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CASE SERIES

Fixed-dose combination of calcipotriene/betamethasone dipropionate foam for the management of mild-to-moderate psoriasis in daily clinical practice: a collection of clinical experiences

Anna Campanati[1], Maria Esposito[2], Giacomo Caldarola[3,4], Sara Cacciapuoti[5], Gabriella Fabbrocini[5]

[1]Dermatological Clinic, Department of Clinical and Molecular Sciences, Polytechnic Marche University, Ancona, Italy; [2]Dermatology – Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [3]Institute of Dermatology, Università Cattolica del Sacro Cuore, Rome, Italy; [4]Dermatology Department, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [5]Department of Clinical Medicine and Surgery – Section of Dermatology, University of Naples Federico II, Napoli, Italy

Abstract

A fixed-dose combination of calcipotriene 0.005%/betamethasone dipropionate 0.064% (Cal/BD) aerosol foam (Enstilar, LEO Pharma) is the only topical therapy approved for the acute (reactive) and proactive management of psoriasis. Although treatment with Cal/BD foam has been characterized in a clinical context, further evidence is needed to determine its optimal use in clinical practice. A group of experts discussed the value of the Cal/BD foam as a topical treatment for mild-to-moderate psoriasis in combination with systemic treatments. The reported experiences support effectiveness of the Cal/BD foam in daily clinical practice, with an improvement in patient quality of life.

Keywords: calcipotriene/betamethasone dipropionate, Cal/BD foam, psoriasis, real-life experience, topical therapy.

Citation

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Introduction

Psoriasis is a chronic immune-mediated inflammatory disease affecting up to 4% of the European population.[1] More than 80% of cases present with plaque-type psoriasis, characterized by erythematous–squamous plaques usually involving elbows, scalp, trunk and knees.[2,3] Even though the condition is not life-threatening, it substantially diminishes the quality of life (QoL) of patients.[4] Thus, the sustained control of signs and symptoms of the disease represents the main therapeutic goal.[5] However, despite the many treatment options currently available for the management of psoriasis, patient satisfaction remains suboptimal.[6]

Most patients present with a localized form of the disease of mild-to-moderate severity (≤10% of body surface area).[7] Current guidelines recommend topical therapies as first-line monotherapy treatment for these patients or in combination with systemic drugs in patients with moderate disease to enhance the therapeutic activity or in case of partial loss of monotherapy effectiveness.[8–11] In addition, topical therapies can be used in patients treated with systemic therapy who present residual disease symptoms in hard-to-treat areas such as the scalp and genital area.[12] The fixed-dose combination of calcipotriol 0.05 µg/g and betamethasone dipropionate 0.5 mg/g (Cal/BD) aerosol foam (Enstilar, LEO Pharma A/S, Denmark; hereafter termed Cal/BD foam) is approved for use in the EU (in adults) and the USA (in adults and adolescents).[13,14] In the recently published PSO-LONG trial, the regular application of Cal/BD foam biweekly for up to 52 weeks (proactive management) was more effective than reactive management (which starts as soon as psoriasis relapses).[15] Based on these results, Cal/BD foam is the only treatment for which the approved label allows either reactive treatment or biweekly maintenance use.[16]

Although treatment with the Cal/BD foam has been extensively characterized in a clinical context, further real-world evidence is needed to determine the optimal use of Cal/BD foam for the management of mild-to-moderate psoriasis in clinical practice.[14]

In May 2022, a group of Italian experts with proven experience in the management of psoriasis met and discussed the positioning of topical therapies in the therapeutic strategy. They explored the value of the Cal/BD foam as a topical treatment for mild-to-moderate psoriasis in combination with systemic treatments for other concomitant conditions. To further characterize and share information on the use of this therapeutic approach in daily clinical practice, starting from the meeting contents, some real-life experiences with the use of the Cal/BD foam are presented and discussed in this article.

Patients and methods

The authors retrospectively selected and reported cases of patients with mild-to-moderate psoriasis treated with the Cal/BD foam up to May 2022. Inclusion criteria were age ≥18 years and an indication of treatment based on clinical practice and physician judgment. Treatment with the Cal/BD foam was prescribed as monotherapy or in addition to other concomitant therapeutic regimens and was administered according to the doses and modalities defined in the Summary of Product Characteristics. Because of the retrospective description of this case series, treatment regimens and patient education were not standardized. The study was conducted following the ethical principles of the revised version of the Declaration of Helsinki. All patients provided written informed consent for treatment and for the publication of clinical data and any accompanying images. All the participants signed an informed consent form. The authors obtained written consent from patients for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available. Patient consent forms were not provided to the journal but are retained by the authors. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines.

Case series

Effectiveness and safety of long-term proactive treatment with the Cal/BD foam

A 60-year-old patient with a 30-year history of mild-to-moderate psoriasis presented in January 2021. The patient had obesity, with hypercholesterolaemia and hypertriglyceridaemia, and did not have psoriatic arthritis. The lesions had a sufficiently stable localization throughout the clinical history of the disease (Figure 1A) and were previously treated with clobetasol propionate, calcipotriol/betamethasone gel, calcipotriol and tacalcitol monohydrate. These approaches gave only a partial clinical benefit with a loss of efficacy in dose reduction. The lesions had a great impact on the patient's QoL due to the hyperkeratosis and were not very responsive to therapy because of a consistent inflammatory background (Psoriasis Area Severity Index (PASI) score: 6.8; Dermatology Life Quality Index (DLQI) score: 25) (Figure 1B).

During the first visit, the patient asked for an effective and safe treatment, which could ensure the long-term persistence of the clinical result, and with less frequent and less severe relapses than previously experienced. Treatment with the Cal/BD foam was prescribed, involving one-daily application for 4 weeks. At the end of this period, the patient was treated with a proactive regimen (application of the treatment twice a week on non-consecutive days) to maintain the clinical results obtained in the induction phase. After 68 weeks of treatment, the patient underwent complete clinical resolution of all lesions, with a substantial improvement in QoL (PASI score: 0; DLQI score: 2). The improvement was clinically and sub-microscopically detectable during capillaroscopy (Figure 2).

Over the 68 weeks of treatment with the Cal/BD foam, the patient experienced two relapses: the first after 2 months of proactive treatment following an episode of SARS-CoV-2 infection; the second 9 months after starting the proactive treatment, following the patient's choice to reduce the applications of Cal/BD foam. In both cases, relapses were managed with daily treatment for 4 weeks, leading to complete remission.

Rapidity of action of Cal/BD foam treatment in case of a disabling flare

This clinical case refers to a 45-year-old woman with a family history of psoriasis and psoriatic arthropathy. She presented with Hashimoto's thyroiditis and irritable bowel syndrome. The patient was first diagnosed with psoriasis in 2008, subsequent to mild and localized skin manifestations in the lower limbs, treated with topical steroids very inconstantly because of the patient's discomfort in using topical products.

In 2017, the patient complained of pain in the interphalangeal joints with swelling of the fingers. Unfortunately, the diagnosis of psoriatic arthritis was reached late, only in 2019, when she started methotrexate therapy at a dosage of 15 mg/week. The patient responded immediately to the therapy, without adverse events.

The disease remained stable until the administration of the booster dose of the SARS-CoV-2 vaccine (March 2020),

Figure 1. Initial presentation of lesions. A Erythematous and desquamating patches on the trunk (I) and elbows (II) at the first presentation. B Consistent inflammatory background reported at capillaroscopy.

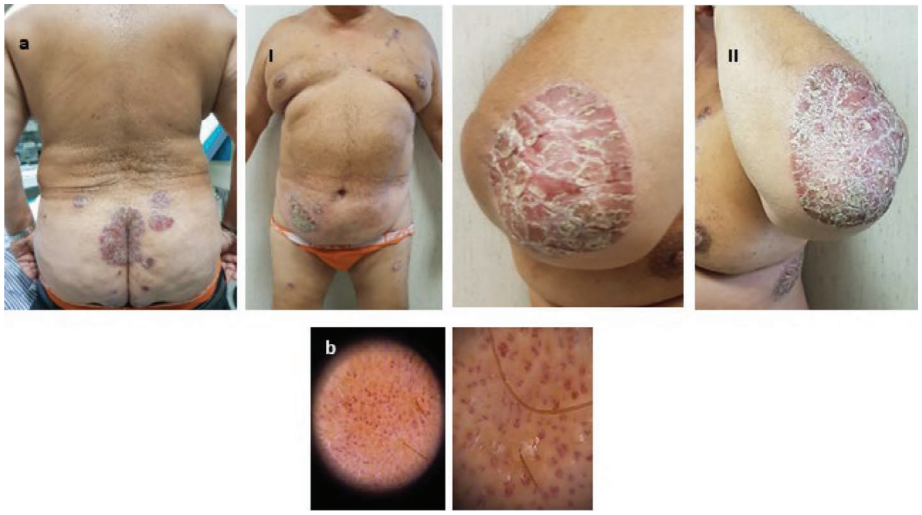
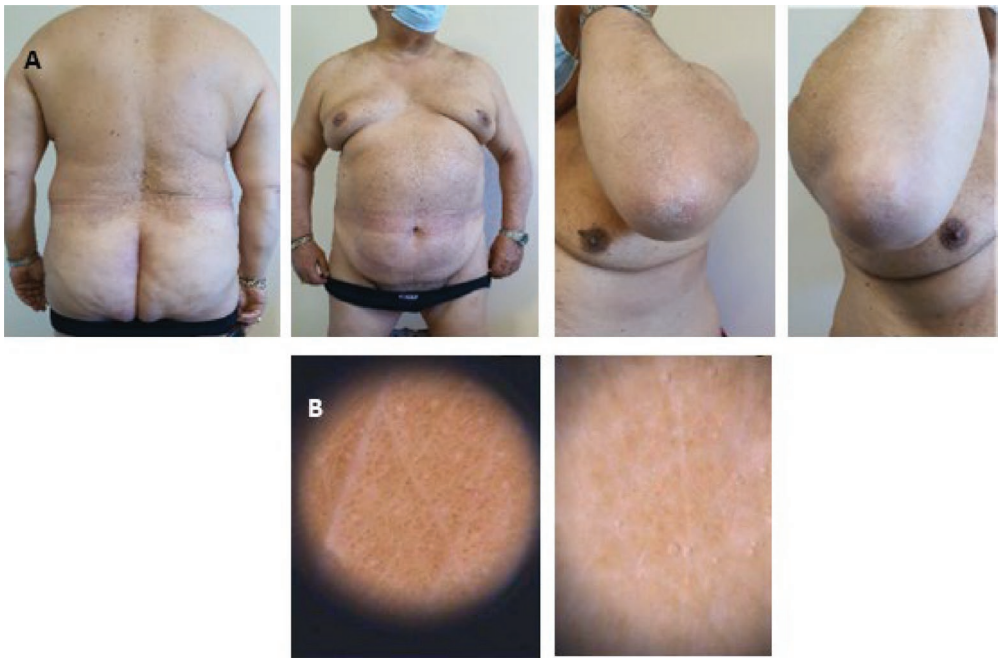


Figure 2. Improvement of lesions. A Complete clinical resolution of the psoriasis plaques after 68 weeks of treatment with the Cal/BD foam. B Resolution of the inflammatory background reported at capillaroscopy.



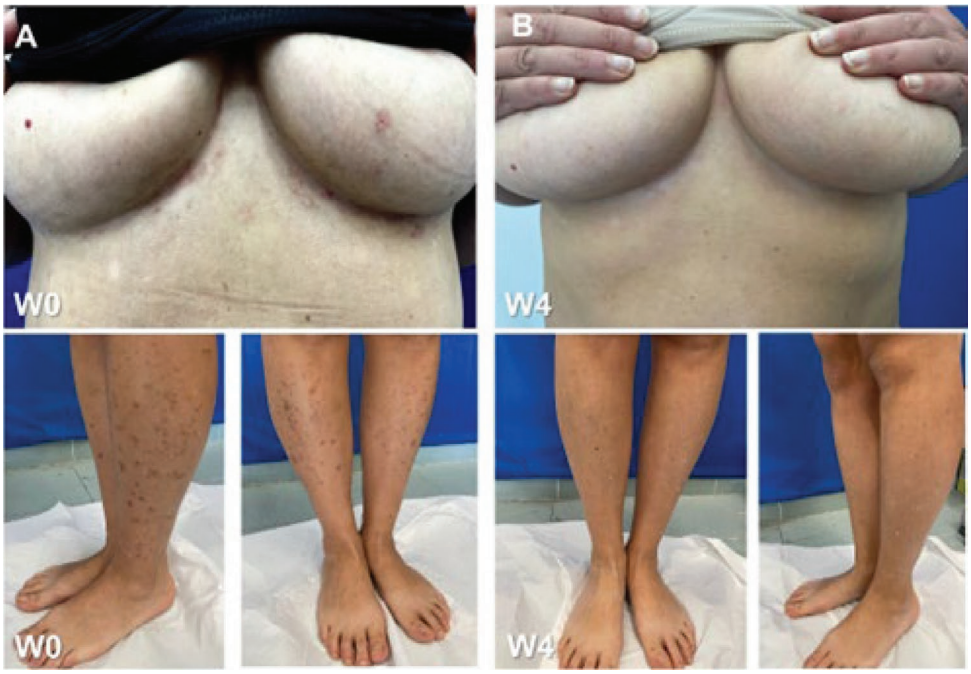
when signs of recurrence in the sub-mammary fold and lower limbs appeared (PASI score: 6; DLQI score: 19; Figure 3A). The treatment plan was then supplemented with Cal/BD foam, with once-daily application for 4 weeks.

After 4 weeks, the patient showed total clearance with only a few post-inflammatory hypochromic sites (PASI score: 0; DLQI score: 2; Figure 3B). The patient showed good therapeutic adherence and particularly appreciated the rapid foam absorption and degree of hydration on the scaly components.

Cal/BD foam treatment for the management of induced moderate psoriasis

A 69-year-old patient presented in June 2019 with itchy atopic dermatitis on the neck and legs, strongly

Figure 3. Recurrence and clearance of psoriasis plaques. A Erythematous patches on the sub-mammary fold and the extensor surface of the limbs at the first presentation (W0). B Total clearance with only a few post-inflammatory hypochromic sites after 4 weeks of Cal/BD foam treatment (W4).



impacting QoL and sleep quality due to itching. The patient tested positive for nickel and potassium dichromate, presented hypertension (under pharmacological treatment), and had undergone osteosynthesis surgery at the right ankle with subsequent bone necrosis. Atopic dermatitis had long been treated only with topical therapies. The patient was given dupilumab therapy, which produced a rapid improvement in skin manifestations and sleep quality after 3 months, with a marked reduction in itching. In September 2019, the patient reported the appearance of scaly plaques on the scalp, compatible with a diagnosis of mild psoriasis. Calcipotriol/betamethasone gel was prescribed.

In November 2019, the patient was in remission of disease and continued maintenance treatment with dupilumab and calcipotriol/betamethasone gel. In January 2022, 3 weeks after the booster dose of the SARS-CoV-2 vaccine, the patient reported a worsening of the clinical picture with a relapse of psoriatic manifestations at the level of the scalp (Figure 4AI) and the appearance of new skin lesions on the trunk, without itchy symptoms, compatible with a diagnosis of psoriasis (Figure 4BI and CI).

The patient tried to apply calcipotriol/betamethasone gel on these new lesions, with poor effectiveness and tolerability due to greasiness. Based on patient preference, therapy with the Cal/BD foam was initiated. After 2 months of treatment, the patient returned to complete remission of the disease, both on the scalp and trunk (Figure 4AII, BII and CII). The Cal/BD foam was well tolerated.

This clinical case suggests that the Cal/BD foam can be combined with a biologic even in the case of induced forms of moderate psoriasis, with superior effectiveness to that reported with the gel formulation.

Activity of long-term treatment with the Cal/BD foam on desquamations and keratolytic component

The clinical case concerns a 73-year-old patient suffering from stable mild-to-moderate plaque psoriasis for about 15 years. The patient presented with plaques in the lower and upper extremities with plantar, palmar and nail involvement (Figure 5A) that had infiltrated papule plaques with mild erythema and an intense hyperkeratotic component with scratching excoriations (PASI score: 6.5; visual analogue scale score related to itching: 7.5). He did not present any sign or symptom of joint involvement. He showed mild hypertension, pharmacologically controlled, and positivity to hepatitis C virus. The patient underwent different therapies to manage psoriasis, including clobetasol ointment, betamethasone + salicylic acid ointment, calcipotriol cream, calcipotriene ointment, salicylic acid 10% in petroleum in combination with topical therapies, cyclosporine 3.5 mg/kg/day (2

Figure 4. First presentation and resolution of psoriasis plaques. A Relapse of the erythematous patch on the scalp after the booster dose of the SARS-CoV-2 vaccine (I) and complete remission after 2 months of Cal/BD foam treatment (II). B, C (I) Erythematous patch on the trunk after the third dose of the SARS-CoV-2 vaccine and (II) complete remission after 2 months of Cal/BD foam treatment.

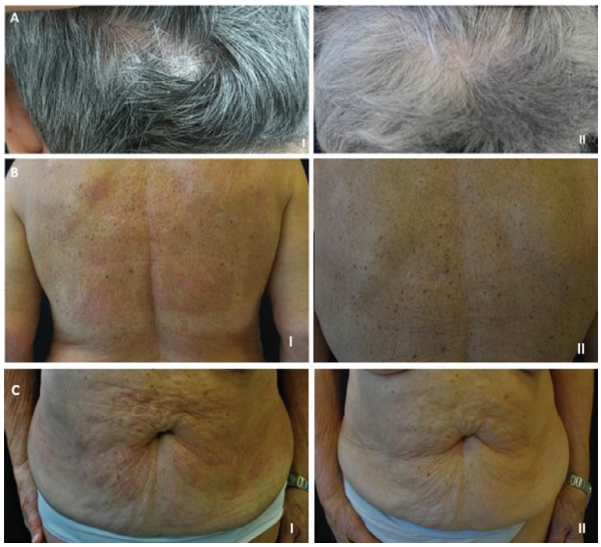
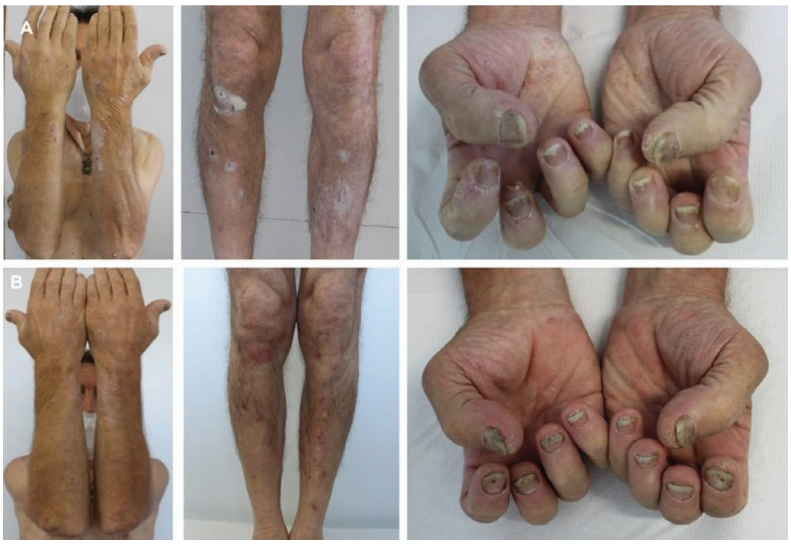


Figure 5. First presentation and improvement of psoriasis plaques. A Erythematous and desquamating patches, with intense hyperkeratotic component and scratching excoriations, on the lower and upper extremities with nail involvement at first observation. B Great reduction of skin plaques, desquamations and keratolytic components after 24 weeks of Cal/BD foam application.



cycles of ~3 months in the previous 2 years), and dimethyl fumarate under a reactive regimen. In combination with systemic therapy for hepatitis C, Cal/BD foam was initiated for 4 weeks, followed by a proactive application (two applications on non-consecutive days per week) for the following 24 weeks. At 4 weeks, the topical therapy showed considerable effectiveness, particularly concerning hyperkeratosis. At week 24, the symptomatology was completely absent, with a remnant of small erythema (PASI score: 0.5; visual analogue scale score related to itching: 0). Reduction of the desquamations and keratolytic components was also evident at the palmar

level (Figure 5B). At the nail level, the patient reported a significant reduction in the pain component (Figure 5B). The patient reported excellent tolerability without any adverse events.

Discussion

Results of different clinical trials and post-hoc analyses report the efficacy of Cal/BD foam treatment in the management of different grades of psoriasis.[17–25] This case series supports the clinical evidence and shows the effectiveness and versatility of Cal/BD foam treatment in managing both mild and moderate psoriasis forms in daily clinical practice, even in the presence of important comorbidities, which require systemic treatments. In these patients, the Cal/BD foam allows the topical management of psoriasis, avoiding the addition of another systemic treatment and/or the interruption of ongoing systemic therapies.

The lack of persistent efficacy over time, risk of cumulative toxicity, and inconvenience of administration are different factors that could limit favourable long-term outcomes with available systemic therapies for moderate psoriasis.[26] Patients described in this series showed the rapid activity of Cal/BD foam treatment administered according to an acute regimen. Moreover, in this series, the Cal/BD foam has been shown to promote great improvement in desquamation and hyperkeratosis.

The proactive treatment showed optimal results with treatment of up to 68 weeks without an adverse event, not even at the submicroscopic level, extending to the clinical practice observed in clinical trials.[24] For instance, in a previous study, dermoscopy and confocal microscopy analyses showed the absence of cutaneous atrophy during proactive treatment with the Cal/BD foam and the consequent improvement in appearance of the psoriatic lesions.[27] According to a proactive regimen, use of the Cal/BD foam has been shown to be effective in reducing residual sub-clinical psoriasis, which supports clinical relapses in patients using on-demand topical medications.[28] These observations, which further support clinical evidence, suggest that the inclusion of a proactive strategy in guidelines for the effective treatment of mild-to-moderate psoriasis is warranted.[10,29]

Topical therapy for psoriasis is often unacceptable to patients, especially the elderly because of application difficulties. It has been reported that the Cal/BD foam provides higher bioavailability, resulting in increased efficacy in plaque psoriasis compared with ointments and gels.[22,23,30] Moreover, Cal/BD foam resulted in one of the most manageable available products, improving patient adherence.[28,31–33] In line with this evidence, the presented clinical cases suggest the feasibility and manageability of the Cal/BD foam formulation, which made the application easier and more immediate for elderly patients (three out of four aged over 60 years) as well as for those with psoriasis in difficult-to-treat areas, such as the plantar, scalp and nails, showing better adherence compared with other topical products or other formulations.

A new Cal/BD cream based on the polyaphron dispersion technology has emerged as a novel formulation for topical treatment of psoriasis and has been available and approved for use in Italy since August 2023. Considering the importance of the vehicle for patient acceptance of topical therapy, the polyaphron dispersion-cream formulation represents a further option for these patients. However, based on the licensed treatment periods for daily use of the two formulations (4 weeks for the foam and 8 weeks for the cream[34]), the foam appears to act faster and this may be associated with rapid improvement in skin symptoms and QoL, potentially increasing treatment adherence. However, head-to-head trials will be required to address this issue.

In conclusion, the Cal/BD foam can be considered a valuable therapeutic option in the treatment of mild-to-moderate forms of the psoriasis, even in the long term, and in patients with concomitant comorbidities, preventing relapses.

Availability of data

All data generated or analysed in this case series are included in this article and/or its figures. Further inquiries can be directed to the corresponding author.

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Celgene, Eli Lilly, Janssen, LEO Pharma and Novartis. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors is available for download at: https://www.drugsincontext.com/wp-content/uploads/2024/02/dic.2023-11-5-COI.pdf

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Correspondence: Anna Campanati, Dermatological Clinic, Department of Clinical and Molecular Sciences, Polytechnic Marche University, Ancona, Italy. Email; anna.campanati@gmail.com

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