2 SYNOPSIS

Title of study:
Evaluation of a developmental 'long lasting' emollient in subjects with dry skin

Investigators:
Dr Suzana Louth

Study Centre(s):
RSSL
The Science and Technology Centre
The University of Reading
Earley Gate, Whiteknights Road,
Reading RG6 6BZ

Publication (reference):
None

Study period :	2009-2010	**Phase of development:** III
Date of first enrolment:	07/12/2009	
Date of last completed:	29/01/2010	

Objective:
The purpose of this study was to determine whether the revised emollient gel formulation, coded DELP, achieves improved skin hydration over time as compared with Doublebase Gel, in patients who, for whatever reason, can only re-apply their treatment as infrequently as twice daily. A secondary objective was to investigate the cosmetic acceptability of the revised formulation.

Methodology:
Part 1
Single centre, double blind left/right concurrent bi-lateral comparison of the effects of a single application of the test and control products on skin hydration in eczema sufferers with dry skin, over 24 hours.
Part 2
Single centre, double blind left/right concurrent bi-lateral comparison of the effects of twice daily application of the test and control products on skin hydration in eczema sufferers with dry skin, for 5 days.

Number of patients planned and analysed:
Approximately 40 patients were planned and 41 were recruited.

Diagnosis and main criteria for inclusion:
The subjects were required to fulfil all the following criteria to be eligible for the study:

- Eczema sufferer.
- Female, and with an insignificant amount of hair on the arms and legs so as not to impair the measurements.
- Between 18 and 65 years of age.
- Dry skin to arms and lower legs (defined as mean corneometer readings of less than 45 units on arms and lower legs).
- Mean baseline corneometer measurements differing by no more than 10 units between left/right arms and legs.

Test product, dose and mode of administration, batch number:
The test product, DELP, is an emollient semi-solid aqueous hydro-gel containing 15% w/w liquid paraffin EP and 15% w/w isopropyl myristate EP and standard excipients, batch number DD21/3.
Single application to the arm (0.05 ml/20 cm^2) in Part 1; twice daily applications of about 1 g to the leg in Part 2.

Duration of treatment:
Up to 5 days (Part 2 only)

Reference therapy, dose and mode of administration, batch number:
The reference product, Doublebase Gel (PL 00173/0183) is an emollient semi-solid aqueous hydro-gel containing 15% w/w liquid paraffin EP and 15% w/w isopropyl myristate EP and standard excipients, batch number DD21C/1. Single topical application to the arm (0.05 ml/20 cm^2) in Part 1; twice daily topical applications of about 1 g to the leg in Part 2.

Criteria for evaluation:
The primary efficacy parameter was the degree and duration of skin moisturisation as determined by the area under the curve of the change from baseline corneometer measurements, which indicates the moisture content of the stratum corneum.

In addition, subjects' scores on the overall acceptability of the two products, whether they would use the product again and which product they preferred were recorded.
Safety monitoring involved questioning patients at each visit to determine if they had experienced any adverse events or adverse drug reactions.

Statistical methods:
The means of triplicate corneometer measurements were used for the determination of the area under the curve of the change from baseline corneometer measurements, calculated using the Trapezoidal rule. Treatment effects were assessed using the within subject error term after adjustment for any effect of arm/leg (right or left), as appropriate for the study design, and were presented with 95% confidence intervals. Normality assumptions were checked. All statistical testing performed was 2-sided using a 5% significance level.

Summary – conclusions:
Efficacy results:
Part 1
A single application of both gels was shown to significantly improve skin hydration (measured by AUC change from baseline corneometer readings over a 24 hour period). The DELP treatment effect was estimated to be an increased AUC of 100 units, which corresponds to a change from baseline difference between the two arms of approximately 4 units and represents an increase in skin hydration for DELP of at least 30% more than that seen with Doublebase Gel. The improved skin hydration of DELP over Doublebase Gel was seen at all of the timepoints studied but was observed to be greater at the 4, 6, 8 and 12 hour timepoints than at the other timepoints studied, but the significant effect was still seen 24 hours after the products were applied.

Summary – conclusions (contd):
Efficacy results (contd):
Part 2
The ITT analysis showed that DELP was statistically significantly better than Doublebase Gel at achieving improved skin hydration as measured by AUC change from baseline corneometer readings over a two day (32 hour) period (planned 5 day study disrupted by adverse weather). The treatment effect is estimated to be an increased AUC of 158 units, which corresponds to a change from baseline difference between the two legs of approximately 5 units over the 32 hour period. This estimated treatment effect shows that the increase in skin hydration for DELP is more than double that achieved by Doublebase Gel.
Changes from baseline corneometer readings to the 1 pm readings on days 1, 2 and 5 in 25 of the 38 subjects for whom these data were available showed DELP was statistically significantly better than Doublebase Gel at achieving improved skin hydration. The treatment effect is estimated to be an increased change from baseline of 8.1 units.

It is clear from the above that after a single application, DELP achieved significantly greater (approximately 30%) skin hydration than Doublebase Gel, and that during twice daily application DELP gave approximately twice the skin hydration as Doublebase Gel.

Overall, the subjects found both of the test products to be acceptable with no statistically significant differences in acceptability between them.

Safety results:
An estimated 326 applications of each product were made during Part 2 of the study, with no significant adverse reactions and no evidence of a difference in safety profile between the two gels.

Conclusion:
Overall it can be concluded that under the conditions of these tests, the results of this study provide strong evidence that DELP is a well tolerated, well accepted, emollient gel that achieved substantially improved skin hydration over time as compared with Doublebase Gel, and is suitable for use by patients who, for whatever reason, can only re-apply their emollient treatment as infrequently as twice daily.

Date of report: July 2010