Review: Clinical Trial Outcomes

CLINICAL INVESTIGATION

Betamethasone valerate foam: a look at the clinical data

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Topical corticosteroids and especially betamethasone valerate (BMV) have been used topically to relieve many inflammatory skin conditions such as psoriasis and atopic dermatitis. The vehicle used to deliver topical drugs can influence the performance of these topical applications. BMV has traditionally been available in creams, ointments, lotions and sprays. In the early 2000s, a topical hydroethanolic BMV foam became commercially available. Subsequently, alcohol-free emulsion- and petrolatum-based foam formulations were also developed. This manuscript reviews the properties of BMV foams and clinical studies that have been conducted to assess their efficacy and safety as treatments for scalp and non-scalp psoriasis, as well as other dermatological inflammatory conditions.

Keywords: betamethasone valerate • foam • psoriasis • topical corticosteroids

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Topical corticosteroids have been ranked in four groups consisting of seven classes ranging from ultra-high potency preparations (class 1) to low-potency preparations (class 7). Betamethasone valerate (BMV) is a mid-potency corticosteroid (class 3–5, depending on the dosage form), used topically to relieve inflammatory skin conditions. It is used as a treatment for psoriasis, atopic dermatitis and other corticosteroid-responsive dermatoses.

The vehicle used to deliver topical drugs can influence the performance of these drugs. The vehicle can have a direct effect on the condition of the skin as a barrier, as it can enhance or retard delivery of the active agent to the target site of action. In addition, it can affect the skin's physical appearance and sensory properties, attributes that can influence patient compliance. Adherence to medication is a major concern in the treatment of dermatological conditions, as it impacts the success of therapy [1]. For example, studies consistently suggest that in psoriasis, up to 40% of patients do not use their medication as directed [2]. Thus, considerable efforts have been applied to the development of optimized topical formulations.

BMV has traditionally been available in creams, ointments, lotions and sprays. In the early 2000s, Luxiq®, a topical hydroethanolic BMV foam, became available. More recently, additional types of foam comprising BMV, including emulsion- and petrolatum-based foams, are currently under development.

This manuscript reviews the properties of BMV foams and the clinical studies that have been conducted to assess their efficacy and safety as treatments for scalp and non-scalp psoriasis, as well as other dermatological inflammations. The information herein was captured from an extensive search of the published academic literature, via PubMed and additional means literature searchs, patent databases and regulatory documents from the US FDA Freedom of Information database.

BMV foam: formulation properties

The use of foam in dermatology was first reported in 1977 by Woodward and Berry, who studied the therapeutic benefit of Betamethasone benzoate, in a hydroethanolic 'quick-break' foam, in comparison with a corresponding semisolid form [3]. The first

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commercial topical dermatological foams were introduced in 2002. These were hydroethanolic foam formulations of clobetasol propionate 0.05% foam (Olux®) and BMV 0.12% foam (Luxiq), which were developed by Connetics Corp. (CA, USA) [3–5]. The vehicle of these foams consists of ethanol (~60%), purified water, propylene glycol, cetyl alcohol, stearyl alcohol, polysorbate 60, citric acid and potassium citrate. The foam is dispensed from an aluminum can that is pressurized by a hydrocarbon propellant (propane and butane) and it is thermolabile; that is, it melts upon exposure to elevated temperature, such as the temperature of the skin [6]. The high concentration of ethanol in the formulation – compared with other vehicles – induces the delivery of corticosteroids through the stratum corneum as demonstrated by *in vitro* studies [6].

Ethanol also promotes fast drying and thereby attempts to address the sticky feeling left by many topical formulations after application. However, alcohol is a defatting agent and may cause skin to become dry and cracked. Due to this undesirable property, hydroalcoholic foams have not been proposed for the treatment of atopic dermatitis, an inflammatory skin disorder most frequently affecting children, which can manifest with pruritic, dry skin usually symmetrically distributed on skin folds and less often other locations. The stinging associated with use of ethanol on atopic skin is another primary reason alcohol-based foams are not recommended for atopic dermatitis.

In addition, because the hydroethanolic foams are thermolabile, their usage is hindered by the recommendation not to dispense them directly onto the hands or to the target skin area, as the foam melts on contact with warm skin, as illustrated in the prescribing information leaflet of Luxiq [7]. The alcohol content of these foams has been associated with transient stinging or burning upon application, which may limit their usefulness for some patients.

Three new versions of BMV foam, an emulsion-based BMV foam and a petrolatum-based BMV foam have been developed by Foamix Ltd (Rehovot, Israel) [8,9]. These compositions include low concentrations of nonionic surfactants to minimize skin irritation. Additionally, Foamix developed a new version of hydroethanolic foam that is not thermolabile, and so its usability is preferred to the original Luxiq. [10,11]

The new emulsion-based formulation of BMV foam, which has the functional properties of a cream, was developed with the aim of treating patients with psoriasis and atopic dermatitis. It contains 30% capric/caprylic trigyceride (MCT oil), which is a skin-conditioning emollient [8,9,12]. The oil provides symptomatic relief of skin dryness, which is often associated with skin diseases such as psoriasis and atopic dermatitis [13,14].

The petrolatum-based BMV foam comprises 85% petrolatum, 3% oil components, and about 3% foam stabilizing agents. It has the functionality of an ointment, which can form an occlusive layer, build up the skin barrier, and retain skin hydration. This foam is water-free and it does not require preservatives [8,9,15].

The Foamix foams are not thermolabile. Unlike Luxiq, they do not readily collapse upon exposure to skin temperature. Instead, they spread easily and absorb rapidly into the skin upon application of mild shear-force, allowing comfortable application and well-directed administration to the target area. The difference between quick breaking thermolabile foam and breakable foam is illustrated in **Figure 1**. In the figure, the breakable foam is stable, resulting in facile application and spreading, while the hydroethanolic foam instantly melts on the fingers (within a few seconds), which makes application to the target site challenging and the foam difficult to spread over large skin areas.

BMV foam for psoriasis

Psoriasis is an inflammatory skin condition. Plaque psoriasis is the most frequent type and clinically presents as thick plaques covered by silvery scales at the sides of preferential sites such as the elbows, knees, lower back, and scalp. Treating scalp psoriasis with traditional creams and ointments is somewhat challenging, as they are difficult to apply under the hair and leave greasy residues, while foam is easier to apply and it does not cause any greasiness. The BMV hydroethanolic foam, Luxiq, was tested in Phase II and III clinical studies in scalp psoriasis and in additional studies that were conducted in patients with non-scalp psoriasis [16–18]. These studies were extensively reviewed by Stein in 2005 [19].

Clinical studies for scalp psoriasis

Among the adverse events associated with topical corticosteroid use, the most serious is hypothalamic–pituitary–adrenal (HPA) axis suppression, which can result in skin atrophy and in extreme cases, may be life threatening. The safety of Luxiq was initially tested by Franz *et al.* in 18 patients with specific emphasis on its potential to cause HPA axis suppression. This study revealed no evidence of increased toxicity or HPA-axis suppression for the BMV foam [16]. Franz *et al.* subsequently conducted a pivotal Phase III clinical trial in scalp psoriasis in 1999 [16]. This study, which was submitted to the FDA for drug approval, was a multicenter, randomized, double-blind, double-dummy, placebo, and active-controlled, parallel-group comparison study of the efficacy and safety of Luxiq in treating scalp psoriasis. In total, 190 male and female patients with moderate to severe scalp psoriasis were enrolled and randomly assigned to four treatment groups in a ratio of 2:1:2:1:

Luxiq, the respective foam vehicle, BMV lotion, and placebo lotion. Applications of the test products were made topically twice daily to the entire scalp for 4 weeks. The study objectives were to evaluate the safety and efficacy of Luxiq in the treatment of psoriasis of the scalp, compared with the foam vehicle, and to a lotion form of BMV and a placebo lotion.

The primary efficacy results, as analyzed by the FDA Medical Officer for the intent-to-treat (ITT) group, are provided in Tables 1–5 [20,21].

As shown in Tables 1–4, Luxiq was significantly more effective in reducing erythema, scaling and plaque thickness than the BMV lotion and the placebo following 4 weeks of treatment. Luxiq and BMV lotion were equally effective in mitigating pruritus (p values were above 0.05).

These findings were corroborated by the investigators' global assessment of success (IGA) and patients' subjective assessment of improvement, as shown in Table 5. The percent of patients with IGA score of 'completely clear' or 'almost clear' after four treatment weeks in the Luxiq group was 67%, significantly better than the 19 and 46% in the foam vehicle and BMV lotion groups, respectively.

The incidence of local adverse events (burning, itching and stinging) was 54% for Luxiq and 75% for the respective foam vehicle, as laid out in Table 6. In most cases the severity of these adverse events was mild.

The FDA Medical Officer therefore concluded that "For clinical signs, results were that BMV foam was significantly superior to the foam vehicle in the change in mean scores from baseline, in the percentage of patients with a score of 0 at the end point, and in the percentage of patients with a core of 0 or 1 at end point for scaling, erythema, plaque thickness, and a composite score." The Medical Officer further determined that BMV foam was significantly superior to BMV lotion in the change in the mean scores from baseline for scaling, erythema, plaque thickness and composite score.

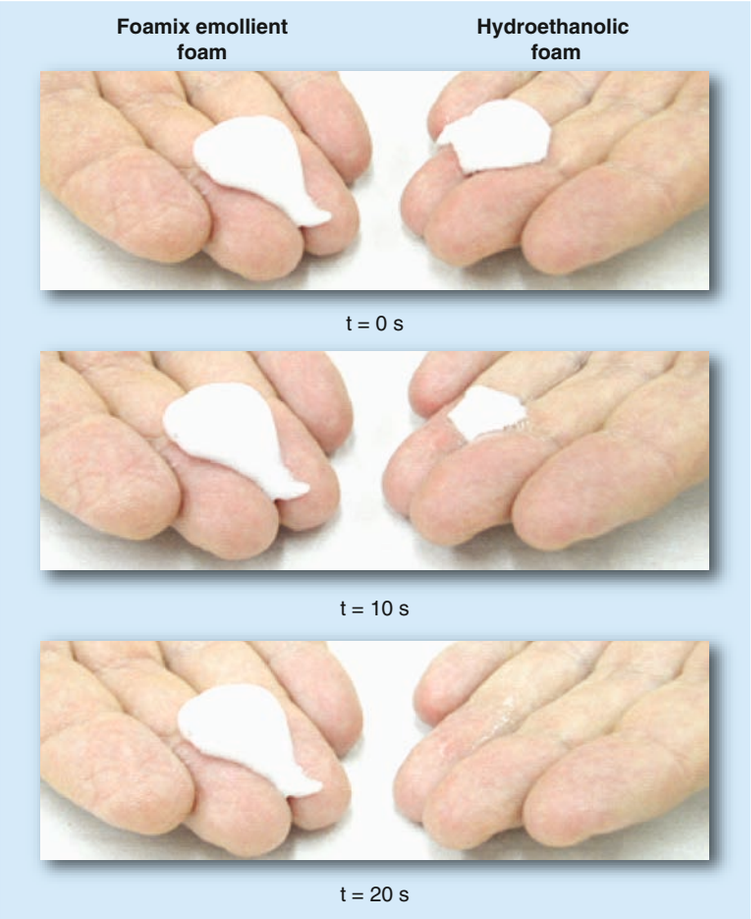

Figure 1. Breakable emollient foam (Foamix Ltd.) versus thermolabile Luxiq®.
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Based on these conclusions, the Medical Officer further stated that "0.1% BMV foam is approvable for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses."

Table 1. Scaling score at baseline and following 4 weeks of treatment (intention-to-treat population).

Treatment	Baseline	End point (4 weeks)	Change from baseline[†]	Score 0 at end point[‡]	Score 0 or 1 at end point[§]
Luxiq®	2.73	0.92	-1.81	30 (47%)	47 (73%)
Foam vehicle	2.88	2.16	-0.71	2 (6%)	8 (25%)
BMV lotion	2.67	1.19	-1.48	22 (35%)	39 (62%)
Placebo lotion	2.81	1.87	-0.94	4 (13%)	11 (35%)

All the values featured in this table are mean values.
[†]Luxiq versus foam vehicle: p = 0.0001; Luxiq versus BMV lotion: p = 0.0848.
[‡]Luxiq versus foam vehicle: p < 0.0001; Luxiq versus BMV lotion: p = 0.2076.
[§]Luxiq versus foam vehicle: p < 0.0001; Luxiq versus BMV lotion: p = 0.1873.
BMV: Betamethasone valerate.
Data taken from [20,21].

Table 2. Erythema score at baseline and following 4 weeks of treatment (intention-to-treat population).

Treatment	Baseline	End point (4 weeks)	Change from baseline†	Score 0 at end point‡	Score 0 or 1 at end point§
Luxiq®	2.48	0.94	-1.55	26 (41%)	48 (75%)
Foam vehicle	2.69	2.13	-0.56	2 (6%)	6 (19%)
BMV lotion	2.48	1.3	-1.17	16 (25%)	39 (62%)
Placebo lotion	2.58	2.03	-0.55	1 (3%)	11 (35%)

All the values featured in this table are mean values.
†Luxiq versus foam vehicle: p = 0.0001; Luxiq versus BMV lotion: p = 0.0399.
‡Luxiq versus foam vehicle: p = 0.0003; Luxiq versus BMV lotion: p = 0.0896.
§Luxiq versus foam vehicle: p < 0.0001; Luxiq versus BMV lotion: p = 0.1292.
BMV: Betamethasone valerate.
Data taken from [20,21].

While this study was sufficient for the FDA to approve Luxiq, it is noted that the approval was based on one pivotal clinical study, which included a total of only 190 patients, and only 64 of them received the actual BMV foam product, which is less than the customary requirement of two adequately controlled Phase III clinical studies.

An open clinical study was conducted to evaluate the efficacy, safety and patient acceptability of Bettamousse®, the European version of the hydroethanolic foam Luxiq (Mipharm SpA, Milano, Italy) in moderate to severe scalp psoriasis. The study, which was conducted in 28 dermatology clinics, was an investigator-blinded, randomized, cross-over study. Bettamousse was compared with standard psoriasis therapies (SPT); that is, corticosteroids or calcipotriol [17]. Each of the 241 patients who were enrolled in this study received 4 weeks of treatment with either Bettamousse or SPT, and then, after a wash-out period of at least 4 weeks, received 4 weeks of treatment with the other drug. Bettamousse was applied twice daily, and SPTs were applied according to their customary treatment regimens.

The effect of each of the treatments (Bettamousse and SPT) on erythema, scaling, itching and burning on a 'target' lesion was assessed by the blinded investigators on a five-grade scale, where 0 equals 'lesion completely cured' and 4 equals 'very severe lesions'. Adverse events were monitored for safety assessment. Finally, the subjective assessment of treatment acceptability by the patients and the influence of each treatment on the Psoriasis Disability Index were determined at baseline and at the end of each treatment period using a Finlay-Khan questionnaire.

The study results indicated that Bettamousse was significantly more effective than SPT. The mean clinical global score (sum of erythema, scaling, itching and burning) was 7.6 ± 2.6 at baseline; it decreased to 1.5 ± 1.9 at the end of treatment, compared with 3.1 ± 2.7 for SPT ($p < 0.001$). Moreover, 88% of the patients had a complete or nearly complete resolution of scaling following Bettamousse treatment in comparison with 66% after SPT therapy ($p < 0.001$). Using the modified Finlay–Kahn questionnaire, Bettamousse was superior to SPT in terms of patient acceptability. It should be noted however that this was an open study and the non-blinded nature of the study might have biased the results. While the evaluation of one end point (the sum score of psoriatic scalp lesions) was performed by investigators unaware of treatment sequences, there is still a risk that a bias did exist. In

Table 3. Plaque thickness at baseline and following 4 weeks of treatment (intnention-to-treat population).

Treatment	Baseline	End point (4 weeks)	Change from baseline†	Score 0 at end point‡	Score 0 or 1 at end point§
Luxiq®	2.63	0.61	-2.02	42 (66%)	52 (81%)
Foam vehicle	2.59	1.84	-0.75	5 (16%)	8 (25%)
BMV lotion	2.54	1.14	-1.4	25 (40%)	39 (62%)
Placebo lotion	2.56	2	-0.65	5 (16%)	8 (26%)

All the values featured in this table are mean values.
†Luxiq versus foam vehicle: p = 0.0001; Luxiq versus BMV lotion: p = 0.0008.
‡Luxiq versus foam vehicle: p < 0.0001; Luxiq versus BMV lotion: p = 0.0044.
§Luxiq versus foam vehicle: p < 0.0001; Luxiq versus BMV lotion: p = 0.0186.
BMV: Betamethasone valerate.
Data taken from [20,21].

Table 4. Composite psoriasis score at baseline and following 4 weeks of treatment (intention-to-treat Population).

Treatment	Baseline	End point (4 weeks)	Change from baseline[†]	Score 0 at end point[‡]	Score 0 or 1 at end point[§]
Luxiq®	7.84	2.47	-5.38	19 (30%)	35 (55%)
Foam Vehicle	8.16	6.13	-2.03	2 (6%)	2 (6%)
BMV Lotion	7.68	3.63	-4.05	14 (22%)	20 (32%)
Placebo Lotion	8.03	5.9	-2.13	1 (3%)	2 (6%)

All the values featured in this table are mean values.

[†]Luxiq versus foam vehicle: p = 0.0001; Luxiq versus BMV lotion: p = 0.0094.

[‡]Luxiq versus foam vehicle: p = 0.0088; Luxiq versus BMV lotion: p = 0.4194.

[§]Luxiq versus foam vehicle: p < 0.0001; Luxiq versus BMV lotion: p = 0.0121.

BMV: Betamethasone valerate.

Data taken from [20,21].

addition, the steroids used as 'SPT' in the Andreassi study were not identified; and if these were less potent steroids, the superior effect of BMV should not be surprising.

Both treatments were well tolerated. Bettamousse was also rated by the patients as more convenient to use for treating scalp psoriasis in comparison with SPT ($p < 0.01$).

Feldman *et al.* investigated the efficacy of Luxiq in the treatment of moderate to severe scalp psoriasis once- or twice-daily [18]. A total of 79 patients were enrolled in seven centers and treated with Luxiq either once or twice a day for 4 weeks. A blinded physician-grader evaluated the erythema, scaling, and plaque thickness before and after treatment using a 5-point severity scale for each of the parameters, where 0 represented 'no scaling, no erythema, and no thickness'; and 4 expressed 'very thick coarse, possibly fissure scales'; 'very dark red beefy erythema'; and 'very thick plaque with sharp edge'. The investigator's and the patients' global assessments were also evaluated.

The study revealed that both once- and twice-daily treatment regimens resulted in clinically and statistically significant improvement of the erythema, scaling and plaque thickness ($p < 0.0001$). The composite score improved significantly from 7.7 ± 2.1 to 3.0 ± 2.2 with twice-a-day use and from 8.1 ± 2.2 to 3.9 ± 2.8 with once-a-day use ($p < 0.0001$ in each regimen); but there was no difference between the treatment regimens ($p > 0.05$) for the difference between groups. Therefore, it was concluded that once-daily administration of Luxiq may be sufficient for scalp psoriasis treatment, thus improving compliance. It is noted, however, that while the study sample size was adequate to determine that both treatments were efficacious, a larger sample size or longer duration of follow-up in this trial would be needed to demonstrate a meaningful difference in efficacy between once- and twice-daily dosing [22].

In a separate study, Feldman *et al.* investigated the equivalence of a given quantity of foam to quantities of cream, lotion, gel and solution by quantifying the number of fingertip units (FTUs) per gram, and measuring the area of coverage of an FTU of each dosage form [23]. The average weight of an FTU of foam was about 50 µg, while the weight of an FTU of cream or gel was nine- to 12-times greater. The area coverage of foam vehicle was less than the area covered by cream and gel.

Table 5. Investigator's global evaluation of improvement following 4 weeks of treatment (intention-to-treat population).

Treatment	Completely clear	Almost clear	Marked improvement	Moderate improvement	Slight improvement	No change	Worse	Score 1 or 2 at end point[†‡]
Luxiq®	26 (41%)	17 (27%)	4 (6%)	4 (6%)	6 (9%)	5 (8%)	2 (3%)	43 (68%)
Foam vehicle	2 (6%)	4 (13%)	1 (3%)	2 (6%)	8 (25%)	12 (38%)	3 (9%)	6 (19%)
BMV lotion	16 (25%)	13 (21%)	4 (6%)	12 (19%)	5 (8%)	11 (17%)	2 (3%)	29 (46%)
Placebo lotion	2 (6%)	4 (13%)	2 (6%)	3 (10%)	5 (16%)	11 (35%)	4 (13%)	6 (19%)

All the values featured in this table are mean values.

Luxiq versus Foam vehicle: p = 0.0001; Luxiq versus BMV lotion: p = 0. 0230.

[†]1 = completely clear; 2 = almost clear.

[‡]Score 1 or 2 at end point; Luxiq versus foam vehicle: p < 0.0001; Luxiq versus BMV lotion: p = 0. 0202.

BMV: Betamethasone valerate.

Data taken from [20,21].

Table 6. Incidence and severity of local burning/itching/stinging.

Treatment	n	Total incidence (n)	Maximum severity (n)		
			Mild	Moderate	Severe
Luxiq®	63	34 (54%)	28 (44%)	5 (8%)	1 (2%)
Vehicle foam	32	24 (75%)	13 (41%)	7 (22%)	4 (12%)
BMV lotion	63	33 (52%)	26 (41%)	6 (10%)	1 (2%)
Placebo lotion	30	20 (67%)	12 (40%)	5 (17%)	3 (10%)

BMV: Betamethasone valerate.
Data taken from [20,21].

In conclusion, three clinical studies presented evidence that BMV foam is effective in the treatment of scalp psoriasis. It is noted that since the approval of this product, additional and newer products for scalp psoriasis, such as clobetasol propionate foam (Olux), a coal tar foam (Scytera™) and a combination calcipotriol plus betamethasone dipropionate (Taclonex® Topical Suspension), have been introduced for scalp psoriasis treatment. Currently, the evidence base lacks any direct comparisons between these products, which would offer useful information for patients and clinicians.

Clinical studies for non-scalp psoriasis

Stein *et al.* conducted a randomized, double-blind, placebo controlled, paired-comparison, split-body study to assess the efficacy and safety of Luxiq in the treatment of patients with symmetrically located mild to moderate plaque psoriasis located in the trunk, upper extremities, lower extremities, elbows, knees, palms or soles [24]. Each of the 40 study patients was assigned to treat one side of the body with Luxiq; the other side was treated with Placebo foam. Luxiq and Placebo were applied twice daily in the morning and evening for 12 weeks.

At the end of the treatment, more than 50% improvement of lesions was demonstrated in 70% of the Luxiq-treated side, compared with 24% of patients with similar improvement on their placebo foam-treated side. Adverse effects were limited to temporary stinging, burning, or itching in several patients. Three patients (7.5%) withdrew from the study because of stinging or itching. These results indicated that Luxiq may be effective in the treatment of non-scalp psoriasis.

The efficacy and safety of an emollient foam composition containing 0.12% BMV developed by Foamix was investigated by Shemer *et al.* [12]. This was a randomized, investigator-blinded, right–left comparison within a patient clinical trial that enrolled 30 patients with mild to moderate psoriasis, who had similar plaque areas of psoriasis on either both knees or both elbows. Foam was administered on one side and a commercially available BMV 0.12% cream (Betnovate, GlaxoSmithKline) was administered on the other side for a period of 6 weeks.

The study reached the conclusion that both treatments were effective in the treatment of the psoriatic lesions (Table 7). After 3 weeks of treatment there was a clinically and statistically significant improvement in all efficacy parameters ($p = 0.03$; Dunnett-t test), including thickness (mean improvement: 42–43%),

Table 7. Efficacy of betamethasone valerate emollient foam versus Betnovate® in the treatment of bilateral elbow and knee psoriasis.

Efficacy	Baseline		3 weeks		6 weeks		Change versus baseline	
	Mean	Range	Mean	Range	Mean	Range	3 weeks (%)	6 weeks (%)
Foam								
Thickness	1.52	0–3	0.87	0–2	1	0–3	-43	-34
Redness	1.27	0–2.5	0.81	0–2	0.93	0–2.5	-36	-26
Scaling	1.32	0–3	0.67	0–2	0.83	0–3	-49	-37
Itch	0.88	0–2.5	0.19	0–1	0.24	0–2	-78	-73
Global	1.22	0–2.5	0.71	0–2	0.85	0–2.5	-42	-30
Area (cm^2)	20.86	3–120	17.54	0–120	18.65	0–120	-16	-11
Cream								
Thickness	1.62	0–3	0.94	0–2	1.09	0–2.5	-42	-33
Redness	1.4	0–2.5	0.79	0–2	1	0–2.5	-44	-29
Scaling	1.4	0–3	0.62	0–2	0.8	0–2.5	-56	-43
Itch	0.92	0–2.5	0.21	0–1	0.23	0–2	-77	-75
Global	1.33	0–2.5	0.75	0–2	0.85	0–2.5	-44	-36
Area (cm^2)	17.48	3–70	14	3–70	13.04	0–70	-20	-25

Data taken from [12].

erythema (mean improvement: 36–44%), scaling (mean improvement: 49–56%), itch (mean improvement: 77–78%), and in the global assessment score (mean improvement: 42–44%). Figure 2 illustrates the therapeutic effect of both treatments photographically. No statistically significant difference was found between treatments ($p = 0.465$; c^2 test), conceivably due to the limited sample size. These improvements persisted following an additional 3 weeks of treatment. Notably, the mean global assessment of change after 3 weeks of treatment on a scale between 0 (no change) and 3 (marked improvement) was 1.35 for the foam and 1.07 for the cream. The investigator identified six "marked improvement" responses for the foam versus three such cases for the comparator cream.

The study assessed treatment compliance by weighing medication containers before and after use. The mean daily amount of foam was approximately 1.1 g; and the corresponding amount of cream was 0.67 g/day. The study also assessed patient usability preferences, via comparing the foam and cream via a patient satisfaction questionnaire. The results of the satisfaction questionnaire indicated that patients are more likely to use the foam preparation rather than the cream based on parameters such as skin absorption, oily residue, shiny look, stickiness and odor, as illustrated in Figure 3. The favorable usability of the foam is a major advantage that contributes to enhanced patient compliance and better clinical outcome of treatment. No drug-related adverse effects were recorded in both treatments.

It was concluded that the BMV emollient foam offers an attractive alternative to mid-potency steroid cream. As such, it is more likely that psoriasis patients will use their medication as frequently as prescribed and will gain the desired therapeutic benefits.

Clinical studies regarding other dermatological indications

This section surveys exploratory studies that were conducted in an effort to assess the clinical utility of BMV foam products in the treatment of various skin conditions other than psoriasis.

Milani *et al.* investigated the efficacy of Bettamousse in the treatment of moderate-to-severe seborrhoeic dermatitis (SD) of the scalp [25]. In total, 180 patients were assessed for the severity of erythema, scaling and itching using a five-point grading score (0 = lesion completely cured; 1 = mild; 2 = moderate; 3 = severe; 4 = very severe lesion); a clinical global score was calculated by summing the scores of all items. Assessments were done at baseline and after 4 weeks of active treatment, followed by 8 weeks of follow up with no treatment.

This study revealed that Bettamousse is effective in the treatment of scalp SD. The clinical global score was reduced significantly from 6.3 ± 1.8 to 1.4 ± 1.4 at the end of 4 weeks of treatment ($p < 0.0001$) and it remained low (1.7 ± 1.8) after the 8-week follow-up period ($p < 0.0001$). In total, 93% of the patients had a clinical global score of 3 or less after 4 weeks of treatment; 88% of patients maintained this low score after 8 weeks of follow up. The majority of patients participating in the study (85%) rated Bettamousse foam as more efficacious and usable than previous treatments used. Thus, the investigators concluded that Bettamousse is a well tolerated and effective treatment of scalp SD.

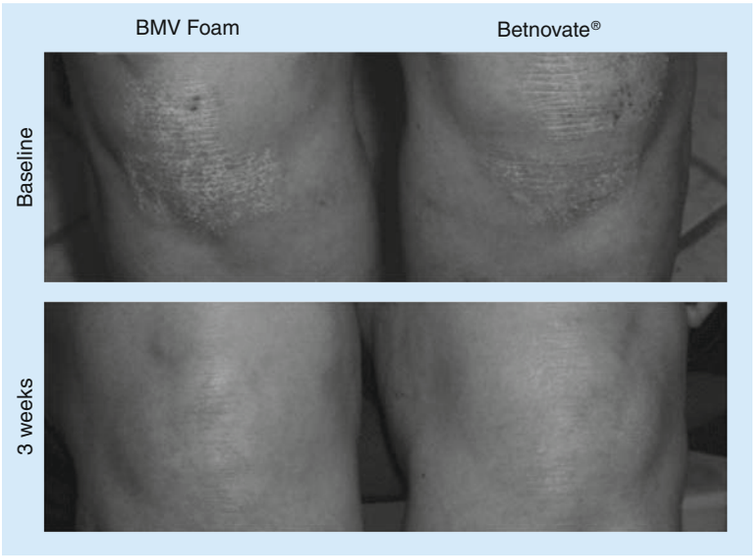

Figure 2. Marked improvement of bilateral psoriasis of the knees, following 3 weeks of treatment with betamethasone valerate emollient foam and Betnovate®.
BMV: Betamethasone valerate.
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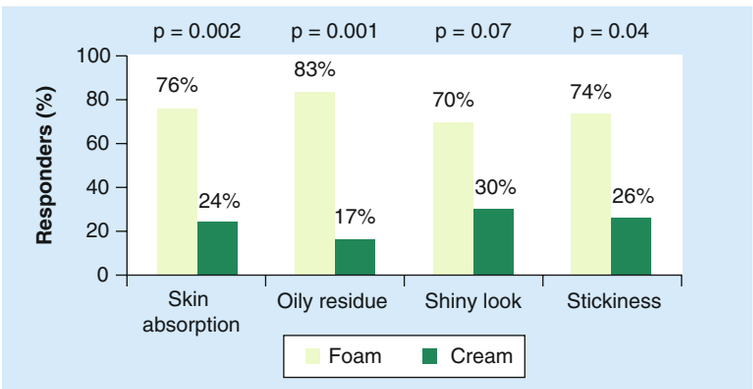

Figure 3. Usability preference – foam versus cream.
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Kudleep *et al.* studied the efficacy and safety of topical BMV foam, intralesional triamcinolone acetonide, and tacrolimus ointment in the treatment of alopecia areata (AA) [26]. A total of 78 patients with localized AA were randomized to receive either topical BMV foam (0.1%) twice daily, intralesional triamcinolone acetonide (10 mg/ml) every 3 weeks, or tacrolimus ointment (0.1%) twice daily, for 12 weeks, followed by 12 weeks of observation without treatment.

Intralesional triamcinolone was the most effective treatment, with 14 patients (56%) who had more than 75% regrowth after 9 weeks and 16 (64%) after 12 weeks of treatment. From the BMV foam group, 12 patients (43%) also gained more than 75% regrowth at the end of treatment, while none of the tacrolimus-treated patients had significant regrowth. Side effects included mild pain and atrophy at injection sites (in the triamcinolone group), pruritus, and burning with BMV foam and tacrolimus,

In conclusion, this study indicated that intralesional triamcinolone acetonide had the greater effect, and that BMV foam was also effective in the management of localized AA.

Conclusion

Hydroethanolic foam formulations of the corticosteroids BMV and clobetasol propionate were the first topical foams available in dermatology. The efficacy of these foams, combined with their favorable tolerability and ease of use, facilitated their utilization as alternatives for traditional creams, lotions, ointments and gels. However, because of their high alcohol content, their use has been limited to scalp psoriasis treatment. New emulsion- and petrolatum-based BMV foams will be useful for treating additional inflammatory skin conditions associated with an impaired epidermal barrier, such as atopic dermatitis and non-scalp psoriasis.

Financial & competing interests disclosure

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Executive summary

- Topical corticosteroids, especially betamethasone valerate (BMV) have been used topically to relieve many inflammatory skin conditions.
- The vehicle used to deliver topical drugs such as creams, ointments, lotions, sprays and foams can significantly influence their performance.
- This manuscript reviewed the properties of BMV foams and discussed the clinical studies that have been conducted to assess efficacy and safety for the treatment of scalp and non-scalp psoriasis, as well as other dermatological inflammatory conditions.
- In conclusion, the efficacy of these foams, combined with their favorable tolerability and ease of use, facilitated their utilization as a treatment option for scalp psoriasis; however, because of their high alcohol content, their use has been limited.
- New emulsion- and petrolatum-based BMV foams will be useful for treating additional inflammatory skin conditions.

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