent in terms of safety by comparing the adverse events reported during the study. Regarding the local reactions, Mann Whitney test showed no statistically significant difference between the two treatment arms at the second and third visit.

This study reflects the excellent safety profile of the product.

Conclusion:

Verisfield's formulation ERYBENZ® Benzoyl peroxide + Erythromycin gel (5+3)% w/w is therapeutically equivalent to BENZADERMINE 30mg-50mg/g, gel, Laboratoires Pharmaceutiques Trenker in terms of safety and efficacy.

Date of the report:	14 November 2011