Pierre Fabre Dermatologie
Represented by the Institut de Recherche Pierre Fabre (IRPF)
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1. TITLE PAGE

CLINICAL STUDY REPORT

EFFICACY AND TOLERANCE OF V0071GM IN INFLAMMATORY SEBORRHEIC DERMATITIS OF THE SCALP

Single centre, intra-individual, half-head-randomised, open, investigator-masked initiation therapy, reference therapy -controlled, proof of concept study.

Investigational Product:	**V0071GM: 0.050% betamethasone (dipropionate) shampoo**
EudraCT Number:	2007-007088-25
Protocol Number:	V00071 GM 201 1A
Phase of Development:	Phase IIa
Date of First Enrolment:	05-May-2008
Date of Last Completed:	23-Jan-2009
Principal Investigator:	Catherine QUEILLE-ROUSSEL, MD *CPCAD, Hôpital L'Archet 2* – 151 route de Saint Antoine de Ginestière – F06200 NICE Tel +33 (0)4 92 03 64 88
Sponsor Representatives for Study Report:	Head of Therapeutic Area: Alain DELARUE, MD, Tel +33 (0)5 34 50 61 88
Date of Report:	22 March 2013

Clinical trial performed in compliance with Good Clinical Practice

2. SYNOPSIS

Name of the Company: Pierre Fabre Dermatologie	**Individual Study Table Referring to part: of the Dossier:**	**(FOR NATIONAL Authority Use only)**
Name of finished product: Not applicable	**Volume:**	
Name of Active Ingredient: 0.050% betamethasone (dipropionate) shampoo (V0071GM)	**Page:**	

Title of Study: "Efficacy and tolerance of V0071GM in inflammatory seborrheic dermatitis of the scalp"

Principal Investigator: Catherine QUEILLE-ROUSSEL, MD

Study centre:
CPCAD – Centre de Pharmacologie Clinique Appliquée à la Dermatologie
Hôpital L'Archet 2 – 151 route de Saint Antoine de Ginestière – BP 3079 – 06202 NICE CEDEX 3 - France

Publication: Not written to date

Study period: 8.5 months	**Phase of development:**
Date of first enrolment 05-May-2008 *Date of last completed*: 23-Jan-2009	Phase IIa

Objectives:

Main objective: To assess the superiority of V0071GM, a 0.050% betamethasone (dipropionate) shampoo, over a 2% ketoconazole (foaming) gel alone in treating inflammatory seborrheic dermatitis (SD) of the scalp.

Secondary objectives:

To assess the efficacy of V0071GM in treating inflammatory SD of the scalp.

To assess the local and general tolerability/safety of V0071GM and the ketoconazole gel.

Methodology:

Single-centre, intra-individual, half-head-randomised, open, investigator-masked, reference therapy-controlled, proof of concept study.

Patients were randomised for the side of application of each of the following treatments:

- 0.05% betamethasone (dipropionate) shampoo (V0071GM) twice weekly application as initiation therapy for 2 weeks, then associated with the 2% ketoconazole gel once weekly for each product for 2 weeks, then the 2% ketoconazole gel alone once weekly application for 4 weeks in maintenance therapy.
- 2% ketoconazole gel alone twice weekly application in initiation therapy for 4 weeks, then once weekly application for 4 weeks in maintenance therapy.

Seven assessment visits were planned: V1/D-14 (selection visit), V2/D0 (inclusion visit), V3/D7, V4/D14, V5/D28 (end of initiation therapy), V6/D42, V7/D56 (end of study visit = end of maintenance therapy).

Number of patients:

As planned, 40 patients were randomised and all were analysed.

Diagnosis and main criteria for inclusion:

Female and male patients aged 18 to 65 years (exclusive), with inflammatory SD bilateral lesions of the scalp involving ≥ 30% of the scalp area, with a ≥ 5-point sum score (erythema + scaling) on an 8-point grading score, and no more than 1-point difference between each half-head area score.

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Test product:
Name: V0071GM (0.050% betamethasone [eq. 0.064% betamethasone dipropionate] shampoo)
Dosage: twice weekly application for the first 2 weeks , then once weekly application for the next 2 weeks
Mode of administration: topical route,
Dose: 3g (3 ml), on a half head wet scalp
Application duration: 5 min with massage, then rinsing
Duration of treatment: 4 weeks (1st to 4th week of the total 8-week study treatment duration) with a total of 6 applications.
0.050% betamethasone shampoo (V0071GM) was applied by a third person from the study team at the investigating centre.
Batch number: SB0645 expiry (EXP). 10/2008

Reference product:

Name: ketoconazole (2% foaming gel; Ketoderm®)

1) Side initiated with V0071GM:
Dosage: once weekly application for 6 weeks since the 3rd study week
Mode of administration: topical route
Dose: 3 g (a half sachet) on a half head or a sachet (6 g) on the total head.
Application duration: 5 min on a wet scalp, then rinsing
Duration of treatment: 6 weeks (3rd to 8th week of the total 8-week study treatment duration) with a total of 6 applications.
- Initiation therapy: ketoconazole was applied by a third person from the study team at the investigating centre for 2 weeks (3rd and 4th weeks of treatment).
- Maintenance therapy: ketoconazole was applied by the patient at home for 4 weeks.

2) Side treated by ketoconazole alone:
Dosage: twice weekly application for 4 weeks as initiation therapy then once weekly application for 4 weeks as maintenance therapy.
Mode of administration: topical route
Dose: 3g (a half sachet) on a half head or 6g (a sachet) on the total head.
Application duration: 5 min on a wet scalp, then rinsing
Duration of treatment: 8 weeks (i.e., the total study treatment duration) with a total of 12 applications.
- Initiation therapy: ketoconazole was applied by a third person from the study team at the investigating centre for 4 weeks (from the 1st to the 4th week treatment).
- Maintenance therapy: ketoconazole was applied by the patient at home for 4 weeks.
Batch number: 7LL5G00 EXP. 12/2009

Associated product:
Soft non medical shampoo (*Ducray Extra-doux*), to wash the scalp and hair: up to 2 to 3 times a week during the study period.

Evaluation criteria (1/2):

Efficacy

Primary efficacycriterion:

Change from baseline in the clinical global sum score on each half head (i.e., Erythema + Scaling scores [see definitions hereafter]) at D14

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Evaluation criteria (2/2):

Secondary efficacy criteria:

- Change in the Clinical Global Sum score (CGSS) on each half head (erythema + scaling) at D7 , D28, D42 and D56,
- Percentage of Patients Completely Cured (CGSS = 0) , by half head, at D7, D14, D28, D42 and D56 ,
- Percentage of Patients Almost Cured (CGSS $\leq$ 2), by half head, at D7, D14, D28, D42 and D56,
- Change in the Scalp Erythema score on each half head at D7, D14, D28, D42 and D56 on a 5 point grading score as following:

  4 = very severe erythema
  3 = severe erythema
  2 = moderate erythema
  1 = mild erythema
  0 = no erythema

- Change in the Scalp Scaling score on each half head at D7, D14, D28, D42 and D56 on a 5 point grading score as following:

  4 = very severe scaling
  3 = severe scaling
  2 = moderate scaling
  1 = mild scaling
  0 = no scaling

- Change in the Scalp Area score on each half head at D7, D14, D28, D42 and D56 on a 5 point grading score as following:

  4 = $\geq$ 70%
  3 = $\geq$ 50% but < 70%
  2 = $\geq$ 30% but < 50%
  1 = $\geq$ 10% but < 30%
  0 = < 10%

- Patient Global Efficacy Assessment choosing the best scalp side improvement at D14, D28 and D56.

Safety:

- Local (scalp and face) tolerability: dryness, itching, burning sensation, papulopustules, pain, seborrhoea (mil/moderate/marked) at each visit
- General tolerability/safety (adverse events only) at each visit

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Summary – Conclusions:

Population characteristics and patient disposition:

Fifty-four (54) patients were screened and 40 were randomised. All the 40 randomised patients (21 females and 19 males, aged 19 to 62 years [mean±SD: 35.7±11.3 years]) completed the whole study:

Efficacy results:

Primary criterion:
At D14, the **mean decrease from baseline** in the **CGSS** with V0071GM was statistically significantly greater than with ketoconazole (-3.4 vs -3.9 with ketoconazole and with V0071GM, respectively; p=0.0060)

Secondary criteria:

CGSS over time
There was a statistically significant difference between treatments in favour of V0071GM at D7 (-2.2 vs -2.8, p=0.0009) and D28 (-4.0 vs -4.4, p=0.0334). At D56, there was a significant difference in favour of the reference product alone (-3.5 vs -3.3, p=0.0163).

Scalp Erythema Score (SES)
There was no statistically significant difference between treatments until D42. At D56, there was a significant difference in favour of the reference treatment (-1.23 vs -1.1, p=0.0251).

Scalp Scaling Score (SSS)
There was a statistically significant difference between both treatments in favour of V0071GM at D7 (-1.2 vs -1.8, p=0.0006) and at D14 (-2.1 vs -2.5, p=0.0021). At D28 and D42 there was no significant difference between treatments but at D56 the mean decrease from baseline was statistically significantly greater for ketoconazole than for V0071GM (-2.3 vs -2.8, p=0.0274).

Scalp Area Score (SAS)
At either post-baseline time point, the SAS decreased from baseline with both treatments with no statistically or clinically significant between-treatment difference .

Patients completely cured
There was no statistically significant difference between treatments in the proportion of patients completely cured at either time point. However, there was a clinically relevant difference in favour of V0071GM at D14 (30.0% vs 17.5%) and D28 (55.0% vs 35.0%).

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Patients almost cured

A statistically significant difference between treatments in the proportion of patients almost cured was observed at D7 and was in favour of V0071GM (29.7% vs 59.5%, p=0.0432). There was no statistically or clinically significant difference at the other time points.

Patient global efficacy assessment

There was a statistically significant difference in favour of V0071GM at D14 (28.2% of most improved side vs 0%, p=0.0009) and at D28 (32.5% of most improved side vs 7.5%, p=0.0124).

Safety results:

A total of 24 AEs in 18 patients was reported during the study. None of these events was related to the study products except two AEs (Headache) where the relationship to study treatment was considered 'unassessable'.

There were neither SAEs, nor AEs leading to the treatment discontinuation.

The analysis of the local tolerability reported by the patients shows a decrease in the severity of dryness, itching, burning sensation, papulopustules and pain from D0 to D56. The number of patients in each category was almost the same for ketoconazole only and V0071GM-initiated treatment sides, except for itching at D28 that was less frequent on the V0071GM-initiated treatment side (17.5% vs 37.5%). No clinical sign of irritation was reported.

Conclusion:

The study demonstrated that the therapeutic effect of V0071GM applied twice-weekly on SD is superior to that of ketoconazole applied twice-weekly after 2 weeks of treatment. This superiority tended to be maintained when administered once-weekly in alternation with ketoconazole once weekly as compared to ketoconazole alone applied twice weekly after 2 additional weeks of treatment.
Local and general tolerability of both products was good.

Date of the report: 22 March 2013