**SYNOPSIS**

Name of Sponsor/Company: LEO Pharma A/S

Name of Finished Product: Taclonex® Scalp Topical Suspension and Daivobet®/Dovobet®/Xamiol® gel

Name of Active Ingredient: Calcipotriol 50 mcg/g plus betamethasone 0.5 mg/g (as dipropionate)

Title of Trial:
Safety and Efficacy of Calcipotriol plus Betamethasone Dipropionate Gel in Adolescent Subjects (Aged 12 to 17 Years) with Scalp Psoriasis.

Investigator:
United Kingdom was the international coordinating investigator.

Trial Centres:
17 centres; 7 in Canada, 5 in France, and 5 in the United Kingdom.

Publication:
None at the time of this clinical study report.

Trial Period:
Date of first enrolment (informed consent signed and CRF started): 22-Nov-2010
Date of last completed: 15-Oct-2012

Phase of development: 2

Objectives:
Primary objective
The primary objective was to evaluate the safety of once daily use of calcipotriol (50 mcg/g) plus betamethasone (0.5 mg/g) (as dipropionate) gel in adolescent subjects (aged 12 to 17 years) with scalp psoriasis.

Secondary objective
The secondary objective was to evaluate the efficacy of once daily use of calcipotriol (50 mcg/g) plus betamethasone (0.5 mg/g) (as dipropionate) gel in adolescent subjects (aged 12 to 17 years) with scalp psoriasis.

Methodology:
This was an international national, multi-centre, prospective, non-controlled, open-label, single-group, 8-week trial in adolescent subjects (aged 12 to 17 years) with scalp psoriasis. The subjects were treated with calcipotriol 50 mcg/g plus betamethasone 0.5 mg/g (as dipropionate) gel once daily for up to 8 weeks.

Number of Subjects (Planned and Analysed):
A sufficient number of subjects were enrolled to ensure 70 subjects were evaluable for evaluation of calcium metabolism. In total, 78 subjects were treated with at least 1 application of investigational product and 74 subjects completed the trial.
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**Diagnosis and Main Criteria for Inclusion:**

- **Psoriasis on the scalp**
  - Signed informed consent given by parent(s) or legal guardian, or by the subject (according to national law) following their receipt of verbal and written information about the trial.
  - Subjects will receive verbal and written information and will provide written assent to the trial.
  - Subjects 12 to 17 years of age.
  - Either sex.
  - Any race or ethnicity.
  - Clinical signs of psoriasis vulgaris on trunk and/or limbs, or earlier diagnosed with psoriasis vulgaris on trunk and/or limbs.
  - At SV2 and Visit 1 a clinical diagnosis of scalp psoriasis which is:
    - amenable to topical treatment with a maximum of 60 g of study medication per week, and
    - of an extent of more than or equal to 10% of the scalp area
    - of at least moderate severity according to the investigator’s global assessment
  - A serum albumin-corrected calcium below the upper reference limit at SV2.
  - Females of child-bearing potential must have a negative urine pregnancy test result and must agree to use a highly effective method of contraception during the trial.

**Investigational Product, Dose and Mode of Administration, Batch Number:**

LEO 80185 gel, calcipotriol 50 mcg/g plus betamethasone 0.5 mg/g (as dipropionate), once daily, cutaneous

Batch numbers used: [redacted] and [redacted]

**Duration of Treatment:**

8 weeks.

**Reference Therapy, Dose and Mode of Administration, Batch No:**

No reference therapy was used.
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Criteria for Evaluation:
The primary response criteria were:
- Adverse drug reactions (ADRs).
- Change in albumin-corrected serum calcium from Baseline (SV2) to Week 4, Week 8, and end of treatment.
- Change in 24-hour urinary calcium excretion from Baseline (SV2) to Week 4, Week 8, and end of treatment.
- Change in urinary calcium:creatinine ratio from Baseline (SV2) to Week 4, Week 8 and, end of treatment.

The secondary safety response criteria were:
- Adverse events (AEs)
- Change in serum phosphate from Baseline (SV2) to Week 4 and Week 8
- Change in 24-hour urinary phosphate excretion from Baseline (SV2) to Week 4 and Week 8
- Change in urinary phosphate:creatinine ratio from Baseline (SV2) to Week 4 and Week 8
- Change in 24-hour urinary hydroxyproline excretion from Baseline (SV2) to Week 4 and Week 8
- Change in urinary hydroxyproline:creatinine ratio from Baseline (SV2) to Week 4 and Week 8
- Change in plasma PTH from Baseline (SV2) to Week 4 and Week 8
- Change in other laboratory parameters from Baseline (SV2) to Week 4 and Week 8
- Reasons for withdrawal
- Change in blood pressure and heart rate from Baseline (SV2) to Week 4 and Week 8

The secondary efficacy response criteria were:
- Subjects with controlled disease (i.e., clear or almost clear) according to the investigator’s global assessment of disease severity at Weeks 2, 4, 8, and end of treatment.
- Percentage change in Total Sign Score (TSS; sum of severity scores for each individual clinical sign, redness, thickness, and scaliness) from Baseline to Weeks 2, 4, 8, and end of treatment.
- Subjects with success (Total Sign Score \( \leq 1 \)) at Weeks 2, 4, 8, and end of treatment.
- Subjects with controlled disease (i.e., clear or very mild) according to the patient’s global assessment of disease severity at Weeks 2, 4, 8, and end of treatment.

Statistical methods:
There was no formal statistical hypothesis to be evaluated. The data were summarised using descriptive statistics.
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SUMMARY – CONCLUSIONS

Study Population:
A total of 78 subjects (mean age 14.6 years) were treated (in 17 centres) with at least one application of investigational product and 74 subjects completed the trial; 2 subjects had emerging exclusion criteria, 1 subject withdrew due to unacceptable adverse events and 1 subject due to other reason(s). Thirteen subjects had controlled disease at Visit 3 or 4 and left the trial as per the specifications in the Clinical Study Protocol.

Efficacy Summary:
Investigator’s Global Assessment (IGA) of Disease Severity
Overall, the majority of subjects had improved during the trial. At end of treatment 84.6% (66 subjects) had controlled disease. There were no clinically relevant differences between males and females or between the age groups.

Investigator’s Assessment of Clinical Signs – Total Sign Score (TSS)
The mean TSS decreased (improved) over time, from 7.1 at Baseline to 1.4 at end of treatment; a 80.4% improvement. The percentage of subjects with success (TSS ≤ 1) improved over time and was 62.8% at the end of treatment.

Patient’s Global Assessment of Disease Severity and Patient Assessment of Itching
Overall, the majority of subjects experienced an improvement during the trial as assessed by the Patient’s Global Assessment of disease severity. The percentage of subjects with controlled disease improved over time and 87.2% (68 subjects) had controlled disease at end of treatment.

Overall, there was an improvement in itching over time as assessed by the patients; at the end of treatment 96.2% (75 subjects) reported to have none or mild itching.

Overall Efficacy Conclusion:
In this non-controlled trial in 78 adolescent subjects, LEO 80185 gel was effective in treating scalp psoriasis.

Safety Summary:
LEO 80185 was well tolerated in this adolescent population; there were no SAEs, few adverse events. Two subjects had lesional/perilesional adverse events on the scalp, 5 subjects had adverse drug reactions, and two subjects withdrew from trial due to adverse events.

No cases of hypercalcaemia were reported and there were no clinically relevant increases in urinary calcium or other parameters of calcium metabolism.

There were no clinically relevant changes in the clinical laboratory values.

Conclusion:
In conclusion, in this non-controlled trial in 78 adolescent subjects, LEO 80185 was safe and effective in the treatment of psoriasis vulgaris on the scalp.