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Once Daily Application of a Combination of Calcipotriol and Betamethasone Dipropionate (Dovobet^{*}, Daivobet[®]) for the Treatment of Psoriasis

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ABSTRACT

This new compound product containing 50 µg/gm calcipotriol and 0.5mg/gm betamethasone dipropionate was recently introduced in Canada for the treatment of psoriasis. Clinical trials demonstrated that this compound was more active than either agent used alone. Recent changes in the product monograph involving the reduction in dose to once daily use has raised questions about the relevance of some previous comparisons of twice daily Dovobet^{}. Pooling the available data from 5,500 patients in clinical trials for Dovobet^{*} will allow an inter-trial comparison of the various treatment arms, demonstrating that Dovobet^{*}, when applied once daily is significantly more effective than with twice daily applications of either its individual components used alone.*

Key Words: psoriasis, calcipotriol, betamethasone dipropionate

Calcipotriol and corticosteroids are both established treatments for psoriasis.¹ Recently, studies have reported that combination therapy applied twice daily with 50 µg/gm calcipotriol and 0.5mg/gm betamethasone dipropionate (Dovobet^{*}, LEO Pharma) is significantly more effective than either monotherapy with each component or the vehicle.²⁻⁴ In Europe, this product is marketed as Daivobet[®].

Once-Daily Dovobet^{*}

In an international, multicenter, prospective, randomized, double-blind, vehicle-controlled, parallel group, 4 week study, Guenther, et al, demonstrated that there was no statistically significant difference in the mean percentage change in the Psoriasis Area and Severity Index (PASI) from baseline to end of treatment between once daily vs. twice daily use of this compound (-5.4%, p=0.052).⁵ There are a number of advantages for reducing the applications to once-daily from twice daily, including reduced cost to the patient, and improved patient compliance. However, the most important is the need to reduce long-term exposure to steroids for psoriasis patients. The irreversible side-effects and tachyphylaxis that are associated with topical steroids should be avoided whenever other proven and safer alternatives exist, since psoriatic patients often self medicate for long periods of time without physician supervision and monitoring.

A recent change in the product monograph involving the reduction in dose to once daily use, raises questions about the relevance of some previous studies that compared twice daily Dovobet^{*} to twice daily use of calcipotriol (Dovonex[®], LEO Pharma) or betamethasone dipropionate (Diprosone[®], LEO Pharma).⁶ These trials all explored the use of Dovobet^{*} for treating large numbers of adult patients with psoriasis. All studies involved the maximal use of 100gm of ointment per week for 4 weeks, had virtually identical inclusion/exclusion criteria, and assessed patients on the basis of the percentage reduction in their Psoriasis Area and Severity Index (PASI) scores. In most cases, a similar group of investigators and site staff was used in the various trials. Together, these factors suggest that a pooling of data to allow the inter-trial comparison of various treatment arms will yield reliable results (see Tables 1 and 2 for meta-analyses of the data).

Comparators	n	Mean % decrease from baseline at week 4
Dovobet*, once daily	1285	69.7±24.3
Betamethasone dipropionate, twice daily	362	61.3±27.9
Calcipotriol, twice daily	919	56.1±27.9

Table 1: Pooled results used to compare once daily Dovobet* with twice daily monotherapies.⁶

The mean difference between treatment groups is provided in Table 2, along with their 95% Confidence Intervals. In both comparisons, the once daily use of Dovobet* demonstrates statistically significant improvement over the twice daily marketed comparator product.

Comparators	Mean % Difference in PASI reduction	95% Confidence Interval	p-value
Dovobet*, q.d. vs. betamethasone dipropionate, b.i.d.	-8.4	-11.3 to -5.4	<0.001
Dovobet*, q.d. vs. calcipotriol, b.i.d.	-14.4	-17.3 to -11.4	<0.001

Table 2: Mean differences between treatment groups.⁶

Treatment Regimen

One potential treatment approach for using Dovobet* and Dovonex[®] to treat psoriasis includes “jump starting” the patient with once-daily Dovobet*, followed by a gradual transition within 4 weeks to Dovonex[®] or emollients for maintenance. Dovobet* can subsequently be reintroduced on weekends as an intermittent pulse therapy when partial relapse or flares occur.

Side-effects

All trials using the twice daily application of Dovobet* demonstrated fewer reported side-effects than with calcipotriol alone.⁷ Once daily applications mean that patients have less exposure to the drugs and presumably less chance developing side-effects, especially those associated with steroids.

Conclusion

Dovobet*, when applied only once daily, is as effective as twice daily applications, and significantly more effective than twice daily applications of calcipotriol or betamethasone dipropionate. In addition, the once-daily application of a single combination ointment is more patient-friendly and likely to encourage compliance.

*registered trademark of LEO Pharmaceutical Products used under the license by LEO Pharma Inc., Thornhill, Ontario, Canada.

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