Adv Ther
DOI 10.1007/s12325-013-0033-4

ORIGINAL RESEARCH

A Novel Formulation of Mometasone Furoate in Psoriasis Patients: A Multicenter, Randomized, Double-Blind Clinical Study

Mats Berg · Åke Svensson · Jan Faergemann

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Received: March 26, 2013

ABSTRACT

Introduction: Further formulations of mometasone furoate are needed for treatment of patients with plaque psoriasis to meet individual patient preferences. This has motivated the development of Ovixan® (Galencia, Malmoe, Sweden), a formulation of mometasone furoate with different cosmetic properties than the commonly used formulation, Elocon® (Merck [Schering Plough], Whitehouse Station, New Jersey, USA). This novel formulation of mometasone furoate was examined in a vasoconstrictor assay comparing its efficacy with that of Elocon. Subsequently, the new formulation was tested in a multicenter, randomized, double-blind clinical study in patients with plaque psoriasis.

Methods: Healthy volunteers were included in the vasoconstrictor study. The treatments were randomly assigned to test fields on the forearms. The test fields were gently cleaned after treatment for 6 h. Skin color was measured during the following 24 h and area under the time curve was calculated. The clinical efficacy and tolerance of Ovixan was as compared to that of Elocon and their vehicles in a double-blind study in patients with plaque psoriasis. Patients with four symmetrically placed lesions on the arms or the legs were treated for 6 weeks. Primary endpoint was the change from baseline of the Total Severity Sign score for each treated lesion. The cosmetic characteristics of the two test preparations were assessed by an independent cosmetological institute.

Results: Ovixan was shown to have skin blanching potency almost identical to the

EudraCT numbers 2008-003823-21 and 2009-016827-72.

M. Berg
Department of Dermatology, Mälarsjukhuset, 63188 Eskilstuna, Sweden

Å. Svensson
Department of Dermatology, MAS University Hospital, 20502 Malmö, Sweden

J. Faergemann (✉)
Department of Dermatology, Sahlgrenska University Hospital, 41345 Gothenburg, Sweden
e-mail: jan.faergemann@derm.gu.se

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Published online: 25 May 2013

vasoconstrictor potency of Elocon. Clinical equivalence of Ovixan to Elocon was demonstrated in the clinical study of the efficacy in patients with plaque psoriasis. A professional testing team clearly documented the cosmetic superiority of Ovixan as compared to Elocon.

Conclusion: The results of the investigations show that Ovixan is equipotent to the commonly used formulation Elocon. However, the cosmetic properties are in favor of Ovixan. The effect of the cosmetic differences on patient preferences and patient adherence to prescribed treatment has to be investigated in further studies.

Keywords: Cosmetic acceptability; Elocon; Mometasone furoate; Ovixan; Randomized clinical study; Plaque psoriasis; Total Severity Sign score; Vasoconstrictor assay

INTRODUCTION

Corticosteroids are one of the most commonly used topical treatments of plaque psoriasis. The action of corticosteroids is wide ranging, including anti-inflammatory and immunosuppressive effects, which are at least partly related to the inhibition of the release of various cytokines. The long-term use of topical corticosteroids has earlier been limited by both topical and systemic side effects with skin atrophy and suppression of the pituitary secretion of adrenocorticotrophic hormone (ACTH) being of particular concern. Therefore, much effort has been focused on developing corticosteroids for topical use where high-strength local effect is combined with low systemic availability. The development of mometasone furoate has been a significant advancement. This corticosteroid combines high potency with low systemic availability after topical administration [1]. The resulting low systemic toxicity leads to an improved risk–benefit ratio as compared to the previous moderately potent topical corticosteroids [2–4]. Owing to its potency, its low percutaneous penetration, low systemic toxicity, and low risk of sensitization, topically applied mometasone furoate cream has emerged as a commonly used formulation for the treatment of plaque psoriasis and other inflammatory skin disorders.

The activity of mometasone furoate and other corticosteroids is influenced by the pharmaceutical formulation used. Penetration enhancers, lipid content, and stability have been found to influence the activity of a topical formulation [3, 5–7]. Of even higher importance for the efficacy of a corticosteroid formulation is the degree of patient compliance. Adherence to topical medication is considered a major problem in the treatment of psoriasis [8, 9]. Prescribing therapy in line with patient preference for treatment vehicle may be a key factor for treatment success [10, 11]. The cosmetic aspect of treatment has been found to have a major impact on the patients' compliance to treatment [12]. The main reasons given by the patients in this pan-European study for not complying with prescribed treatment were lack of efficacy and poor cosmetic characteristics of the treatments. The patients expressed their desire to have less greasy, sticky, and smelly treatments with high efficacy to be more compliant [12]. Those results are in line with the results from an earlier questionnaire study in patients with psoriasis [13]. Of the 692 patients, only 26% preferred ointments, clearly fewer than the 43% who preferred the less greasy cream formulations. This underlines the need for a variety of improved formulations of

mometasone furoate and other corticosteroids in order to meet varying patient preferences [13].

The need for further formulations of mometasone furoate has triggered pharmaceutical development work. Recently, the development of a less fatty cream with mometasone furoate 0.1% has been reported [14, 15]. In parallel, another cream formulation, Mometasone 0.1% cream Galenica (in the following text referred to as Ovixan® [Galencia, Malmoe, Sweden]), has been developed with different cosmetic properties than the commonly used, commercially available mometasone formulation, Elocon® (Merck [Schering Plough], Whitehouse Station, New Jersey, USA). The authors report here the results from a multicenter, randomized, double-blind clinical study of Ovixan in patients with mild-to-moderate plaque psoriasis. The clinical study of the efficacy and safety of Ovixan was preceded by a comparative investigation of the vasoconstrictor potency of this novel cream as examined in the vasoconstrictor assay [16, 17]. The aim of the investigations was to investigate if Ovixan was clinically equivalent to Elocon.

MATERIALS AND METHODS

Ovixan 1 mg/g Cream

Ovixan is a cream containing 1 mg/g mometasone furoate. Ovixan is an oil in water (o/w) emulsion with coconut oil dispersed in the continuous water phase. Coconut oil accounts for approximately 8% (m/m) and water for approximately 50% (m/m) of the total cream composition. Propylene glycol is used as solvent for mometasone furoate.

The composition of Ovixan is distinctly different from the composition of Elocon, a commonly used mometasone formulation. Elocon is a water in oil (w/o) emulsion, where white soft paraffin is the main component of the continuous oil phase, accounting for approximately 54% (m/m). The aqueous phase, containing only approximately 3% (m/m) water of the total composition, is dispersed in the continuous oil phase. In this formulation, hexylene glycol is used to dissolve mometasone furoate.

Vasoconstrictor Assay

The vasoconstrictor effect of Ovixan and other study preparations and of comparators was examined by the dermatological contract research organization, bioskin GmbH, Hamburg, Germany. The study protocol was approved by the Ethical committee of the Hamburg Medical Council. The study was performed in accordance with the "Somerset West" Declaration of Helsinki (October 1996) as revised in 2000, as well as German regulations. The International Conference on Harmonization (ICH) guideline for Good Clinical Practice (GCP) (January 1997) was observed. Informed consent was obtained from all patients for being included in the study. The trial has the EudraCT number 2008-003823-21. The study was conducted between August 27 and September 9 2008.

Healthy male and female volunteers from Hamburg, Germany, with healthy skin and demonstrated adequate vasoconstriction after treatment with topical corticosteroids were selected according to defined inclusion and exclusion criteria, and were included in the study. Exclusion criteria included immunocompromised patients, the use of a potent topical corticosteroid formulation within the last 4 weeks, systemic use of anti-inflammatory drugs within the last 2 months,

and non-reliable patients, e.g., due to drug or alcohol abuse. This single-center, vehicle-controlled study was double-blind for the study preparations and observer-blind for the comparators with random assignments of the treatments to test fields on the right and left forearm. All included subjects completed the study and were included in the intent-to-treat (ITT) analysis. Study preparations were (1) Ovixan, (2) vehicle to Ovixan, (3) 0.1% mometasone furoate generic composition, and (4) vehicle to 0.1% mometasone furoate generic composition. Commercially available reference preparations were (1) Kenacort®-T 0.1% cream (GlaxoSmithKline, London, UK), a class II steroid (European classification); (2) Elocon 0.1% cream, a class III steroid; and (3) Dermovat® 0.05% cream (GlaxoSmithKline, London, UK), a class IV steroid. A single topical non-occlusive application of approximately 50 μL was made to test fields measuring approximately 2 cm^2 located on the volar surface of the forearms. There were altogether nine test fields per patient, including two untreated test fields. The treatment lasted for 6 h where after the test fields were gently cleaned. Skin color in the test fields 1, 2, 4, 6, 18, and 24 h after treatment was measured using a Chroma-Meter CR 300 (Konica Minolta, Ramsey, New Jersey, USA). The primary efficacy variable was the degree of redness of the skin, measured as the area under the time curve (AUC) of the baseline-corrected, untreated control site-corrected chromaticity (*a* values).

Statistical Analysis

For each treatment group the AUC was calculated for the respective *a* values using the trapezoid rule and descriptive statistics were carried out. The hierarchal approach was performed for both active study preparations and corresponding active ingredient-free vehicles. The overall significance level of $P < 0.05$ could be kept for each active study preparation with this ordered test procedure.

The Multicenter, Randomized, Double-Blind Clinical Study of Ovixan

Overall Study Design

This study was a phase 3 clinical study designed to verify the clinical equivalence of Ovixan to the commonly used Elocon 0.1% cream (in the following text referred to as Elocon). The study protocol was approved by the Ethical committee in Gothenburg, Sweden, on January 12, 2010. The study was performed in accordance with the "Somerset West" Declaration of Helsinki (October 1996) as revised in 2000, as well as applicable local laws and regulations. The ICH guideline for GCP (January 1997) was observed. Informed consent was obtained from all patients for being included in the study. The trial has the EudraCT number 2009-016827-72. The study was conducted between March 1 and June 9, 2010.

In the study, the effect of Ovixan was compared to Elocon in patients with mild-to-moderate plaque psoriasis, defined as having a Psoriasis Area and Severity Index (PASI) score <10. The design was a multicenter, randomized, double-blind, non-inferiority, intra-individual study with efficacy as primary objective. The patient required four $(2 + 2)$ symmetrical lesions. The lesions had to be symmetrically located on the arms or the legs. Each of the lesions had to have a Total Severity Sign (TSS) score of ≥ 5, and a diameter of at least 3 cm. The lesions were required to be at least 5 cm apart on the same extremity. Two of the symmetrically located lesions were treated with

Ovixan or Elocon, and the other two lesions with the vehicle of Ovixan or the vehicle of Elocon, in a blinded fashion. Patients who were being treated for their psoriasis at the time of screening had to undergo a 2-week wash-out period for topical treatment (restricted to the four lesions that were to be studied) before being randomized into the study to be able to evaluate the effect of the study medications properly. During the wash-out period, the patient used the emollient Canoderm® 5% cream (ACO, Stockholm, Sweden) on the lesions to be studied. The patient was instructed to apply the study treatment as a thin layer on the plaque psoriasis lesions in the evening once daily during the first 3 weeks, then once every second day for 1 week, followed by twice a week for the remaining 2 weeks. The total treatment period was 6 weeks. The emollient Canoderm 5% cream was used in the morning and the study medications in the evening on the lesions that were treated. No other emollient was allowed on the test areas. Lesions other than the test lesions were treated as before. The patients visited the investigator four times during the study. The first visit was the screening visit that took place $\leq$6 weeks prior to day 0. Randomization was made at the second visit at day 0, and treatment was started. Visit 3 was made at day 21 ($\pm$2 days), and visit 4 at day 42 ($\pm$2 days). Table 1 gives a flow chart of the study events.

Study Participants

Male and female patients, at least 18 years old, with mild-to-moderate plaque psoriasis on four lesions on the arms or legs were included into the study after having given their informed consent. Female patients of childbearing age were required to have a negative pregnancy test before being included into the study. No systemic antipsoriatic treatments were allowed for 4 weeks before entering the study. Patients were not included if they (a) had neglected the wash-out period of treatments other than with the emollient Canoderm on the lesions to be studied, (b) had any clinically significant deviation from normal that might interfere with the study evaluation, (c) had any current or past medical condition which might significantly affect the response to the study medication, (d) had any other form of psoriasis other than plaque psoriasis, (e) had any other active skin disease, (f) had known allergic reaction to mometasone furoate or any of the excipients, (g) had any existing contraindication for Elocon or Canoderm, (h) were in a situation where optimal participation in the study would be difficult, (i) were lactating, (j) was participating or had been participating within 4 weeks in another clinical study, (k) had suspected alcohol or drug abuse, (l) were part or a family member of the staff of the participating centers, (m) were treated with systemic or locally acting medications, which might influence the study aims, within 2 weeks before the start of the study, and (n) were females of childbearing age not using highly effective contraception.

The patients were recruited at the dermatology clinics of three hospitals in the southern part of Sweden. Two of the hospitals were university hospitals and the third a regional hospital of high standards.

Study Objectives

The primary objective of the study was to show that Ovixan had a clinical effect equivalent to that of Elocon in patients with mild-to-moderate plaque psoriasis. Primary efficacy variable was TSS score on each of the four study lesions as assessed by the investigator at each visit. Efficacy was measured by evaluating

Table 1 Flow chart: study events

Study events	Visit 1 Screening ≤6 weeks prior to day 0	Visit 2 Baseline (day 0)	Visit 3 (day 21 ± 2)	Visit 4 (day 42 ± 2)
Patient informed consent	x			
Allocation of a screening number	x			
Demographic data	x			
Urine pregnancy test	x	x		x
Medical and psoriasis history	x			
Physical examination	x			x
PASI	x			
Eligibility criteria	x	x		
Allocation of patient number		x		
Vital signs (Blood pressure, pulse)		x		x
TSS	x	x	x	x
PGA1 (Investigator)		x	x	x
PGA2 (Patient)		x	x	x
Cosmetic questionnaire			x	
Adverse events		x	x	x
Tolerability questionnaire		x	x	x
Concomitant medication		x	x	x
Dispensing of study product kit	x[a]	x	x	

PASI psoriasis area and severity index, *PGA1* physician global assessment of improvement, *PGA2* patient global assessment of improvement, *TSS* Total Severity Sign score

[a] Canoderm 5% cream was dispensed and used during the wash-out period by six patients

the change from baseline in TSS score for each of the lesions at each visit. TSS scale assesses signs (redness, scaling, and thickness) and symptoms (itching) of psoriasis on a 3-point scale. The scores for all signs and symptoms are summed to obtain the TSS score, which ranges from 0 to 12, where a higher score indicates greater severity.

Secondary objectives were supporting evidence of efficacy and assessment of safety, measured as tolerability, by a comparison between Ovixan and Elocon. Efficacy was also measured by evaluating the change from baseline in Physician Global Assessment of Improvement (PGA1) score assessed by the investigator, and by the patient by using Patient's Global Assessment of Improvement (PGA2). Cosmetic preference was measured by asking the patient about the cosmetic qualities of the study medication in a questionnaire at the third visit after 21 days of treatment.

Randomization and Blinding

After the Informed Consent Form had been signed, the patient was identified by a screening number. The screening number was allocated in

a non-consecutive order. Patient eligibility was established before treatment randomization. Patients were randomized sequentially and a computer-generated randomization list was prepared that identified which of the lesions should be treated with Ovixan or Elocon, or the two vehicle-creams. The randomization list was blind to each member of the study team until clean file was declared. The randomization schedule was not disclosed to the investigators except for individual patients in case of emergency.

The tubes with the study medication were distributed twice, at visit 2 and at visit 3. The patient was given four identical tubes marked with "RIGHT 1" or "RIGHT 2" or "LEFT 1" or "LEFT 2" and with different colors on the labels, to be used on the lesions. The patient was given detailed written instructions on how to apply the treatment. The treatment code was not broken until all measurements had been performed, data had been entered into the database, and the database was declared clean.

Sample Size and Statistical Analyses

It was estimated that 60 patients should be included in order to reach 50 fully evaluable ITT patients. With this number of ITT patients it would be possible to reach 90% probability for detecting a clinically meaningful difference between two treatments. A two-sided $P < 0.05$ was considered statistically significant. No adjustments for multiple comparisons were made. The statistical evaluations were made with SPSS (IBM, Armonk, New Jersey, USA).

The primary endpoint in the study was the change in TSS score from baseline. The TSS score was calculated on each lesion at each visit. The absolute and the relative changes (in percent) in TSS total score were calculated separately for each lesion. The hypothesis that the change between baseline and end of treatment was equal for the treatments was tested by means of the paired Student's t test using the relative change. The primary set of patients was the patients classified as ITT. The ITT set consisted of all correctly included and randomized patients with baseline and at least one post-randomization assessment on each of the lesions of the primary efficacy variable, the TSS score. To investigate the robustness of the results, the hypotheses were tested by means of the Per Protocol (PP) subset of patients as well.

Before finally declaring clinical equivalence between Ovixan and Elocon (and, hence, superiority over the vehicle of Elocon) the assay sensitivity had to be shown to be sufficient. This prerequisite was assessed by testing the hypothesis that the Elocon was equal to the vehicle of Elocon. If this hypothesis could be rejected, assay sensitivity could be declared. The hypothesis was tested by means of the Student's t test and declared significant if the two-sided P value was ≤ 0.05.

Sensory Cosmetic Characterization of Ovixan and Elocon

The Swedish Institute for Food and Biotechnology AB, Gothenburg, Sweden, was commissioned to undertake a study to characterize the sensory properties of Ovixan as compared to Elocon. A panel of four specially selected and trained assessors examined in a blind fashion the two test formulations. The sensory attributes that best described the sensory characteristics for the two products were selected for quantification on a six-graded scale. The procedure followed a well-established standard procedure in the food and cosmetics industry [18].

RESULTS

Vasoconstrictor Assay

Altogether, 38 subjects were screened for inclusion into the study. Thirty healthy volunteers were enrolled into the study and completed the study as planned. There were three minor protocol deviations which were not considered to be relevant for study outcome. None of the subjects were excluded from the analysis of the results. Therefore, the ITT and PP analyses were made on the identical patient populations.

The age of the patients ranged from 20 to 60 (mean 39, SD 9) years, weight from 54 to 118 (mean 77, SD 12) kg, and height from 162 to 193 (mean 175, SD 9) cm. Nine subjects used concomitant medication during the study. This medication was not considered to affect study outcome.

The AUC of the baseline-corrected and untreated control site-corrected *a* values measured 1, 2, 4, 6, 18, and 24 h after removal of treatments reflected the course of blanching over the measurement period. Figure 1 shows the mean AUC with the 95% CI. All corticosteroid formulations showed clear blanching. No relevant blanching was seen in the test fields treated with the two active ingredient-free vehicles. The blanching effect observed in the fields treated with Ovixan (mean AUC 49.9) was slightly higher than the blanching effect of the class II comparator, Kenacort-T (mean AUC 47.9), slightly lower than the blanching effect of the class III comparator, Elocon (mean AUC 53.0), and lower than of the class IV comparator, Dermovat 0.05% cream (mean AUC 64.3). However, the differences between the mean potencies did not reach statistical significance. In addition, the blanching effect observed in the fields treated with 0.1% mometasone furoate generic composition (mean AUC 46.7), was not statistically different from what was obtained with Ovixan or with Elocon, or with the other comparators.

The hierarchal testing for Ovixan showed that this preparation was superior in effect above the cream vehicle (Table 2). Ovixan was shown to be non-inferior to the comparator, Kenacort-T 0.1% cream, a class II steroid. There was no statistical difference in mean AUC between Ovixan and the class III comparator, Elocon, or between Ovixan and the class IV comparator, Dermovat. However, the results had insufficient power to permit the statistical conclusion of non-inferiority of Ovixan to Elocon.

The hierarchical testing for 0.1% mometasone furoate generic composition showed this preparation to have very similar effect as Ovixan. Considering better cosmetic properties, Ovixan was selected for further development and testing in the randomized clinical trial versus Elocon.

There were no adverse events and no other observations related to safety in this study. The final physical examination at the end of the study did not show relevant findings in any of the subjects.

The Multicenter, Randomized, Double-Blind Clinical Study of Ovixan

Study Participants

Sixty-two patients were screened, and all patients but one were eligible to participate in the study: 48 men and 13 women. All patients had mild-to-moderate plaque psoriasis on four lesions (2 + 2, symmetrically placed lesions) on the arms and/or the legs. Each of the lesions was at a minimum of 3 cm in diameter, and with a mean TSS score for each lesion of 7.7. Six out of

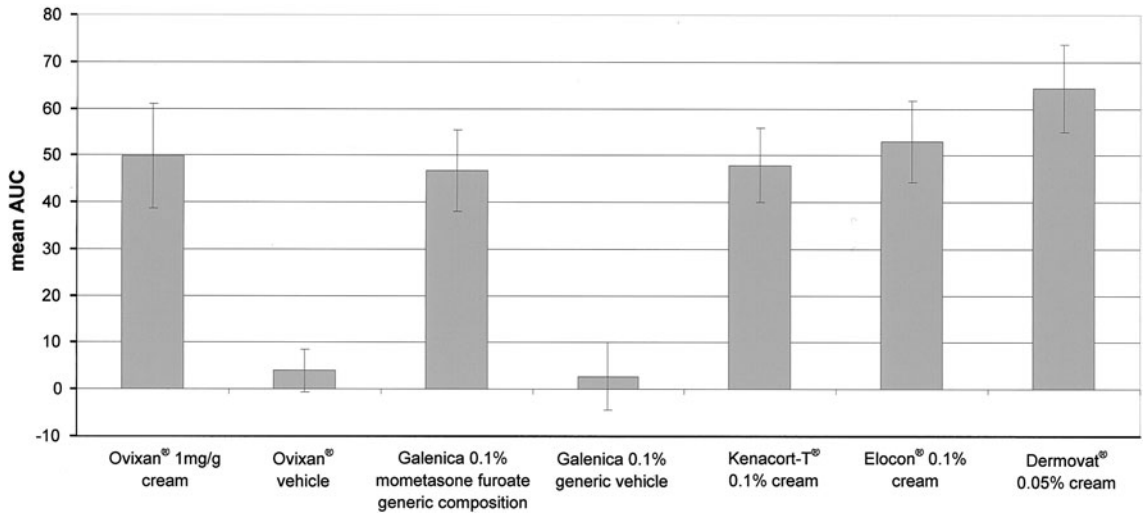

Fig. 1 Mean AUC of *a* values and 95% confidence intervals. *AUC* area under the time curve

61 patients (10%) needed a wash-out period of 2 weeks before start of treatment due to previous treatment for their psoriasis, while 55 out of 61 could start the treatment close to the screening visit. The first patient was screened on March 1, 2010 and the last visit for the last patient was on June 9, 2010.

Efficacy was evaluated on the ITT set of patients. Fifty-eight patients were included in the ITT analysis. Three patients were excluded as there was no post-baseline data for these patients. One of the 58 patients did not show up at the last visit without any reasons given. Therefore, the TSS score at the last visit was assessed in only 57 patients.

The PP analysis set of patients at the end of treatment (at visit 4) consisted of 52 patients. Six patients among the 58 patients in the ITT set of patients were excluded because of protocol violations. Four of those patients did not show up at visit 4 within the time frame set to be acceptable; 42 ± 2 days. The fifth patient dropped out after the third visit and before the fourth visit. No reasons were given for not coming to the scheduled fourth visit. The sixth patient withdrew from the study after 27 days of treatment. Disappointment with treatment efficacy of one or more of the four treatments given, having a traffic accident, and having a tooth infection were given as reason for dropping out from the study.

Safety was evaluated on all 61 patients who had applied at least one layer of any of the study creams.

The 58 patients in the ITT set of patients had a mean age of 58 years (range 32–79). No medical history or abnormal vital signs excluded the patients from participating in the study. PASI mean score was 5 at baseline.

Efficacy Results

A prerequisite for making an evaluation of efficacy was the demonstration that the sensitivity of this clinical assay was sufficiently high. This was to be assessed by testing the hypothesis that the efficacy of Elocon was equal to the vehicle of Elocon. If this hypothesis could be rejected, sufficient assay sensitivity could be declared. Thus, there must be sufficient statistical strength in the results to reject the hypothesis that the effect of Elocon was equal to that of the vehicle for Elocon, i.e. to have a

Table 2 Inferential analyses of AUC, baseline-corrected, untreated control site-corrected redness value (*a* values) for Ovixan

Test treatment T	Reference treatment R	Mean AUC treatment T	Mean AUC treatment R	Mean AUC difference R-T	Conf. Interv. R-T	Reference value[a]
Ovixan	Vehicle	49.9	4.0	−45.9	−56.7, −35.2	0.0[b]
Ovixan	Kenacort-T 0.1% cream	49.9	47.9	−2.0	−8.5, 4.5	9.6[c]
Ovixan	Elocon	49.9	53.0	3.1	−5.9, 12.0	10.6[c]
Ovixan	Dermovat 0.05%	49.9	64.3	14.4	7.3, 21.5	12.9[c]

AUC area under the time curve

[a] Reference value is 0 in case of the comparison to vehicle and 20% of the mean AUC of the reference treatment for the other comparisons

[b] If the upper confidence interval (coverage probability = 95%) is below 0 then the superiority of Ovixan to its vehicle is proven

[c] If the upper confidence interval (coverage probability = 90%) is below the reference value then the non-inferiority of Ovixan to the reference treatment is proven

P value ≤0.05. When comparing the effect of Elocon to that of the vehicle for the Elocon, the *P* value was $P = 0.03$ (Table 3). This means that the hypothesis that the efficacy of Elocon was equal to the efficacy of the vehicle of Elocon could be rejected. Thus, it could be concluded that this clinical assay had sufficient sensitivity.

The mean TSS scores in the four groups at the start of treatment and at the end of treatment are given in Table 3. There was no significant difference in TSS score reduction by Ovixan and Elocon. The *P* value for the difference between these two groups was 0.96. Analysis of the PP set of patients showed that the difference between Ovixan and Ovixan vehicle in TSS score reduction reached statistical significance (Table 4). The other comparisons gave similar results as at the ITT analysis.

Secondary efficacy variables were PGA1 and the PGA2. The PGA1 score at the end of the treatment was compared to the score at the start of treatment. The relative score reduction caused by treatment with Ovixan and for Elocon, 23 and 26%, respectively, was more pronounced than the score reduction caused by the corresponding vehicles, 12 and 14%, respectively. The *P* value for the difference between the active treatments was $P = 0.076$. The *P* values for the relative change when comparing the active treatments to their vehicles were <0.05. Similar results were obtained when analyzing the reduction in PGA2 score caused by Ovixan and Elocon and their vehicles. Thus, the PGA1 and the PGA2 supported the results of the primary variable: the reduction of TSS score.

At visit 3, after 3 weeks of treatment, the patients filled out a questionnaire on the cosmetic properties of the study medications. There were no notable differences between the perception of the cosmetics of the two active treatments, Ovixan and Elocon, as assessed

Table 3 TSS score in 58 ITT patients at start of treatment with Ovixan and Elocon, and their vehicles, and after treatment for 6 weeks

Treatment	At start of treatment mean ± SD	After treatment for 6 weeks, mean ± SD
Ovixan	7.7 ± 1.2	6.6 ± 1.8[ac]
Ovixan vehicle	7.7 ± 1.1	7.2 ± 1.6[a]
Elocon	7.7 ± 1.1	6.5 ± 1.7[bc]
Elocon vehicle	7.7 ± 1.1	7.2 ± 1.7[b]

ITT intent-to-treat, *TSS* Total Severity Sign score
[a] Ovixan vs. Ovixan vehicle, ITT; $P = 0.06$
[b] Elocon vs. Elocon vehicle, ITT; $P = 0.03$
[c] Ovixan vs. Elocon, ITT; $P = 0.96$

Table 4 TSS score from baseline (visit 2) to end of treatment after 6 weeks (visit 4): Per Protocol analysis ($n = 52$)

Comparison	Mean per cent difference in TSS score at visit 4 (%)	95% Conf. interval for the mean per cent difference (%)	*P* value
Ovixan versus Elocon	0.1	−3.2, 3.4	0.96
Elocon versus Elocon vehicle	−8.1	−15.2, −1.3	0.02
Ovixan versus Ovixan vehicle	−8.2	−15.4, −0.8	0.03

TSS Total Severity Sign score

under the conditions in this clinical trial focused on efficacy evaluation.

Safety Results

No serious adverse events were reported during the conduct of the study. Of the 14 reported adverse events, seven were judged as moderate and seven as mild. Only two adverse events were judged as possibly related to the treatment. The first adverse event was a case of pruritus judged to be mild, and the second was worsening of psoriasis, judged to be moderate. It can be concluded that the adverse events reported were mild or moderate, and in no case severe and in most of the cases not related to the treatment. All four treatments were equally well tolerated.

Sensory Cosmetic Characterization of Ovixan and Elocon

The sensory characterization showed clear differences in the perceived properties of the two creams tested. Elocon had a stronger and more pungent odor than Ovixan, which had an odor perceived to be less intense and milder. Elocon was glossy, grainy, and buttery, and seemed to be melting when applied. Ovixan had a colder, whiter appearance and was perceived to be less greasy at application. The greasy feeling of Elocon was still prominent 90 min after application. Elocon, but not Ovixan left a white film on the skin after application.

DISCUSSION

Topical mometasone furoate has emerged as standard medication for psoriasis and other inflammatory skin disorders owing to its strength and low potential to cause adverse systemic effects [4]. The clinical efficacy of mometasone furoate and other corticosteroids is dependent not only on the strength of the steroid but also on the acceptability among patients of the formulation used and of the cosmetic properties it has [8, 12, 13]. Adherence to topical medication is a major problem in the treatment of psoriasis because of dissatisfaction with the formulation used [9, 10, 13]. The

importance of finding and prescribing the optimal formulation for the individual patient meeting the patient's preferences has been stressed [9–11]. Thereby, the adherence to the prescribed medication is likely to be increased and, thus, also the treatment efficacy and patient satisfaction [9, 10, 12]. The need for a variety of formulations for treatment of psoriasis is obvious [11, 13]. Mometasone furoate is presently available as cream, ointment, lotion, and foam. Efforts are being made to improve the available cream formulations and increase their acceptance among psoriasis patients [3, 14, 15, 19]. In this report, the authors have presented results from development work of a new mometasone furoate cream formulation, Ovixan, with different cosmetic properties than the commonly used formulation Elocon.

The intent behind Ovixan was to develop a mometasone furoate cream formulation in which the cream was not greasy and messy, was absorbed rapidly, and had no unpleasant cosmetic characteristics. Such a formulation would be particularly suitable for daytime use on psoriasis vulgaris located in areas where more lipid formulations would be cosmetically unsuitable, or would risk soiling the clothing. Such a formulation should be a light cream with high water content. In Ovixan the water concentration is approximately 50%, in comparison with the water concentration of Elocon, 3%. Recently, the results from investigations of yet another new mometasone furoate preparation have been presented [14]. This preparation, characterized as a light cream, has a water concentration of 33%. With Ovixan, a further step is taken as this preparation contains 50% water. Ovixan could, therefore, be characterized as an extra light cream.

A formulation with high water content, i.e., a cream, has occasionally been considered to be less clinically effective than formulations with high fat content, e.g. Elocon [10, 11]. Therefore, there was a need to demonstrate the clinical equivalence of the extra light cream, Ovixan, as compared to Elocon. The results presented in this report show Ovixan to be equipotent to Elocon.

The results obtained with Ovixan shows that mometasone in this formulation has a skin blanching efficacy comparable to that of the comparator Elocon when assayed in the vasoconstrictor assay, although the results had insufficient power to permit the statistical conclusion of non-inferiority of Ovixan to Elocon. However, Ovixan was demonstrated to be equipotent to Elocon in the clinical study when assessing the reduction of TSS score, the primary efficacy variable. The results proved the clinical equivalence between Ovixan and Elocon in patients with plaque psoriasis. This makes Ovixan an addition to the therapeutic armamentarium available for treatment of psoriasis. It has been stressed that an optimal treatment of psoriasis requires a spectrum of topical drugs and their formulations in different vehicles [13]. Ovixan constitutes an addition to this spectrum. Patient preferences and effects on patients' adherence to prescribed treatment should be examined in further studies. Limitations of this study include the number of patients, which could be increased. A more equal number of males and females, as well as an increase in the number of younger patients would increase the possibility to obtain a difference between the two formulations.

CONCLUSION

Ovixan cream has been shown to be equally effective as the commonly used mometasone cream, Elocon, in the treatment of patients with plaque psoriasis. However, the cosmetic

properties of the two formulations were different, and Ovixan had a superior cosmetic acceptance than Elocon.

ACKNOWLEDGMENTS

The studies and article publication charges were funded by Galenica AB, 205 12 Malmö, Sweden. Dr Faergemann is the guarantor for this article, and takes responsibility for the integrity of the work as a whole.

Conflict of interest. Mats Berg declares no conflict of interest. Åke Svensson declares no conflict of interest. Jan Faergemann is a consultant to Galenica AB.

Compliance with ethical guidelines. The study protocol was approved by the Ethical committee of the Hamburg Medical Council. The study was performed in accordance with the "Somerset West" Declaration of Helsinki (October 1996) as revised in 2000, as well as German regulations. The International Conference on Harmonization (ICH) guideline for Good Clinical Practice (GCP) (January 1997) was observed. Informed consent was obtained from all patients for being included in the study.

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