### SYNOPSIS

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<td>DAIVOBET/DOVOBET gel</td>
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**Title of study/Protocol Code Number:**
Calcipotriol plus Betamethasone Dipropionate Gel in Scalp Psoriasis. A Phase II Proof of Concept Study of Calcipotriol 50 mcg/g plus Betamethasone 0.5 mg/g (as Dipropionate) Gel in the Treatment of Patients with Scalp Psoriasis / MBL 0401 INT.

**International Co-ordinating Investigator:**
[Redacted], MD, Consultant Dermatologist, Waterford Regional Hospital, Ireland.

**Centre details [number by country]:**
- Canada: 6 centres
- Finland: 3 centres
- France: 6 centres
- Ireland: 3 centres

**Publication references [intended references]:**
To be decided.

**Study period details [date of first enrolment, date of last patient completed]:**
- First patient included 26 February 2004.
- Last patient attended last visit 03 July 2004.

**Phase of development:**
Phase II

**Objectives/hypothesis, if applicable:**

**Primary objective:**
To compare the clinical efficacy of once daily treatment for up to 8 weeks of DAIVOBET/DOVOBET (calcipotriol plus betamethasone dipropionate) gel with betamethasone dipropionate in the same gel vehicle in patients with scalp psoriasis.

**Secondary objective:**
To compare the safety of once daily treatment for up to 8 weeks of DAIVOBET/DOVOBET (calcipotriol plus betamethasone dipropionate) gel with betamethasone dipropionate in the same gel vehicle in patients with scalp psoriasis.

**Study methodology [design, assessments, stratification]:**
The study was designed as an international, multi-centre, prospective, randomised, double-blind, 2-arm, parallel group, 8-week study.

The investigator made the following clinical assessments:
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- assessment of the extent of scalp psoriasis
- assessment of the clinical signs (redness, thickness and scaliness on the scalp)
- global assessment of disease severity
- safety assessment

The patient made the following clinical assessments:
- Overall assessment of treatment response.

**Number of patients enrolled [total and by treatment groups]:**
A total of 218 patients were enrolled and randomised at visit 1 (DAIVOBET/DOVOBET gel: 108; Betamethasone in the gel vehicle: 110).

**Diagnosis and main criteria for patient selection:**
Hospital out-patients or patients attending the private practice of a dermatologist, aged 18 years or above, with a diagnosis of stable psoriasis on the scalp amenable to topical treatment with a maximum of 100 g of medication per week. The extent of involvement should be more than 10% of the scalp. Lesions should be assessed by a Total Sign Score for redness, thickness and scaliness of 4 to 12 inclusive but each individual sign should be more than or equal 1. Disease severity should be graded as mild, moderate, severe, or very severe according to the investigator’s global assessment of disease severity.

**Investigational product [name], dose [amount and frequency, dosage form], method of administration, lot numbers:**
DAIVOBET/DOVOBET gel (Calcipotriol 50 mcg/g (as hydrate) plus betamethasone 0.5 mg/g (as dipropionate)), topical application once daily on the lesions on the scalp. Lot number: [redacted]

**Reference product [name], dose [amount and frequency, dosage form], method of administration, lot numbers:**
Betamethasone 0.5 mg/g (as dipropionate) in the gel vehicle, topical application once daily on the lesions on the scalp, lot number: [redacted]

**Duration of treatment:**
Up to 8 weeks.

**Criteria for evaluation [efficacy evaluation, primary and secondary response criteria]:**
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**Efficacy:**

- The absolute change in Total Sign Score from baseline (visit 1) to end of treatment (visit 6).

**Secondary Response Criteria:**

- The percentage change in Total Sign Score from baseline (visit 1) to end of treatment (visit 6).
- The absolute change in Total Sign Score from baseline to each subsequent visit and to end of treatment.
- The absolute change in the individual signs (redness, thickness and scaliness) of Total Sign Score for each visit and at end of treatment.
- The absolute change in score for extent of scalp psoriasis from baseline to each subsequent visit and to end of treatment.
- The proportion of patients with ‘Controlled disease’ (‘Absence of disease’ or ‘Very mild disease’) according to investigator’s global assessment of disease severity at each visit and at end of treatment.
- The proportion of patients with Treatment success (‘Marked improvement’ or ‘Almost clear’ or ‘Cleared’) according to investigator’s global assessment of treatment response at each visit and at end of treatment.
- The distribution of investigator’s global assessment of disease severity.
- The distribution of patient’s overall assessment of treatment response.

**Safety:**

**Safety Evaluation Criteria:**

- Incidence and severity of any reported adverse events.
- The reason for withdrawal from the study.

**Statistical methodology [as in protocol, or, especially, if different than originally presented in protocol]**

The primary efficacy criterion was analysed for the ITT population and the per-protocol population. The absolute change in Total Sign Score was analysed using analysis of covariance and non-parametric analysis (Kruskal Wallis test).
The secondary criteria were analysed only for the ITT population using either analyses of covariance or logistic regression models/Cochran-Mantel-Haenszel test.

Summary – Conclusions

Primary efficacy criteria:
The study shows that DAIVO BET/DOVO BET gel has a significantly better efficacy than betamethasone dipropionate in the gel vehicle after up to 8 weeks of treatment for the primary efficacy criterion: absolute change in Total Sign Score. The difference between means was -0.56 (95% CI: -1.10; -0.02) with P-value = 0.042. When analysed for the per-protocol population very similar results were obtained; the difference between means was -0.60 (95% CI: -1.14; -0.06) with P-value = 0.028. The onset of action was fast for both products but after 2 weeks DAIVO BET/DOVO BET gel was significantly more effective than betamethasone dipropionate in the gel vehicle (P-value = 0.005). Also after 4 and 6 weeks the tendency of DAIVO BET/DOVO BET gel being more effective was observed.
A significant centre-treatment interaction was observed. For the analysis of the absolute change in Total Sign Score, the majority of the centres provided estimates in favour of DAIVOBET/DOVOBET gel with one centre showing statistically significantly better efficacy in the DAIVOBET/DOVOBET gel.

Secondary efficacy criteria:
The percentage change in Total Sign Score gave a difference of -7.90 (95% CI: -16.30; 0.50) and a P-value=0.065. The difference between groups for the absolute change in redness at end of treatment was statistically significant (P-value=0.012) in favour of DAIVOBET/DOVOBET gel. For the absolute change in thickness, absolute change in scaliness, and absolute change in extent from baseline to end of treatment no statistically significant difference was found between the two treatment groups at end of treatment. However, in all cases a trend towards better efficacy of DAIVOBET/DOVOBET gel was seen.

The distribution of the Investigators Global assessment of disease severity at end of treatment was in favour of DAIVOBET/DOVOBET gel. In the DAIVOBET/DOVOBET gel group 83.3% of the patients achieved ‘Controlled disease’ defined as ‘Absence of disease’ or ‘Very mild disease’ on the Investigator Global assessment of disease severity scale. In comparison 74.6% in the betamethasone dipropionate treated group achieved ‘Controlled disease’. The difference of 8.8 (95% CI: -2.0;19.5) was not statistically significant (P-value=0.11). The Log-Rank test of time to ‘Absence of disease’ (P-value=0.031) showed that patients achieved ‘Absence of disease’ faster to DAIVOBET/DOVOBET gel than to betamethasone. According to the patients overall assessment of treatment response DAIVOBET/DOVOBET gel was significantly better than betamethasone dipropionate. At end of treatment, the percentage treatment success (defined as ‘Cleared’, ‘Almost clear’ plus ‘Marked improvement’) was 92.5% assessed by the patients treated with DAIVOBET/DOVOBET gel compared to 82.6% assessed by the patients treated with betamethasone dipropionate. The difference of 10.0 (95% CI: 1.3;18.7) was statistically significant (P=0.027).
The adverse event profiles for the two groups were very similar. Lesional/perilesional adverse drug reactions were reported by 6.5% of the patients in the DAIVOBET/DOVOBET gel group compared to 9.1% of the patients in the betamethasone group. The difference was not statistically significant (P-value=0.48). Skin adverse drug reaction on the scalp was reported by approximately 7% in both groups. The most reported lesional/perilesional adverse drug reaction and skin adverse drug reaction on the scalp was ‘Pruritus’. No serious adverse events were reported.

Conclusion: [relationship of risks and benefits]
The results indicate that DAIVOBET/DOVOBET gel is superior to betamethasone dipropionate in the gel vehicle in the treatment of scalp psoriasis. Superiority of the DAIVOBET/DOVOBET gel was also observed when comparing absolute change in redness from baseline to end of treatment. In addition, it was shown that the patients treated with DAIVOBET/DOVOBET gel achieved ‘Absence of disease’ faster than patients treated with betamethasone dipropionate, and the patients overall assessment for treatment success was statistically significant in favour of DAIVOBET/DOVOBET gel.

The adverse event profiles for the two products were very similar.
In conclusion, the benefit/risk ratio has been demonstrated to be in favour of the DAIVOBET/DOVOBET gel.

Report date: