Calcipotriene-Betamethasone Dipropionate Topical Suspension in the Management of Psoriasis: A Status Report on Available Data With an Overview of Practical Clinical Application

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Practice Points

- Calcipotriene 0.005%—betamethasone dipropionate 0.064% topical suspension (C/Bd-TS) applied once daily has been shown in multiple studies to be effective, well tolerated, and safe for the treatment of plaque psoriasis (PP) involving the scalp and/or other body sites such as the trunk and extremities. Studies have included all severities of PP, with both investigator and subject assessments shown to be favorable overall.
- Most studies were completed in adults over a duration of 8 weeks; however, clinical trials also have been performed with C/Bd-TS in adults treated for up to 52 weeks for scalp psoriasis, in a subgroup of Hispanic/Latino and black/African American adult patients with scalp psoriasis, and in adolescents with scalp psoriasis.
- · Studies evaluating application of C/Bd-TS once daily for PP affecting nonscalp sites have primarily involved use on the trunk and extremities.
- The adaptability for scalp and body application allows for use in many cases of a single topical product without needing to prescribe a second leave-on medication specifically for use on the scalp.

Psoriasis is a multifactorial process associated with immunologic dysregulation. Chronic plaque psoriasis (PP) is the most common clinical presentation. Plaque psoriasis is characteristically a chronic disease associated with periods of persistence and episodes of

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soriasis is a common inflammatory skin disorder that appears to be induced by multifactorial pathophysiologic processes associated with immunologic dysregulation. 1 It can affect patients of any age, gender, and ethnicity, and it presents clinically with a variety of visible manifestations. The disease course and severity of psoriasis varies among affected patients.¹ Chronic plaque psoriasis (PP), also referred to as psoriasis vulgaris, is the most common clinical presentation.^{1,2} Although many patients are affected by psoriasis that is widespread and in some cases severe, the majority of affected patients exhibit localized involvement that usually affects less than 2% to 5% of the body surface area. Although the skin at any anatomic location can be affected, commonly involved sites are described by the mnemonic term SNAKES (scalp, nails, anogenital region, knees, elbows, sacral region).^{2,3}

Because the majority of patients with PP present with localized disease, topical therapy is the foundation of treatment in most cases. Topical corticosteroids (TCs) are the most commonly utilized agents, supported by a long track record of favorable efficacy and safety over approximately 6 decades. 4,5 However, optimal management of PP with TCs requires use of a formulation that is of adequate potency, is adaptable for application to the affected body sites, and is properly monitored and adjusted to avoid potential TC-induced adverse effects. 4-6 Nonsteroidal topical therapies such as vitamin D analogues (eg, calcipotriene) and retinoids (eg, tazarotene) are commonly integrated into topical regimens to reduce the application frequency and duration of TC use as well as to sustain efficacy.^{5,7,8} Plaque psoriasis is characteristically a chronic disease associated with periods of persistence and episodes of flaring; therefore, intermittent use of TC therapy along with concurrent or sequential use of a nonsteroidal topical agent are commonly employed to achieve and sustain control of the disorder. 7-9

In the last decade, several advances have revolutionized the management of psoriasis, especially for PP patients with extensive involvement who require systemic therapy and/or phototherapy as well as for those with psoriatic arthritis. ^{10,11} The availability of biologic agents such as tumor necrosis factor α inhibitors and certain interleukin inhibitors (eg, IL-12/IL-23) have been at the forefront of major advances in PP treatment, with some agents also blocking the progression of joint destruction associated with psoriatic arthritis. ¹⁰⁻¹² However, even when patients with PP respond favorably to biologic therapy, it is not uncommon for them to still be affected by some persistent PP. In these cases, although much of the chronic PP may clear with use of the biologic

agent, persistence of psoriatic plaques may involve the lower extremities, scalp, and/or trunk, with topical therapy often added to augment the therapeutic response. 13-15

This article provides a review of a patented topical suspension combination formulation that contains calcipotriene hydrate 0.005%, a vitamin D analogue, and betamethasone dipropionate (Bd) 0.064%, a high-potency TC. In 2008, the US Food and Drug Administration approved the once-daily application of calcipotriene 0.005%-Bd 0.064% topical suspension (C/Bd-TS) for the treatment of PP; this formulation is approved for use on the scalp and body in patients 18 years of age and older. According to the product insert, the recommended maximum duration of treatment with C/Bd-TS once daily is 8 weeks, and patients may not exceed a maximum weekly dose of 100 g.16 It is important to note that the terms calcipotriene and calcipotriol refer to the same molecule and are used interchangeably in the literature. Formulation characteristics of C/Bd-TS, perspectives on modes of action, outcomes from pivotal trials, and efficacy and safety data reported from additional studies are discussed in this article.

What are the formulation characteristics of C/Bd-TS?

Each gram of C/Bd-TS contains 52.18 µg of calcipotriene hydrate (equivalent to 50 µg of calcipotriene) and 0.643 mg of Bd (equivalent to 0.5 mg of betamethasone), formulated together in a viscous, nearly odorless, almost clear to slightly off-white suspension. The excipients are hydrogenated castor oil, polypropylene glycol 11 stearyl ether, α-tocopherol, butylhydroxytoluene, and mineral oil, collectively producing a gel base in which both active ingredients are suspended.¹⁶ Although the viscous quality of the suspension warrants some additional effort for removal during hair washing, the tenacious gel-like viscosity assists in removing scale on psoriatic plagues, which is often adherent, especially on the scalp. Additionally, it is important that C/Bd-TS be shaken well before use. 16 Initially, C/Bd-TS was studied and marketed in the United States for treatment of scalp psoriasis; however, the indication was expanded to include treatment of PP on the rest of the body, supported by evidence from randomized controlled trials (RCTs). 16-23

Vitamin D analogues (eg, calcipotriene/calcitriol) have been shown to be photolabile when exposed to UV light, especially UVA. They also have been shown to be chemically incompatible and less stable when admixed with a variety of other active ingredients and/or vehicles used to treat PP, including hydrocortisone valerate ointment 0.2%, ammonium

lactate lotion 12%, and salicylic acid compound ointment 6%. ²⁴⁻²⁶ As a result, it is important for clinicians to consider avoidance of concomitant topical calcipotriene application with use of a TC unless the stability of the active ingredients has been tested when the formulations are combined. Calcipotriene 0.005%/Bd 0.064% topical suspension utilizes vehicle technology that maintains the stability and activity of both calcipotriene and Bd within the suspension formulation. ^{16,26}

What is the rationale behind combining calcipotriene and Bd in a single formulation for the treatment of PP?

The potential advantages of C/Bd-TS include the combined modes of action of 2 different active ingredients used for treatment of PP, complementary immunomodulatory effects as compared to use of a TC or vitamin D analogue alone, ease of use with a single product applied once daily, adaptability of the vehicle for use on scalp and/or body skin, and improvement in quality-of-life (QOL) measures.²⁷⁻³⁴

Combined Modes of Action—Calcipotriene 0.005%—Bd 0.064% topical suspension combines the modes of action of a high-potency topical suspension and a vitamin D analogue for the treatment of PP in a single stable gel formulation that is approved in the United States for treatment of PP in adults. ¹⁶ The multiple anti-inflammatory properties of corticosteroids as well as the efficacy and safety of TC therapy for psoriasis have been well described. ^{4,6,7,9,27} The antiproliferative and anti-inflammatory properties of vitamin D analogues that appear to correlate with therapeutic effects in the treatment of PP also have been discussed in the literature. ²⁸

Complementary Immunomodulatory Effects—More recent studies using various research assays have provided further evidence supporting relevant immunomodulatory properties of calcipotriene alone and in combination with Bd that favorably modify immune dysregulation pathways described more recently in the pathogenesis of PP.^{1,29,30} Treatment of psoriatic plaques with calcipotriene has been shown to suppress the increased production of peptide alarmins (psoriasin and koebnerisin) in psoriatic skin and their T_H17-mediated regulation in epidermal keratinocytes, thus interfering with the S100 amplification loop that appears to produce inflammation in psoriasis.²⁹ In T-lymphocyte cultures evaluating exposure to calcipotriene and Bd both alone and as a combined therapy, calcipotriene inhibited IFN-y, IL-8, IL-17, and IL-22 expression, and it reversed the corticosteroid-induced suppression of IL-4, IL-5, IL-10, and IL-13; Bd inhibited both IL-6 and tumor necrosis factor α expression. The outcomes demonstrated that the combination of calcipotriene and Bd inhibited the endogenous release of T_H1 -and T_H17 -associated cytokines that are associated with psoriatic inflammation and together induced a more favorable anti-inflammatory cytokine profile. Although the broad range of anti-inflammatory effects provided by a TC of adequate potency, such as Bd, can clear or markedly improve PP, the concurrent use of calcipotriene was shown to provide additional immunomodulatory effects that suppressed the key T_H17/T_H1 pathophysiologic mediators of psoriatic inflammation and simultaneously induced a T_H2/T regulatory response that is believed to provide therapeutic benefit. 29,30

Ease of Use and Vehicle Adaptability—A once-daily regimen and a vehicle formulation adaptable for use on both the scalp and body are advantageous in enhancing the potential for greater patient adherence.31,32 The adaptability of the C/Bd-TS for use on the scalp and/or body is supported by several studies encompassing a large number of actively treated subjects. Calcipotriene 0.005%-Bd 0.064% topical suspension has been extensively studied in patients with PP on the scalp and/or body as evidenced by a pooled analysis of 9 eight-week RCTs (scalp, n=6; body, n=3) that encompassed 2777 total subjects treated once daily for PP (scalp, n=1953; body, n=824). ²³ Additionally, C/Bd-TS applied once daily was evaluated in an open-label, single-arm, 8-week, phase 2 study of adolescents (N=78; age range, 12–17 years [mean age, 14.6 years]) with scalp psoriasis (mean affected scalp area, 43.7%). The investigator global assessment of treatment success (clear or almost clear) and the patient global assessment of treatment success (clear or very mild) were essentially identical among participants and investigators with 85% and 87% reported after 8 weeks, respectively; approximately 50% of participants achieved treatment success after 2 weeks based on both the investigator global assessment and patient global assessment.³³

Improvement in QOL Measures—Quality-of-life measures were compared in an 8-week RCT of participants with at least moderate scalp psoriasis treated with C/Bd-TS once daily (n=207) or calcipotriene solution twice daily (n=107). Significantly greater improvement in QOL scores compared to baseline were noted at all time points using the Skindex-16 questionnaire in participants treated with C/Bd-TS compared to calcipotriene solution (total score, P<.001 at weeks 2 and 4 and P=.008 at week 8; symptoms score, P<.001 at weeks 2 and 4 and P=.005 at week 8).³⁴ A 4-week, open-label, noninterventional cohort,

Reference (Year)	Study Design	Study Population	Efficacy Data	Tolerability/Safety Data
Buckley et al ¹⁷ (2008)	Double-blind RCT; 2 arms; once-daily treatment with C/Bd-TS (n=108) or Bd-TS alone (n=110); 8-wk treatment period	Adults with scalp PP; all severities	Primary parameter: absolute change in total sign score from baseline to wk 8 (score rated erythema, scaling, thickness); difference between means (~0.56) greater for C/Bd-TS (P=.042); treatment success (clear, almost clear, marked improvement) significantly greater in C/Bd-TS group (92.5% vs 82.6%; P=.027)	Skin-related AEs in 7 C/Bd-TS participants (6.5%) and in 8 Bd-TS participants (7.3%) with pruritus being the most commonly reported AE (3 patients in each group [2.8% and 2.7%, respectively]); no serious AEs were noted
Fleming et al ¹⁸ (2010)	Double-blind RCT; 4 arms; once-daily treatment with C/Bd-TS (n=162), Bd-TS alone (n=83), C-TS alone (n=79), or vehicle (n=40); 8-wk treatment period	Adults with PP on the trunk/extremities; all severities (moderate severity, 59% of participants); mean PASI: 7.7-7.9	Primary parameter: responders defined as IGA rating at wk 4 and wk 8 of clear or minimal if baseline was at least moderate and clear if baseline was mild; responders at wk 4: C/Bd-TS (16%), Bd-TS (9.6%), C-TS (3.8%), and vehicle (2.5%); responders at wk 8: C/Bd-TS (27.2%), Bd-TS (16.9%), C-TS (11.4%), and vehicle (0%), wk 8 result comparisons with C/Bd-TS statistically significant (P=.027, P=.006, and P<.001, respectively); mean PASI change at wk 8: C/Bd-TS (-55.3%), Bd-TS (-49.8%), C-TS (41.2%), and vehicle (-1.9%)	Most AEs were ranked as not related to study medication and were rated as mild to moderate severity; 12 skin-related AEs in C/Bd-TS group (7.4%), 7 in Bd-TS group (8.4%), 8 in C-TS group (10.1%), and 10 in vehicle group (25.0%); reports included dry skin, skin burning, pruritus, erythema; no severe AEs were reported
Menter et al ¹⁹ (2013)	Double-blind RCT; 4 arms; once-daily treatment with C/Bd-TS (n=482), Bd-TS (n=479), C-TS (n=96), or vehicle (n=95); 8-wk treatment period	Adults with PP on the trunk, arms, or legs; severity: mild (~22% of participants) and moderate (>75% of participants); mean PASI: 7.8–8.5; mean BSA: 11.1%–12.6%	Primary parameter: IGA ratings at wk 4 and wk 8 of clear or almost clear if moderate at baseline and clear if mild at baseline and a ≥2-grade change from baseline defined as CD; CD at wk 4: C/Bd-TS (13.3%), Bd-TS (12.5%), C-TS (5.2%), and vehicle (2.1%); CD at wk 8: C/Bd-TS (29%), Bd-TS (21.5%), C-TS (14.6%) and vehicle (6.3%); wk 8 result comparisons with C/Bd-TS were statistically significant (P<.008 for all 3 arms); participants with 50% PASI reduction at wk 8: C/Bd-TS (67.1%), Bd-TS (58.6%), C-TS (54.9%), and vehicle (33.8%)	Most AEs were rated as not related to the study medication and were ranked as mild to moderate severity; skin-related AEs were rare in all groups; 1 serious AE (nephrolithiasis) was rated as possibly related to the study medication (Bd-TS); most common AE was increased parathyroid hormone levels noted in 1.5%, 1.3%, 0%, and 1.1% in C/Bd-TS, Bd-TS, C-TS, and vehicle groups, respectively; analysis of parathyroid hormone levels showed marked intrapatient variability with no overall trend in changing values after treatment and no differences between the study groups
Jemec et al [∞] (2008)	Double-blind RCT; 4 arms; once-daily treatment with C/Bd-TS (n=541), Bd-TS (n=556), C-TS (n=272), or vehicle (n=136); 8-wk treatment period	Adults with scalp psoriasis; moderate severity (50.7%–57.4% of participants) and severe (28.8%–36.0% of participants); scalp surface area affected: ≥50% in 37.4%–42.3% of participants	Primary parameter. IGA rating of absent or mild disease at wk 8: C/Bd-TS (71.2%), Bd-TS (64.0%), C-TS (36.8%), and vehicle (22.8%); superiority of C/Bd-TS over other groups observed at wk 2 onward; IGA wk 8 result comparisons with C/Bd-TS were statistically significant (P=.011, P<.0001, and P<.0001, respectively); PGA ratings at wk 8 were similar to IGA ratings for clear or almost clear	Majority of AEs were rated as not related to study medication; pruritus was the only skin-related AE reported in >1% of C/Bd-TS and Bd-TS groups; pruritus, skin burning, and skin irritation were reported most often in the C-TS group; no serious AEs were reported; no concerning changes in albumin-corrected serum calcium levels were noted

Reference (Year)	Study Design	Study Population	Efficacy Data	Tolerability/Safety Data
van de Kerkhof et al ²¹ (2009)	Double-blind RCT; 3 arms; once-daily treatment with C/Bd-TS (n=568), Bd-TS (n=568), or C-TS (n=286); 8-wk study period	Adults with PP of the scalp; moderate severity (51.4%–54.8% of participants) and severe (29.9%–33.6% of participants); scalp surface area affected: ≥50% in 35.6%–39.0% of participants	Primary parameter: IGA rating of absence of disease or very mild disease at week 8: C/Bd-TS (68.4%), Bd-TS (61.0%), and C-TS (43.4%); efficacy of C/Bd-TS was greater than Bd-TS and C-TS at wk 2; IGA wk 8 result comparisons with C/Bd-TS were statistically significant (P=.0079 and P<.0001, respectively)	Most AEs were rated as not related to the study medication; skin-related AEs were most common in the C-TS group (12.8% overall; pruritus, 8.9%); no concerning changes in albumin-corrected serum calcium levels were noted
Langley et al ²² (2011)	Investigator-blinded RCT; 3 arms; once-daily treatment with C/Bd-TS (n=183), tacalcitol ointment (n=184), or vehicle (n=91); 8-wk treatment period	Adults with PP affecting > 10% of the trunk and/ or arms and/or legs; moderate severity or greater (severe, 27.3%—31.5% of participants); mean PASI: 8.93–9.84; mean BSA: 9.0%–9.5%	Primary parameter: IGA rating of clear or almost clear at wk 8: C/Bd-TS (39.9%), tacalcitol (17.9%), and vehicle (5.5%); IGA wk 8 result comparisons with C/Bd-TS were statistically superior to both other groups (P<.001 for both groups); more participants treated with C/Bd-TS achieved PASI 50 and PASI 75	No serious AEs were reported; skin-related AEs were reported more commonly in the tacalcitol group (17.4%) vs C/Bd-TS group (8.8%) vs vehicle group (15.4%); no rebound (psoriasis return >125% of baseline PAS) over 8-wk posttherapy observation phase; median time to relapse in participants clear or almost clear at wk 8 was 61–63 d for all treatment groups
Kragballe and van de Kerkhof≅ (2014)	Pooled safety analysis (9 total trials with 8-wk treatment periods); oncedaily treatment with C/Bd-TS (scalp, n=1953; body, n=824), Bd-TS (scalp, n=1214; body, n=662), C-TS (scalp, n=979; body, n=175), vehicle (scalp, n=173; body, n=226), C solution (scalp, n=104), or tacalcitol ointment (body, n=184)	Adults with PP of the scalp and body	N/A	Most AEs were mild to moderate in severity; lowest % of skin-related AEs in C/Bd-TS group vs all comparators in scalp PP (5% vs 6%-19%) and second lowest for body PP (5% vs 3% in Bd-TS group); similar pattern for ADRs with C/Bd-TS lowest among scalp PP groups (8% vs 9%-27%) and second lowest among body PP groups (6% vs 4% in Bd-TS group); no major safety signals were noted with a low incidence of AEs and ADRs
Gooderham et al ³³ (2014)	Phase 2, open-label; 1 arm; once-daily treatment with C/Bd-TS (N= 78); 8-wk treatment period	Adolescents with PP of the scalp (age range, 12-17 y); moderate severity or greater; ≥10% of scalp affected (mean scalp area, 43.7%)	85% of participants achieved IGA of clear or almost by wk 8; 50% achieved clear or almost clear at wk 2	No cases of hypercalcemia were noted; no clinically relevant increases in albumin-corrected serum calcium, 24-h urinary calcium excretion, or urinary calcium:creatinine ratio were noted; no clinically relevant changes in serum biochemistry or hematologic parameters were noted; application-site pruritus was noted in 1 participant (1.3%)

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Study Design Population
Adults with moderate to severe scalp PP
Hispanic and black adults with moderate to severe scalp PP
Adults with extensive PP; 15%–30% BSA affected

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postmarketing ("real life") study of 721 patients treated at 333 dermatology centers with C/Bd-TS showed a 69.5% improvement in the scalp life quality index score compared to baseline (P < .0001), with 89.5% and 90.4% of participants reporting that C/Bd-TS was better/much better than previously used therapies for scalp psoriasis and easy/very easy to use, respectively.³⁵ An 8-week RCT trial evaluated C/Bd-TS once daily compared to calcipotriene alone, betamethasone dipropionate alone, and vehicle in 1152 participants with mild to moderate PP involving the trunk and extremities. Participants treated with C/Bd-TS (n=442) demonstrated superior reductions in QOL scores using the dermatology life quality index at weeks 4 and 8 compared to those treated with Bd alone (n=418) or vehicle (n=77)but not compared to calcipotriene alone (n=80).¹⁹

What data are available on the efficacy and safety of C/Bd-TS?

Several clinical studies have evaluated the efficacy, tolerability, and safety of C/Bd-TS applied once daily for PP of the scalp and body (ie, trunk, extremities). Most studies were completed over a duration of 8 weeks in adults¹⁶⁻²³; however, studies also have been performed in adolescents,³³ in adults treated for up to 52 weeks,³⁶ and in a subgroup of Hispanic/Latino and black/African American patients with scalp psoriasis.³⁷ The Table provides a detailed summary of primary efficacy data along with important tolerability and safety considerations based on study outcomes.

What practical recommendations can be made regarding the use of C/Bd-TS for PP?

Calcipotriene 0.005%-Bd 0.064% topical suspension applied once daily provides a formulation that allows for treatment of PP involving both the scalp and body using a single product, which provides an element of convenience and is likely to enhance compliance and reduce costs compared with the use of 2 separate products. The efficacy and safety of C/Bd-TS has been well established in several studies, 16-23,37 including a 52-week trial in patients with scalp psoriasis.³⁶ The combination of calcipotriene and Bd appears to favorably address the pathophysiologic pathways involved in psoriasis.^{29,30} Calcipotriene 0.005%-Bd 0.064% topical suspension is a rational option for the treatment of PP in patients with localized disease or in patients treated systemically or with phototherapy for more extensive disease who exhibit persistence or recurrence of scattered areas of PP.6-9,14,15 Appropriate use of C/Bd-TS is likely to achieve favorable efficacy with a low risk of tolerability reactions and a very low risk of major adverse drug reactions. 16-23,36-38

REFERENCES

- Guttman-Yassky E, Krueger JG. Psoriasis: evolution of pathogenic concepts and new therapies through phases of translational research. Br J Dermatol. 2007;157:1103-1115.
- 2. Menter MA. An overview of psoriasis. In: Koo JYM, Levin EC, Leon A, et al, eds. *Moderate to Severe Psoriasis*. 4th ed. Boca Raton, FL: CRC Press Taylor & Francis Group; 2014:1-21.
- 3. Sandoval LF, Feldman SR. General approach to psoriasis treatment. In: Koo JYM, Levin EC, Leon A, et al, eds. *Moderate to Severe Psoriasis*. 4th ed. Boca Raton, FL: CRC Press Taylor & Francis Group; 2014:3-8.
- 4. Zeichner JA, Lebwohl MG, Menter A, et al. Optimizing topical therapies for treating psoriasis: a consensus conference. *Cutis*. 2010;(3 suppl):5-31.
- 5. American Academy of Dermatology Work Group, Menter A, Korman NJ, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 6. guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions [published online ahead of print February 8, 2011]. J Am Acad Dermatol. 2011;65:137-174.
- Del Rosso J, Friedlander SF. Corticosteroids: options in the era of steroid-sparing therapy. J Am Acad Dermatol. 2005;53(1, suppl 1):S50-S58.
- Menter A, Korman NJ, Elmets CA, et al; American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. section 3. guidelines of care for the management and treatment of psoriasis with topical therapies [published online ahead of print February 13, 2009]. J Am Acad Dermatol. 2009;60:643-659.
- 8. Koo J. New developments in topical sequential therapy for psoriasis. *Skin Therapy Lett.* 2005;10:1-4.
- Mason AR, Mason J, Cork M, et al. Topical treatments for chronic plaque psoriasis. Cochrane Database Syst Rev. 2009;2:CD005028.
- 10. Belge K, Brück J, Ghoreschi K. Advances in treating psoriasis. F1000Prime Rep. 2014;6:4.
- Mease PJ, Armstrong AW. Managing patients with psoriatic disease: the diagnosis and pharmacologic treatment of psoriatic arthritis in patients with psoriasis. *Drugs*. 2014;74:423-441.
- 12. Boehncke WH, Qureshi A, Merola JF, et al. Diagnosing and treating psoriatic arthritis: an update. *Br J Dermatol*. 2014;170:772-786.
- 13. Feldman SR. Effectiveness of clobetasol propionate spray 0.05% added to other stable treatments: add-on therapy in the COBRA trial. *Cutis.* 2007;80(suppl 5):20-28.
- 14. Feldman SR, Gelfand JM, Stein Gold L, et al. The role of topical therapy for patients with extensive psoriasis. *Cutis*. 2007;79(suppl 1[ii]):18-31.
- 15. Kircik L. Topical calcipotriene 0.005% and betamethasone dipropionate 0.064% maintains efficacy of etanercept after step-down dose in patients with moderate-to-severe

- plaque psoriasis: results of an open label trial. *J Drugs Dermatol*. 2011;10:878-882.
- Taclonex [product insert]. Parsippany, NJ: LEO Pharma Inc; 2014.
- 17. Buckley C, Hoffmann V, Shapiro J, et al. Calcipotriol plus betamethasone dipropionate scalp formulation is effective and well tolerated in the treatment of scalp psoriasis: a phase II study. *Dermatology*. 2008;217:107-113.
- 18. Fleming C, Ganslandt C, Guenther L, et al. Calcipotriol plus betamethasone dipropionate gel compared with its active components in the same vehicle and the vehicle alone in the treatment of psoriasis vulgaris: a randomized, parallel group, double-blind, exploratory study. Eur J Dermatol. 2010;20:465-471.
- Menter A, Stein Gold L, Bukhalo M, et al. Calcipotriene plus betamethasone dipropionate topical suspension for the treatment of mild to moderate psoriasis vulgaris on the body: a randomized, double-blind, vehicle-controlled trial. J Drugs Dermatol. 2013;12:92-98.
- Jemec GBE, Ganslandt C, Ortonne JP, et al. A new scalp formulation of calcipotriene plus betamethasone compared with its active ingredients and the vehicle in the treatment of scalp psoriasis: a randomized, double-blind, controlled trial. J Am Acad Dermatol. 2008;59:455-463.
- 21. van de Kerkhof PC, Hoffmann V, Anstey A, et al. A new scalp formulation of calcipotriol plus betamethasone dipropionate compared with each of its active ingredients in the same vehicle for the treatment of scalp psoriasis: a randomized, double-blind, controlled trial. *Br J Dermatol.* 2009;160:170-176.
- 22. Langley RG, Gupta A, Papp K, et al. Calcipotriol plus betamethasone dipropionate gel compared with tacalcitol ointment and the gel vehicle alone in patients with psoriasis vulgaris: a randomized, controlled clinical trial. *Dermatology*. 2011;222:148-156.
- 23. Kragballe K, van de Kerkhof P. Pooled safety analysis of calcipotriol plus betamethasone dipropionate gel for the treatment of psoriasis on the body and scalp. *J Eur Acad Dermatol Venereol.* 2014;28:10-21.
- 24. Lebwohl MG, Corvari L. Compatibility of topical therapies for psoriasis: challenges and innovations. *Cutis*. 2007;79(suppl 1[ii]):5-10.
- 25. Patel B, Siskin S, Krazmien R, et al. Compatibility of calcipotriene with other topical medications. *J Am Acad Dermatol.* 1998;38(6, pt 1):1010-1011.
- Traulsen J. Bioavailability of betamethasone dipropionate when combined with calcipotriol. *Int J Dermatol.* 2004;43:611-617.
- 27. Sandoval LF, Feldman SR. Topical corticosteroids. In: Koo JYM, Levin EC, Leon A, et al, eds. *Moderate to Severe Psoriasis*. 4th ed. Boca Raton, FL: CRC Press Taylor & Francis Group; 2014:21-36.

- 28. deShazo R, Krueger GG, Duffin KC. Topical agents. In: Koo JYM, Levin EC, Leon A, et al, eds. *Moderate to Severe Psoriasis*. 4th ed. Boca Raton, FL: CRC Press Taylor & Francis Group; 2014:41-65.
- 29. Hegyi Z, Zwicker S, Bureik D, et al. Vitamin D analog calcipotriol suppresses the Th17 cytokine-induced proinflammatory S100 "alarmins" psoriasin (S100A7) and koebnerisin (S100A15) in psoriasis. *J Invest Dermatol*. 2012;132:1416-1424.
- Lovato P, Norsgaard H, Ropke M. Key immunomodulatory effects exerted by calcipotriol in combination with corticosteroid on human cells. Poster presented at: 21st European Academy of Dermatology and Venereology Congress; September 27-30, 2012; Prague, Czech Republic.
- 31. Renton C. Diagnosis and treatment of adults with scalp psoriasis. *Nurs Stand*. 2014;28:35-39.
- 32. Feldman SR, Housman TS. Patients' vehicle preference for corticosteroid treatments of scalp psoriasis. *Am J Clin Dermatol.* 2003;4:221-224.
- 33. Gooderham M, Debarre JM, Keddy-Grant J, et al. Safety and efficacy of calcipotriene plus betamethasone dipropionate topical suspension in adolescents with scalp psoriasis: an open, non-controlled, 8-week trial. Poster presented at: American Academy of Dermatology 72nd Annual Meeting; March 21-25, 2014; Denver, CO.
- Ortonne JP, Tan J, Nordin P, et al. Quality of life of patients with scalp psoriasis treated with calcipotriene plus betamethasone dipropionate gel compared to calcipotriene solution. J Am Academy Dermatol. 2008;58(2, suppl 2):AB134.
- 35. Mrowietz U, Macheleidt O, Eicke C. Effective treatment and improvement of quality of life in patients with scalp psoriasis by topical use of calcipotriol/betamethasone (Xamiol®-gel): results [in German]. *J Dtsch Dermatol Ges*. 2011;9:825-831.
- Luger TA, Cambazard F, Larsen FG, et al. A study of the safety and efficacy of calcipotriol and betamethasone dipropionate scalp formulation in the long-term management of scalp psoriasis. *Dermatology*. 2008;217:321-328.
- 37. Tyring S, Mendoza N, Appell M, et al. A calcipotriene/ betamethasone dipropionate two-compound scalp formulation in the treatment of scalp psoriasis in Hispanic/ Latino and Black/African American patients: results of the randomized, 8-week, double-blind phase of a clinical trial. *Int J Dermatol.* 2010;49:1328-1333.
- 38. Silver S, Tuppal R, Gupta AK, et al. Effect of calcipotriene plus betamethasone dipropionate topical suspension on the hypothalamic-pituitary-adrenal axis and calcium homeostasis in subjects with extensive psoriasis vulgaris: an open, non-controlled, 8-week trial. J Drugs Dermatol. 2013;12:882-888.

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