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ORIGINAL RESEARCH

Beyond-Mild Psoriasis: A Consensus Statement on Calcipotriol and Betamethasone Dipropionate Foam for the Topical Treatment of Adult Patients

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ABSTRACT

Introduction: There are clear treatment options for mild psoriasis where topical therapies are the mainstay, and for severe psoriasis where systemic therapy (biologic or non-biologic) is necessary. However, there is less clarity in the 'grey zone' of patients in the moderate or so-called '*beyond-mild*' segment. There are frequent delays to the initiation, discontinuation, switching and dose change in treatment, and many patients fail to continue treatment because of concerns about safety or lack of efficacy. Treatment with topical therapies, such as calcipotriol and betamethasone dipropionate (Cal/BD) combinations, may be suitable for these patients.

Method: These consensus recommendations on the use of topical therapies including Cal/BD foam for *beyond-mild* psoriasis originated from a modified Delphi process of European clinical experts. In the process, the experts iteratively refined a series of draft statements, which had to receive ≥ 80% approval to be incorporated into the consensus.

Results: The experts identified three main themes: Cal/BD foam as monotherapy, as an add-on to non-biologic systemic therapies and as an add-on to systemic biologics. The consensus emphasises disease factors and patient

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preference in treatment choice, summarises the evidence base for Cal/BD foam monotherapy for flare treatment as well as long-term management, and identifies the potential for improved treatment outcomes, such as reduced time to onset of action and reduced systemic dose to minimise side effects for add-on Cal/BD therapy to non-biologic systemics. The recommendations regarding add-on Cal/BD foam to biologics are similar to those for non-biologic systemic therapies, but also include suggestions for patients on biologics who are late responders. As clinical choices of Cal/BD combination vary, we have here often used 'Cal/BD' without reference to any particular formulation.

Conclusions: These recommendations aim to give practical guidance to those treating patients with *beyond-mild* psoriasis, to support patients' use of topical preparations and to optimise treatment outcomes.

Keywords: Moderate psoriasis; Severe psoriasis; Consensus recommendations; Topical treatments; Calcipotriol; Betamethasone dipropionate

Key Summary Points

Why carry out this study?

Determining optimal treatment for moderate plaque psoriasis can be challenging as there exists a grey area between the mild and severe ends of the spectrum, hereby referred to as '*beyond-mild*', where optimal patient management is uncertain.

Following growing evidence for the use of calcipotriol and betamethasone dipropionate (Cal/BD) foam for *beyond-mild* psoriasis, we conducted a modified Delphi review to identify key themes and recommendations for treatment based on currently available data and expert clinical experience and opinion.

What was learned from the study?

Three key themes regarding the use of Cal/BD foam in the *beyond-mild* psoriasis patient were identified. These were the use of Cal/BD foam as: (1) monotherapy, (2) add-on to non-biologic systemic therapies and (3) add-on to biologics.

Across these three themes, the authors make 14 key recommendations for the use of CAL/BD foam in adult patients (summarised in Tables 1,2,3).

These recommendations are intended to help provide healthcare professionals (HCPs) with guidance to support their use of the topical medication Cal/BD foam, as monotherapy or as add-on treatment with non-biologic or biologic systemic therapy for *beyond-mild* psoriasis, and ultimately to optimise treatment outcomes for these patients.

INTRODUCTION

Psoriasis is a chronic, inflammatory, immune-mediated disease which primarily affects the skin and joints, and occurs in 2–4% of the Western population [1]. In addition to bothersome physical symptoms, psoriasis is often associated with significant psychosocial burden as a result of social stigmatisation, and difficulties with body image and self-esteem are experienced by many patients. Psoriasis may, therefore, have a profound impact on the patient's quality of life (QoL) [2, 3].

Although there are clear treatment options for mild and severe psoriasis, there exists a 'grey zone' between these two types. The American Academy of Dermatology classifies moderate psoriasis as that which affects from at least 5% to less than 10% of body surface area (BSA), while European guidelines classify moderate-to-severe psoriasis as that which affects more than 10% of BSA [4, 5]. Topical therapies are the mainstay for mild-to-moderate psoriasis [6], but

can also be used as an add-on to systemic therapy (non-biologic or biologic) [5, 7]. Topical steroids are effective and inexpensive but have limitations in terms of locations, such as the face and intertriginous areas, where they are not recommended (except for very short-term use) owing to local side effects [8]. In other areas, topical steroids may be applied for longer periods but are recommended for use beyond 12 weeks only under careful medical supervision [9]. Multiple topical agents are used in psoriasis to supplement and reduce over-reliance on topical steroids. These agents include vitamin D analogues, retinoids such as tazarotene and off-label use of calcineurin inhibitors [8, 9]. Other topical treatments include salicylic acid, dithranol and coal tar preparations [9].

A common treatment pathway for mild forms of plaque psoriasis is daily treatment either with a topical corticosteroid or a fixed topical combination of calcipotriol and betamethasone dipropionate (Cal/BD) with evaluation of response in 2–8 weeks. If there is a response to treatment, frequency of treatment can be reduced, for example to twice weekly. If not, UV or systemic therapy at an expert centre may be needed [8]. For patients with more severe psoriasis, non-biologic systemic treatments are sometimes recommended as first-line therapy (e.g. methotrexate, cyclosporin and acitretin). Biologics are also recommended for these patients when they fail to respond or have contraindications to/side effects from non-biologic systemics [10–13].

Patients in the 'grey zone' between mild and severe may be eligible for topical or systemic therapy, or a combination of both. Following a review of the academic literature, three psoriasis specialists, in collaboration with LEO Pharma and a market research company (Cello Health Insight, London, UK), developed the concept of '*beyond-mild*' psoriasis to describe this population [14]. The literature review selected studies with the following characteristics: patients with moderate-to-severe disease; $N > 50$ patients; treatment either available or with potential to be licensed by the European Medicines Agency. More weight was given to studies with an active comparator (not placebo/vehicle), and informative severity measures and outcomes [14].

While attention in recent years has focused on biologics for the treatment of moderate-to-severe psoriasis, advances have also been made in the development of topical agents [15], such as fixed-dose combinations of Cal/BD in gel, ointment and foam formulations, and of halobetasol propionate and tazarotene. In addition, the use of steroid-sparing agents can reduce the risk of corticosteroid-related adverse effects [9]. The recent PSO-LONG phase III trial demonstrated that long-term proactive management over 52 weeks with fixed-dose Cal/BD foam was superior in (1) prolonging time to first relapse, (2) reducing number of relapses and (3) increasing days in remission, compared with vehicle foam, in adults with plaque psoriasis, with a favourable safety profile [16].

Additionally, there is growing clinical evidence to support the use of Cal/BD formulations for the treatment of patients with moderate-to-severe psoriasis, both as monotherapy (particularly the foam) [17] and as add-on therapy to non-biologic systemic [18] or biologic treatments [19]. In addition, real-world data demonstrate the use of Cal/BD foam for patients with *beyond-mild* psoriasis as monotherapy or as part of a multi-therapy strategy with other topical or systemic agents [12].

Based on the data available for Cal/BD formulations, and to arrive at a clinical consensus for the use of Cal/BD foam in *beyond-mild* psoriasis, we conducted a modified Delphi review based on currently available data and expert clinical experience and opinion. While more detailed data are available for the Cal/BD foam formulation than for other topical treatments, recommendations may be applicable to other topical treatments in the context of *beyond-mild* psoriasis.

METHODS

The Consensus Process

An advisory group of nine European-based expert dermatologists from five countries (France, Germany, Italy, Spain and UK) met in September 2019. Advisors had extensive clinical

experience in treating mild-to-severe psoriasis. Initial discussions focused on the identification of clinical care gaps or themes in relation to the treatment of *beyond-mild* psoriasis, where the development of key recommendations for treatment of *beyond-mild* psoriasis could be considered valuable. The advisors then evaluated each clinical theme and generated supporting statements to provide clinical guidance. Using a modified Delphi methodology [20], draft statements were then reviewed and refined, if necessary, based on clinical value and evidence.

The advisors voted on the draft statements. Consensus was defined as $\geq$ 80% agreement with the summary statement. During the voting process, each advisor assigned an 'agreement score' from 1 to 5 to each statement, where 1 denoted their strong disagreement and 5 denoted strong agreement. Individual scores were then collated and assigned to one of three groups: 1–2, 3 and 4–5. A strong level of agreement to a given statement was achieved if $\geq$ 80% of advisors scored within the 4–5 range. Statements for which an agreement was not achieved were discussed, revised and voted on again. If agreement was not achieved after this second vote, a lack of agreement was recorded. Some slight amendment of statements has been made during preparation of this publication to maintain consistency. This paper is formed of the opinions of the authors themselves and contains no research or study elements that would require ethics committee approval.

RESULTS

Three key themes regarding the use of Cal/BD foam in the *beyond-mild* psoriasis patient were identified. These were the use of Cal/BD foam as: (1) monotherapy, (2) add-on to non-biologic systemic therapies and (3) add-on to biologics.

Cal/BD Foam as Monotherapy

The advisors provided four key recommendations on use of Cal/BD foam as monotherapy (Table 1). These recommendations are listed below.

Table 1 Overview of key recommendations for the use of Cal/BD foam as monotherapy

Cal/BD foam as monotherapy	Agreement score[a]
1A. Use of Cal/BD foam as monotherapy should be guided by HCPs' consideration of disease factors, including PASI > 10 or BSA > 10% or DLQI > 10	8/9 (89%)[b]
1B. Cal/BD foam, given as monotherapy, is safe and effective up to 4 weeks for patients with *beyond-mild* psoriasis (as supported by RCTs, RWE and guidelines)	9/9 (100%)
1C. Cal/BD foam may be used to bridge the time to starting subsequent systemic treatment	9/9 (100%)
1D. Use of Cal/BD foam as monotherapy should be guided by the patient, considering their:	9/9 (100%)
•preference for a topical agent over a systemic therapy	
•goals and expectations for treatment	
•desire for an easier-to-use formulation	

BSA body surface area, *Cal/BD* calcipotriol and betamethasone dipropionate, *DLQI* Dermatology Life Quality Index, *HCP* healthcare professional, *PASI* Psoriasis Area and Severity Index, *RCT* randomised controlled trial, *RWE* real-world evidence

[a] Number of experts indicating that they 'strongly agree' (4–5)

[b] One advisor felt that *beyond-mild* disease severity, i.e. the target patient group for Cal/BD foam treatment, had not yet been fully defined

Recommendation 1A: Use of Cal/BD Foam as Monotherapy Should Be Guided by HCPs' Consideration of Disease Factors, Including PASI > 10 or BSA > 10% or DLQI > 10

Variation in the measurement of the severity of psoriasis is reflected in a range of definitions in current guidelines [2, 8, 9, 21]. In practice, healthcare professionals (HCPs) should consider a number of parameters when assessing psoriasis severity, as well as traditional tools that assess the objective characteristics of the disease, such as BSA and the Psoriasis Area and Severity Index (PASI). Psoriasis severity can also be underestimated if prior treatment failure history and/or relevant impact of psoriasis on QoL is not taken into account [22]. The location of lesions and a measurement of QoL, such as the Dermatology Life Quality Index (DLQI), are important for accurate assessment of psoriasis severity [22].

Some guidelines already consider QoL in psoriasis management. The European consensus on treatment goals for moderate-to-severe psoriasis follows the 'rule of tens' – BSA > 10, PASI > 10 or DLQI > 10 – in its definition of moderate-to-severe psoriasis [22]. The British and Canadian guidelines acknowledge the importance of areas of involvement and psychosocial impact, as criteria for severity classification and treatment decisions [10, 23]. While Cal/BD foam is an option for those with *beyond-mild* psoriasis, it is important to note that topical monotherapy may not be appropriate in patients with extensive lesions. Cal/BD foam is not indicated for use in patients with BSA > 30%, nor on the face or genitalia [24].

Recommendation 1B: Cal/BD Foam, Given as Monotherapy, Is Safe and Effective up to 4 weeks for Patients with Beyond-Mild Psoriasis (as Supported by RCTs, Real-World Evidence and Guidelines)

Current guidelines recommend the use of topical monotherapy as first-line therapy in localised disease, and advise that improvement in symptoms should be expected within 4 weeks of initiating topical therapy [7, 25]. Clinical evidence supports the use of Cal/BD foam as monotherapy in patients with more severe disease/moderate-to-severe psoriasis, due to its efficacy, rapid onset of action and favourable safety profile [14, 17, 26–28]. For example, in a subgroup analysis of the PSO-ABLE study in patients with moderate-to-severe disease, a higher proportion of patients achieved PASI 75 with Cal/BD foam compared with gel at weeks 4, 8 and 12, and also had superior DLQI scores [17].

A real-world, prospective, observational study assessed the efficacy and safety of Cal/BD foam in 410 patients with mild-to-severe plaque psoriasis in daily clinical practice conditions. After 4 weeks of treatment, 43% of patients with severe psoriasis (Investigator's Global Assessment (IGA) score = 4) were clear/almost clear of lesions and had improvements in IGA [16].

Recommendation 1C: Cal/BD Foam May Be Used to Bridge the Time to Starting Subsequent Systemic Treatment

Dermatologists may use topical treatments to 'bridge' the time to a patient first starting systemic therapies [29, 30]. Topical treatments may also be used as a bridge to cover a treatment gap or to control disease flare when, in some healthcare systems, formal approval is required from payers before systemic therapy is initiated or changed [31]. Real-world evidence (RWE) demonstrates that specialists may use topical agents to bridge the waiting time to systemic treatment with a non-biologic (64% of HCPs) or a biologic (63%) [14].

Recommendation 1D: Use of Cal/BD Foam as Monotherapy Should Be Guided by the Patient, Considering Their Preference for a Topical Agent Over a Systemic Therapy, Goals and Expectations for Treatment, and Desire for an Easier-to-Use Formulation

Patient preference is an important consideration when choosing a treatment [32]. For example, a patient may be reluctant to start systemic treatment and wish to see if treatment with topicals alone can resolve their disease. It is important to note, however, that when systemic treatment is needed it should not be delayed.

A shared decision-making process involving patient preference and clinician judgement may

enhance outcomes, such as treatment satisfaction and adherence (a key factor for treatment efficacy) [32]. Suboptimal adherence is often the reason why real-life outcomes fail to reflect outcomes seen in clinical trials [33].

Cal/BD Foam as an Add-on to Non-biologic Systemic Therapies

The advisors provided six key recommendations on use of Cal/BD foam in combination with non-biologic systemic therapies. Four of the recommendations relate to the use of the foam in patients being initiated on non-biologic systemics, and two concern its use in patients already receiving non-biologic systemics (Table 2). These recommendations are listed below.

Recommendation 2A: Consider Cal/BD Foam as an Add-on When Starting a Non-biologic to Enhance Treatment Outcome and Time of Onset of Response

Many patients with psoriasis receiving systemic agents, such as methotrexate, do not experience an optimal response to treatment; some studies suggest only about 40% of patients achieve PASI 75 [34, 35]. In addition, some systemic treatments can have a slow onset of action, taking months to achieve maximum therapeutic response [22]. For patients initiated on a slower acting non-biologic, starting a topical therapy at the same time may achieve a quick and effective response when required. For example, Kircik found that adding Cal/BD foam to apremilast at the time of initiation in patients with moderate psoriasis improved the speed of onset and efficacy of overall treatment, as well as patient DLQI scores [18].

Recommendation 2B: Consider Combining Cal/BD Foam with a Non-biologic as an Add-on to Improve Treatment Outcomes in Patients Who Are Late Responders

Certain patients may experience a delayed response to systemic therapies (excluding cyclosporin) [36]. In these cases, add-on topical therapy should be offered to optimise treatment outcomes, as this may avoid the need to switch to another systemic agent [7, 37].

Table 2 Overview of key recommendations for the use of Cal/BD foam in combination with non-biologic systemic therapies

Cal/BD foam in combination with non-biologic systemic therapies	Agreement score[a]
2A. Consider Cal/BD foam as an add-on when starting a non-biologic to enhance treatment outcome and time of onset of response	9/9 (100%)
2B. Consider combining Cal/BD foam with a non-biologic as an add-on to improve treatment outcomes in patients who are late responders	8/9 (89%)
2C. For responder patients experiencing loss of efficacy on a non-biologic therapy, treatment may be optimised by the addition of Cal/BD foam	9/9 (100%)
2D. In responder patients not satisfied with non-biologic treatment (assessed using e.g. PASI, QoL and HADS), addition of Cal/BD foam may be considered	8/9 (89%)
2E. Consider combining Cal/BD foam and a non-biologic systemic therapy, as it may allow a systemic dose reduction or minimise side effects	9/9 (100%)
2F. Consider combining Cal/BD foam and a non-biologic systemic therapy to control residual disease	9/9 (100%)

Cal/BD calcipotriol and betamethasone dipropionate, *HADS* Hospital Anxiety and Depression Scale, *PASI* Psoriasis Area and Severity Index, *QoL* quality of life

[a] Number of experts indicating that they 'strongly agree' (4–5)

Recommendation 2C: For Responder Patients Experiencing Loss of Efficacy on a Non-biologic Therapy, Treatment May Be Optimised by the Addition of Cal/BD Foam

The 'drug survival' (duration of adherence) of non-biologics can be reduced in some patients. These patients may be candidates for add-on topical treatments [19]. The Swiss Dermatology Network for Targeted Therapies, a national psoriasis registry of patients with moderate-tosevere psoriasis treated with either a non-biologic or biologic, found that drug survival for non-biologic systemic treatments, including methotrexate, was 19.2 months [38]. Cal/BD foam may be a useful option in cases when the efficacy of the current non-biologic treatment has decreased over time.

Recommendation 2D: In Responder Patients Not Satisfied with Non-biologic Treatment (Assessed Using e.g. PASI, QoL and HADS), Addition of Cal/BD Foam May Be Considered

Some responder patients may be dissatisfied with their treatment despite achieving full or partial clinical success (e.g. PASI 75 or PASI 50–75, respectively). Suboptimal patient satisfaction with systemic therapies has been reported [39]. There is a need for more patient-centred assessments (e.g. the DLQI and Hospital Anxiety and Depression Scale (HADS) questionnaires) in a 'treat-to-target' approach to help better gauge patient satisfaction with treatment [40–42]. For patients not satisfied with their treatment outcome, the use of Cal/BD foam as an add-on to their non-biologic treatment may be an option.

Recommendation 2E: Consider Combining Cal/BD Foam and a Non-biologic Systemic Therapy, as it May Allow a Systemic Dose Reduction or Minimise Side Effects

If topicals increase the efficacy of a systemic non-biologic therapy, a lower dose of that systemic may achieve comparable clinical response to monotherapy. This may lower the risk of adverse events. Such use of topicals is supported in a review describing the combination of topicals with non-biologics. Adding a topical to methotrexate, phototherapy, acitretin or cyclosporin increased the overall/combined treatment efficacy and enabled use of a lower dose of the non-biologic systemic [19].

Recommendation 2F: Consider Combining Cal/BD Foam and a Non-Biologic Systemic Therapy to Control Residual Disease

Patients with psoriasis with resistant lesions and/or residual disease may experience reduced health-related QoL (HRQoL). Such patients may respond after addition of topical agents to conventional systemic treatments [5], and may also benefit from their use in managing isolated, difficult-to-treat areas [4, 7].

Topical treatments may also be added to non-biologic systemics for the control of psoriasis exacerbations. Psoriasis activity fluctuates over time, and topical therapies can be used at the first sign of increased activity to prevent disease escalation. Patients can, therefore, use topicals to minimise flares and maximise control of the condition [43].

Cal/BD Foam as an Add-on to Biologics

The experts provided four recommendations on use of Cal/BD foam in combination with biologics. Two of the recommendations are about Cal/BD foam in patients initiated on biologics, while the remaining two concern use in patients already receiving biologics (Table 3). These recommendations are listed below.

Recommendation 3A: Consider Using Cal/BD Foam as an Add-on When Starting a Biologic to Enhance Treatment Outcomes and Time to Onset of Response

There may be situations where use of a topical agent as an add-on is beneficial for patients with extensive psoriasis who are receiving biologics [5]. When a biologic is newly started, addition of a topical agent may increase the overall efficacy of treatment (and overall disease improvement) by treating residual disease or potentially reducing the time to onset of action of a slower-acting biologic [5, 44].

In clinical practice, the effectiveness of biologics can be lower than the efficacy reported in clinical trials [45]. Based on Physician Global

Table 3 Overview of key recommendations for the use of Cal/BD foam in combination with biologics

Cal/BD foam in combination with biologics	Agreement score[a]
3A. Consider using Cal/BD foam as an add-on when starting a biologic to enhance treatment outcomes and time to onset of response	9/9 (100%)
3B. Consider combining Cal/BD foam as an add-on when starting a biologic to improve treatment outcomes in late-responder patients who may not immediately respond to a biologic	8/9 (89%)[b]
3C. For responder patients experiencing reduced efficacy on a biologic, treatment may be optimised by the addition of Cal/BD foam	9/9 (100%)
3D. In responder patients not satisfied with their biologic treatment (assessed using e.g. PASI, QoL, HADS), addition of Cal/BD foam may be considered	9/9 (100%)[c]

Cal/BD calcipotriol and betamethasone dipropionate, *HADS* Hospital Anxiety and Depression Scale, *PASI* Psoriasis Area and Severity Index, *QoL* quality of life

[a] Number of experts indicating that they 'strongly agree' (4–5)

[b] One advisor was uncertain about the use of 'immediately respond' as a time period, explaining the response rate may vary in different patients, e.g. in late responders

[c] 7/9 advisors initially voted 'strongly agree', after initially failing to reach consensus. Following discussion, 'should' was amended to 'may' to allow for individual situations. In the second vote, all advisors (9/9; 100%) were in agreement

Assessment (PGA), the efficacy of adalimumab was 73% in a randomised controlled trial (RCT), but 48% in a real-world study [45]. Clinical trial findings support the use of add-on topical therapy with biologics to enhance treatment effectiveness. A phase IIIb, multicentre RCT in patients with moderate-to-severe plaque psoriasis demonstrated that short-term use of topical clobetasol propionate (0.05%) with etanercept provided additional clinical benefit at week 12 in terms of PASI 75, PGA 'clear/almost clear' and BSA, compared with etanercept alone [46].

Some biologics can have a time to onset of action of up to 25 weeks [47]. Adding a topical treatment to a slow-acting biologic at treatment initiation may help achieve the quickest and greatest therapeutic response. The BELIEVE study reported that the addition of Cal/BD foam to adalimumab in patients with moderate-to-severe psoriasis resulted in more rapid and efficacious responses in the first 4 weeks versus patients receiving adalimumab alone ($p = 0.021$) [48].

Combination of a topical treatment with systemic therapy is a frequently used strategy for moderate-to-severe psoriasis (BSA > 10%) according to a recent survey of international dermatologists [49].

Recommendation 3B: Consider Combining Cal/BD Foam as an Add-on When Starting a Biologic to Improve Treatment Outcomes in Late-Responder Patients Who May Not Immediately Respond to a Biologic

The response to biologics can be delayed [50]. An initial lack of response to biologics may impact a patient's treatment satisfaction and adherence, and may prompt a switch away from their current biologic. The use of Cal/BD foam in these circumstances may improve outcomes and prevent the need for switching.

Recommendation 3C: For Responder Patients Experiencing Reduced Efficacy on a Biologic, Treatment May Be Optimised by the Addition of Cal/BD Foam

The 'drug survival' (duration of adherence) of certain biologics can be reduced because of factors such as anti-drug antibodies [51–53]. A meta-analysis of 37 studies, which pooled drug survival of biologics for treatment of psoriasis in 32,631 patients, found that drug survival for all

four of the biologics studied was reduced from year 1 to year 4 [52, 53]. These results are consistent with findings from the Danish DERMBIO registry, which reported that the efficacy of biologics diminishes over time and that this reduced efficacy is responsible for the majority of patient discontinuations [53].

Finally, add-on topical treatment with biologics may also be used to enhance treatment outcomes for patients experiencing secondary loss of efficacy or a seasonal fluctuation/flare/exacerbation of their disease while receiving a biologic [54].

Recommendation 3D: In Responder Patients Not Satisfied with Their Biologic Treatment (Assessed Using e.g. PASI, QoL, HADS), Addition of Cal/BD Foam May Be Considered

Achieving patient satisfaction with systemic therapies can be challenging, and lack of patient satisfaction with biologic treatment represents a significant problem. It can adversely affect patient adherence, patient preferences and HRQoL [55].

Evidence from BioCAPTURE, a daily-practice registry consisting of patients with psoriasis treated with biologics, suggests that poor satisfaction, measured by the Treatment Satisfaction Questionnaire for Medication (TSQM) among female patients, may contribute to their earlier discontinuation of biologic treatment versus male patients [56]. A prospective, open-label study evaluated Cal/BD foam efficacy in patients who were already receiving biologics, but in whom treatment responses were inadequate. Add-on therapy with Cal/BD foam was found to improve both patient HRQoL and treatment satisfaction (as measured by DLQI and TSQM-9 at weeks 4 and 16) [57].

DISCUSSION

Treatments for psoriasis are constantly evolving, and up-to-date recommendations on therapy are therefore imperative. This is particularly the case for the *beyond-mild* population, for whom there is a lack of clarity on treatment options. We identified situations in which the *beyond-mild* psoriasis population may benefit from the use of a topical treatment, either alone or in addition to an existing systemic therapy. Topical treatment with Cal/BD combinations including Cal/BD foam is an add-on option to non-biologic and biologic therapy to improve outcomes, reduce the time to onset of action, and reduce the dose of systemic therapy to minimise side effects; it may also help enhance outcomes in patients with a delayed response to biologic therapy. These recommendations do not address circumstances in which treatments may be restricted or contraindicated.

The side effects associated with a treatment are a key factor in determining its successful use, and patients may avoid a treatment because of adverse reactions. Additionally, some systemic treatments are contraindicated in patients with comorbidities. For example, oral methotrexate should be given 'with great caution if at all' when patients have hepatic disease, and it is associated with pulmonary fibrosis in rare circumstances [58]. Pregnancy or drug interactions may also limit treatment options [59]. Contraindications specific to biologics may include situations in which requirements for laboratory monitoring during treatment or refrigerated storage are not feasible [60], while cost may be an additional barrier [61].

Topical treatments have fewer associated side effects and contraindications than systemic therapies, but concerns remain over long-term patient adherence [62]. Ease of use, time to achieve satisfactory efficacy, cost and patient acceptability may be barriers to adherence, and patients may prefer some formulations to others [63]. The area to be treated is also a consideration: patients may prefer to use and be more adherent to shampoo products for scalp psoriasis [9]. Other limitations of topicals include the occurrence of 'topical fatigue' or tachyphylaxis and restrictions in the total BSA that can be treated [24]. However, novel topical treatments may have improved acceptability to patients over traditional creams or ointments because of enhanced ease of application or absence of odour [29, 63].

Altogether, topical treatments play a substantial role in the treatment of *beyond-mild* psoriasis. Novel topicals offer HCPs increasing

flexibility to tailor treatments for patients with more severe psoriasis. The benefits of topicals may include reductions in dose-related adverse events as a result of lower systemic use.

Limitations

Our recommendations and consensus statements are based on data on short and long-term effectiveness, safety and current clinical use of Cal/BD foam for *beyond-mild* psoriasis patients. Some of the recommendations are possibly generalisable to other formulations or therapies, but they were not discussed at length. Now that this group of *beyond-mild* patients has been described, it would be useful to develop a pathway for them that addresses their clinical management more comprehensively.

CONCLUSION

Novel topical treatments may offer HCPs increased flexibility to tailor treatments for their patients with *beyond-mild* psoriasis. These recommendations are intended to help provide HCPs with guidance to support their use of the management of plaque psoriasis with topical treatment. Topical treatment with Cal/BD foam was qualified to be an appropriate alternative as monotherapy or as add-on treatment with non-biologic or biologic systemic therapy for *beyond-mild* psoriasis, and ultimately to optimise treatment outcomes for these patients.

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