**Pierre Fabre Dermatologie**
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# 1. TITLE PAGE

## ABRIGED CLINICAL STUDY REPORT

**Efficacy and safety of 8% clobetasol nail lacquer formulation versus vehicle in nail psoriasis**

**Investigational product**: V0074VE (clobetasol)

**Study Design**: single-centre, double-blind, vehicle-controlled, intraindividual pilot study

**Protocol number**: V00074 VE 2 02 04A
**EudraCT No.:** 2006-006569-18
**Phase of development**: II

**Date of first enrolment**: May 03, 2007.

**Date of last completed**: November 12, 2007

**Coordinator Investigator**: Pr J.P. Ortonne (CHU de l'Archet 2 – service de dermatologie F-06 202 Nice - ☎ 33 (0) 492 036 240)

**Sponsor Representatives for study report**: Clinical study coordinator: M. Condomines (☎ 0 534 506 209)
Project Statistician: C. Lauze (☎ 0 562 245 463)
Medical Writer: C. Touzet M.D. (☎ 0 534 506 353).

**Date of report: February 20, 2012**

Study performed in compliance with Good Clinical Practice.

# 2. SYNOPSIS

| | | |
|---|---|---|
| **Name of Company: Pierre Fabre Dermatologie** | **Individual Study Table Referring to Module 5 of the Dossier** | **(For National Authority Use Only)** |
| **Name of finished product:** | | |
| **Name of active substance** *(or ingredient)***:** | **Vol.: .....Page: .....** | |
| **Title of study:** | **Efficacy and safety of 8% clobetasol nail lacquer formulation versus vehicle in nail psoriasis** | |
| Coordinating Investigator**:** | Pr J.P. Ortonne (CHU de l'Archet 2 – service de dermatologie F-06 202 Nice). | |
| **Study centre:** | CHU de l'Archet 2– service de dermatologie F-06 202 Nice. | |
| **Publication :** | No publication concerning the study was written to date. | |
| **Studied period :**<br>**date of first enrolment**<br>**date of last completed** | 6 months<br>May 03, 2007.<br>November 12, 2007. | **Phase of development: II** |
| **Objectives:** | Primary objective: to assess the efficacy of a 24-week daily application of clobetasol 8% nail lacquer versus placebo in fingernail psoriasis.<br>Secondary objectives :<br>- to assess local and general safety of clobetasol 8% nail lacquer,<br>- to assess systemic exposure to clobetasol 8% nail laquer 24-week treatment. | |
| **Methodology:** | Single-centre, double-blind, placebo-controlled, intraindividual pilot study to compare clobetasol 8% nail lacquer with the placebo in patients with finger nail psoriasis (clobetasol 8% left --placebo right versus placebo left – clobetasol 8% right).<br>5 visits, including a phone contact. | |
| **Number of patients :** | 30 patients were planned to be selected. 30 patients were selected and randomised, respectively 15 in each randomised group. | |
| **Diagnosis and main criteria for inclusion:** | The main inclusion criteria were ambulatory patients over 18 year-old, men or women, suffering from psoriasis skin disease for at least 6 months, with at least one fingernail psoriatic involvement on each hand,, with at least one nail on the same finger of each hand (both considered as target nails) presenting an onycholysis area ≥ 25% or/and a subungual hyperkeratosis ≥ 2 mm. Patients were without any topical treatment for nail psoriasis (corticoids, retinoids, vitamin D derivatives) or any systemic treatment for psoriasis (biologics, methotrexate, cyclosporin, retinoids, PUVA therapy) within one month preceding the inclusion visit, and without any injection of corticosteroids in the nail within the two months preceding the inclusion visit. | |
| **Test product, Dose, Mode of administration,, Batch number:** | clobetasol 8% , nail lacquer.<br>CLP060, expiry date February 28, 2009. | |
| **Duration of treatment:** | 24 weeks. | |
| **Reference therapy, Dose, Mode of administration, Batch number:** | placebo, nail lacquer<br>CLP059, expiry date February 28, 2009. | |
| **Criteria for evaluation** *(1/2)***:** | **Primary efficacy criterion**<br>– dEPGA *(dynamic expert physician global assessment) of the target nails (defined as a nail on the same finger of each hand with an onycholysis area ≥ 25% or/and a subungual hyperkeratosis≥ 2 mm)* and of each hand at Week 24. | |
| | ***V00074 VE 2 02 04A* – synopsis page 1/2** | |

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**Criteria for evaluation** *(2/2)***:**

Secondary efficacy criteria

- dIPGA *(dynamic investigator physician global assessment)* of the target nails and of each hand at Weeks 6, 12, 24,
- sEPGA *(static Expert Physician Global Assessment)* of the target nails and of each hand at baseline and Week 24
- sIPGA *(static investigator physician global assessment)* of the target nails and of each hand at baseline, Weeks 6, 12, 24.
- Clinical score *(for nail matrix,pitting, trachyonychia, red spots in lunula and for nail bed onycholysis, splinter hemorrhages, salmon patch or oil drop, subungual hyperkeratosis assessed by Inog physician)* for each hand at baseline, Weeks 6, 12, 24.
- number of cured or almost cured nails and cured or almost cured hands at Week 24
- improvement of onycholysis and hyperkeratosis at baseline, Weeks 6, 12, 24.
- Patient global self-assessment at Week 24.

Compliance at each visit from V1 onward,

Safety

- adverse events (except baseline) and local tolerance (periungual irritation, skin atrophy, number of telangiectasia) at each visit,
- blood clobetasol measurement at baseline, Weeks 12 and 24.
- Physical Examination at baseline and Week 24

**Statistical methods:**

- Baseline characteristics: $\chi^2$ test, Fischer's exact test, Student's t test, Cochran Mantel-Haenzel test. normality tests Shapiro Wilks test or Wilcoxon's rank test,
- dEPGA, dIPGA, sEPGA, sIPGA, number of healthy nails, Patient global self-assessment, local tolerance: Wilcoxon test using Koch's method (**Koch 1972**),
- Clinical score .parametric, improvement of onycholysis and hyperkeratosis analysis of variance for cross over design,
- healthy hands, compliance, adverse events physical examination: descriptive statistics,
- clobetasol measurement at baseline, Weeks 12 and 24.

**Summary - Conclusions:**

Thirty (30) patients were selected, randomised and treated with both study drugs, each on a different hand. One of these patients withdrew prematurely from the study (see safety results). 20/30 were men and 10/30 were women, aged 53.1 (sd = 13.5) years on average, ranging from 23.4 to 73.9 years old. Patients suffered from psoriasis for 171.8 (sd = 112.55) months ranging from 11.6 to 416.8 months.

**Efficacy results**

No clinically relevant difference was observed between the two treatments in regard to the main criterion (dEPGA), as well as in regard to the other efficacy criteria.

**Safety results**

Thirty-two (32) treatment emergent adverse events were experienced by **17** patients. No serious adverse event was notified during the study period. One of these patients withdrew prematurely from the study due to a severe cutaneous psoriasis (placebo left-clobetasol right).

Among these adverse events, 6 in 6 patients were clinically relevant, *i.e.* 5 patients with exacerbations of the cutaneous psoriasis, 1 of them (premature withdrawal) presented several localisations of the psoriasis and a Willebrand disease. The 6$^{th}$ patient suffered from a Waldenström's macroglobulinaemia. None of these adverse events was considered by the investigator as drug related. The only adverse event considered by the investigator as related to the study drug was a blue coloration of all the nails occurred in 1 patient.

Clobetasol was detected? in blood in 13 patients, respectively in 3 patients at V3, in 5 patients at V5 and in 5 patients at both V3 and V5. Values were ranged between 0.0522 ng.mL$^{-1}$ and 0.249 ng.mL$^{-1}$.

**Conclusion**

The descriptive analysis of the efficacy data did not evidence any difference between clobetasol 8% nail lacquer and placebo. Clobetasol 8% nail lacquer used once daily for 24 weeks is safe and well tolerated.

**Date of report: February 20, 2012**