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# Non-psoriatic uses of calcipotriol: a concise updated review

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## Abstract

Calcipotriol (calcipotriene) is a synthetic vitamin D3 derivative that is a standard treatment option for psoriasis. It is generally well tolerated with minimal side effects. Due to its ability to reduce keratinocyte proliferation and induce keratinocyte differentiation as well as its immunomodulatory effects, calcipotriol has been used to treat a variety of skin disorders such as atopic dermatitis, actinic keratoses, lichen planus, seborrheic keratoses, and vitiligo [1]. We surveyed the literature examining the use of calcipotriol for non-psoriatic dermatologic disease.

*Keywords: alopecia, calcipotriol, calcipotriene, dermatitis, eczema, vitamin D, vitíligo*

## Introduction

Calcipotriol is a synthetic vitamin D3 derivative that was first approved by the FDA in 1993 for the treatment of psoriasis. Its mechanism of action, similar to its natural form calcitriol (1,25-dihydroxycholecalciferol), is through regulation of genes involved in keratinocyte proliferation via binding to the vitamin D3 receptor, which plays a role in hair follicle and epidermal differentiation [2,3].

Calcitriol is synthesized by the body through a series of conversion steps initiated by exposure to ultraviolet B radiation. It primarily functions to regulate bone growth and calcium in the intestine, kidneys, and parathyroid [4]. Calcitriol also acts as an immunosuppressant by increasing regulatory T cells and decreasing pro-inflammatory cytokines, including interferon gamma. It leads to class switching from T helper 1 and 17 cells to T helper 2 cells [5]. These effects can be enhanced by combining with topical steroids [6]. It also has antiproliferative effects on keratinocytes [7].

Calcipotriol has a shorter half-life than calcitriol and has less pronounced effects on calcium metabolism, which makes calcipotriol a superior therapeutic option [1]. Calcipotriol is available in ointment, cream, and solution formulations at a standard concentration of 50μg/g (0.005%). Formulations that are commercially available in the U.S. include Dovonex, Calcitrene, and Sorilux.

Calcipotriol is generally well tolerated with short- and long-term usage with the majority of adverse effects being moderate in intensity and cutaneous. Common local side effects of calcipotriol include burning, pruritus, edema, xeroderma, irritation, dermatitis, and erythema [3]. Rare side effects include hypercalcemia and parathyroid hormone suppression. However, most reports of these side effects involved weekly dosages of >100 grams of 0.005% topical formulation of calcipotriol [8]. In patients requiring weekly dosages >100 grams of 0.005% topical calcipotriol, it is recommended to obtain weekly serum calcium levels for the first three weeks of therapy as most cases of hypercalcemia have been diagnosed after 4-19 days of treatment [8]. Calcipotriol is pregnancy category C due to studies of oral calcipotriene in rats and rabbits demonstrating skeletal abnormalities [9]. However, no effects were seen when dosed at levels similar to expected human systemic exposure from dermal application of calcipotriene [9].

Due to its ability to reduce keratinocyte proliferation and induce keratinocyte differentiation as well as its immunomodulatory effects, calcipotriol can be used for many skin disorders beyond psoriasis [1]. We surveyed the literature examining the use of

calcipotriol for non-psoriatic dermatologic diseases as outlined in Tables 1 and 2.

## Discussion

### Actinic keratoses

Small studies of topical calcipotriol in the treatment of actinic keratoses (AKs) have shown mixed results. An investigator-blinded, half-face/scalp study (N=9) demonstrated a statistically significant decrease in total number of AKs compared to placebo after application of calcipotriol cream twice daily for 12 weeks. Two of the eight participants completing the study had a >50% decrease, three had a 25-50% decrease, and three had a <25% decrease in total AK lesions [10]. Conversely, a double-blind study conducted on renal transplant recipients with AKs (N=13) demonstrated no significant improvement in any of the treatment groups after patients applied calcipotriol twice daily alone or in combination with all-trans retinoic acid cream [11].

In a double-blind randomized controlled trial (RCT), 132 patients were randomized into the treatment group with 5-fluorouracil(5-FU)/calcipotriol cream (N=65) or the control group with 5-FU/Vaseline (N=67). The drug combination for 5-FU/calcipotriol was prepared by mixing 0.005% calcipotriol ointment with 5% 5-FU cream in a 1:1 weight ratio while the drug combination for 5-FU/Vaseline was prepared by mixing Vaseline with 5% 5-FU cream in a 1:1 weight ratio, both in accordance with United States Pharmacopeial Convention 795 guidelines for compounding topical medications [12]. Participants were asked to apply the cream twice daily for four days. Upon evaluation during week eight, the treatment group (N=64) versus the control group (N=66) demonstrated the following mean reduction in the number of AKs: 87.8% versus 26.3% on the face, 76.4% versus 5.7% on the scalp, 68.8% versus 9.6% on the right upper extremity, and 79% versus 16.3% on the left upper extremity. Additionally, the treatment group had more participants obtaining complete clearance and had higher activation of CD4 T-cell immunity against AKs [12]. Of the 130 patients completing the eight-week study, 84 were reassessed three years later [13]. Among those who treated their scalp and face, those in the treatment group (N=30) had a significant reduction in risk of squamous cell carcinoma (HR 0.215, CI 0.048-0.0972) compared to those in the control group (N=40). However, a statistically significant reduction in squamous cell carcinoma risk was not appreciated across all anatomic sites combined. The results of these studies suggest that calcipotriol (monotherapy or in combination with 5-FU) may be a consideration for the treatment of AKs.

In a retrospective chart review, the efficacy of calcipotriene 0.005% foam and/or 1% 5-FU cream after cryotherapy was examined in 175 patients with AKs [14]. Group One (N=50) was treated with cryotherapy alone, Group Two (N=50) was treated with cryotherapy and 1% 5-FU cream, Group Three (N=50) was treated with cryotherapy and combination of 1% 5-FU cream and calcipotriene 0.005% foam, and the Group Four (N=25) was treated with cryotherapy and calcipotriene 0.005% foam. After cryotherapy, Groups Two, Three, and Four used the topical medications in three-week cycles consisting of five days of application on the face and seven days of application elsewhere and then no treatment for the remainder of the three-week period. The three-week treatment cycles were continued for 300 days. In addition, all patients applied zinc healing cream as needed and sunblock every morning. During treatment days 101-200, only Group Three had a significant mean reduction in the number of AKs compared to Group One (-9.55, P=0.002). During treatment days 201-300, Group Two (-7.54, P=0.047), Group Three (-14.70, P=0.001), and Group Four (-14.18, P=0.004) had a significant mean reduction in the number of AKs compared to Group One. Reported side effects included pruritus, itching, and erythema; all resolved within each three-week treatment cycle. Group Two had the greatest rate of adverse effects (30%), followed by Group Three (10%); Group Four had the lowest rate (8%). The results of this study suggest that the addition of calcipotriene to 5-FU after cryotherapy improved its efficacy and expedited the onset of its therapeutic effects (**Table 1**).

### Alopecia areata

Calcipotriol has also been used to treat alopecia areata (AA) with variable efficacy. A retrospective

study evaluated 48 patients with mild-to-moderate AA treated with calcipotriol cream twice daily [15]. By week 12 of treatment, 30 (62.5%) patients had >75% hair regrowth, and 13 of these achieved total hair regrowth. Another 18 (37.5%) patients had some evidence of a positive response. In a similar but prospective study design, application of 0.005% calcipotriol lotion applied to AA areas twice daily for 12 weeks demonstrated hair regrowth in 13 of 22 (59.1%) patients and seven of the 13 achieved hair growth sufficient to cover the scalp or conceal the alopecic patches [16]. Nine of 22 (40.9%) patients had no response or worsening disease.

An intrasubject-controlled, prospective study compared the efficacy of topical calcipotriol versus topical clobetasol for AA affecting the scalp [17]. Thirty-five patients applied calcipotriol 0.005% ointment to one side of the scalp and clobetasol propionate 0.05% ointment to the contralateral side twice daily for 24 weeks. At the end of weeks 12 and 24, 54.29% and 64.29% of patients in the calcipotriol group achieved >75% hair regrowth compared to 45.71% and 62.86% in the clobetasol group, respectively. The difference between the two treatment groups was not significant.

Contrarily, a double-blind, placebo-controlled clinical trial (CT) of 20 patients with alopecia universalis or alopecia totalis applied calcipotriol to one side of the scalp and a matching placebo ointment to the contralateral scalp twice daily for 12-26 weeks [18]. No subject demonstrated a positive response.

Calcipotriol may enhance the efficacy of topical steroids in the treatment of AA. An RCT evaluated the combination of 1:1 ratio of 0.1% mometasone cream and 0.005% calcipotriol ointment (N=50) versus mometasone alone (N=50) for the treatment of AA affecting <50% of the scalp [19]. All participants applied topical mometasone 0.1% cream each morning and the dual-treatment group additionally applied calcipotriol 0.005% ointment each night. The duration of treatment was 24 weeks with follow-up visits at 6, 12, and 24 weeks. The mometasone plus calcipotriol group demonstrated significantly greater decrease in mean Severity of Alopecia Tool (SALT) score from baseline to 24 weeks compared to mometasone alone, 7.22 to 2.98 and 6.05 to 2.66, respectively (P<0.001).

Calcipotriol has also been studied in comparison to and in combination with narrowband ultraviolet B (NB-UVB) for AA [20]. Patients (N=60) were randomized to one of four groups: NB-UVB, 0.005% calcipotriol ointment, combination of NB-UVB and 0.005% calcipotriol ointment, or placebo ointment. Calcipotriol was applied twice daily to affected areas and was not to be applied until two hours after NB-UVB treatment in the combination group. All treatments were found to be efficacious and showed statistically significant decreases in SALT scores compared to baseline and compared to the placebo group. However, no treatment group was statistically superior (**Table 1**).

### Hand eczema

One study showed that calcipotriol may be as effective as desoximetasone for chronic hand eczema. A double-blind, randomized trial compared the effectiveness of 0.005% calcipotriol ointment to 0.25% desoximetasone ointment for the treatment of chronic hand eczema [21]. Thirteen participants applied calcipotriol to one hand and desoximetasone to the other twice daily for eight weeks followed by four weeks of petrolatum ointment twice daily to both hands. Follow-up visits occurred at week two, six, eight, and twelve. At week eight, hand eczema severity index (HECSI) scores decreased by 76% compared to baseline in both the calcipotriol and desoximetasone groups. There were no statistically significant differences in HECSI scores or subjective scoring of improvement between the calcipotriol and desoximetasone groups (**Table 1**).

### Lichen planus

Bayramgureler et al. assessed the efficacy of calcipotriol for the treatment of lichen planus in an open pilot trial [22]. After application of topical calcipotriol ointment twice daily and 25mg hydroxyzine twice daily for three months, complete clearing with residual hyperpigmentation was observed in five patients (31.25%), partial response in four patients (25%), and no improvement in seven patients (43.75%). Calcipotriol was also reported to be effective for an 80-year-old patient with

hypertrophic lichen planus with sustained clearance after twice daily application for seven months [23].

Theng et al. concluded calcipotriol and betamethasone valerate may be similarly effective for the treatment of lichen planus [24]. Thirty-one patients were enrolled into a randomized trial with 15 patients receiving calcipotriol treatment and 16 receiving betamethasone for 12 weeks. Results demonstrated flattening in 46.7% and 50.0% of subjects in the calcipotriol and betamethasone groups, respectively. Only one patient had complete clearance in the calcipotriol group. None achieved complete clearance in the betamethasone group (**Table 1**).

**Lichen sclerosus**

In an open label trial, 23 patients with genital lichen sclerosus applied 0.005% calcipotriol ointment once daily for one week, increasing to twice daily as tolerated for a total of 16 weeks. At the end of the trial, both men and women had statistically significant decreases in symptom scores. The women also had a statistically significant decrease in total sign score [25]. Similarly, in a case of extragenital lichen sclerosus on the back in a 69-year-old female, 0.005% calcipotriol ointment was employed twice daily under occlusion for 12 weeks with gross resolution of nearly all lesions [26]. In vivo confocal laser scanning microscopy showed a decrease in hyperkeratosis, resolution of epidermal hypertrophy, and decreased dermal sclerosis. At the six-month follow-up, there was no disease progression (**Table 1**).

**Seborrheic dermatitis**

An open pilot study (N=10) was conducted to assess the efficacy of calcipotriol in treating seborrheic dermatitis [27]. Five patients received calcipotriol cream while the other five received calcipotriol solution twice daily for 15 days. Two of five patients in the cream group and four of five in the solution group showed major improvement and/or complete clearance within an average of eight days. One patient in the solution group had severe skin irritation requiring treatment cessation.

In contrast, a RCT (N=40) did not demonstrate the efficacy of calcipotriol cream for facial seborrheic dermatitis after application twice daily for two weeks [28]. Only one of 19 calcipotriol-treated patients showed a marked improvement whereas six vehicle-treated patients demonstrated complete clearance and two showed 40% improvement.

Calcipotriol was inferior to betamethasone in another randomized trial [29]. Sixty patients were randomly assigned to apply either calcipotriol or betamethasone twice daily for four weeks. However, seven patients withdrew from the calcipotriol group due to adverse effects or an unacceptable treatment response. For patients with mild improvement, treatment was continued for another four weeks. At four weeks, 20 patients (67%) in the betamethasone group had complete clearance compared to seven patients (23%) in the calcipotriol group. An additional three patients in the calcipotriol group achieved complete clearance at eight weeks. Two patients in the calcipotriol group and seven patients in the betamethasone group relapsed at follow-up four weeks after stopping treatment (**Table 1**).

**Seborrheic keratoses**

An open-label controlled trial compared topical calcipotriol, topical tazarotene, and topical imiquimod with cryosurgery for the treatment of seborrheic keratoses [30]. Fifteen patients were enrolled in the study with each patient having two seborrheic keratoses treated with calcipotriol (one treated once daily, and one treated twice daily) for four months. Treatment with calcipotriol did not result in any improvement in seborrheic keratoses.

Another controlled trial (N=116) was conducted to assess the efficacy of vitamin D3 ointments (tacalcitol, calcipotriol, and maxacalcitol) applied once or twice daily in comparison to petrolatum with 10% salicylic acid in petrolatum as a control [31]. Twelve of the 34 patients (35.3%) that received calcipotriol had a >80% decrease in the number of seborrheic keratoses whereas 17 of 34 (50%) patients had a decrease between 40-80%. Only five of 34 (14.7%) had a <40% decrease in the number of seborrheic keratoses. Effectiveness of calcipotriol was comparable to that of maxacalcitol whereas tacalcitol was less effective. There were no observed changes in the control group (**Table 1**).

**Vitiligo**

Gargoom et al. conducted a trial with 18 children ages three to 12 [32]. Calcipotriol was applied twice

daily as an ointment (N=9) or cream (N=9) for four months. Of the 14 patients who completed the course, three showed complete resolution, four showed 50-80% improvement, three showed 30-50% improvement, and four showed no improvement. The authors concluded that calcipotriol could be useful in treating children with vitiligo who cannot be treated with steroids or psoralen plus ultraviolet A (PUVA).

However, in a prospective, right/left comparative open study including 24 patients, treatment of one lesion with topical calcipotriol was compared to one lesion that was left untreated. An average treatment duration of 3.9 months resulted in repigmentation in only three of the 24 patients [33]. In another controlled trial comparing calcipotriol to clobetasol ointment, calcipotriol was minimally effective [34].

Several studies suggest calcipotriol is an effective adjuvant therapy when combined with PUVA. A RCT evaluated PUVA in combination with calcipotriol versus PUVA treatment with placebo [35]. Twenty-seven patients were given a calcipotriol treatment one hour before PUVA twice weekly with repigmentation evaluated as initial (25%) and complete (75-100%). Combination calcipotriol and PUVA treatment resulted in initial repigmentation in 81% of patients and complete repigmentation in 63% of patients whereas PUVA monotherapy resulted in 7% initial and 15% complete repigmentation. There were multiple other controlled trials in which calcipotriol was an effective adjuvant therapy when applied twice daily with PUVA treatment thrice weekly [36-39]. However, a study of twice-weekly PUVA monotherapy compared to twice-daily calcipotriol cream combined with twice-weekly PUVA demonstrated no additional response in the combination group compared to PUVA monotherapy [40].

Combination therapy with calcipotriol and NB-UVB has also been extensively studied with mixed results. Multiple controlled trial have demonstrated superior efficacy of calcipotriol combined with NB-UVB compared to NB-UVB monotherapy [41-43]. In these studies, repigmentation of ≥ 50% was detected as early as six months after initiating treatment with calcipotriol once or twice daily and NB-UVB thrice weekly. However, several other studies failed to demonstrate the benefit of NB-UVB with adjunctive calcipotriol compared to NB-UVB monotherapy [44-48].

Results of studies of calcipotriol combined with excimer laser have also been mixed. One controlled trial reported increased efficacy with 12 weeks of excimer light plus topical calcipotriol followed by 12 weeks of calcipotriol monotherapy in comparison to 12 weeks of excimer light plus topical clobetasol followed by 12 weeks of clobetasol [49]. However, in an RCT, combination treatment with excimer light and calcipotriol for 24 weeks was not more effective than excimer light monotherapy [50], (**Table 1**).

**Other dermatologic diseases**

Case reports have demonstrated variable success with topical calcipotriene in a variety of other dermatologic skin diseases. These include acanthoma [51,52], acanthosis nigricans [53,54], angioimmunoblastic T-cell lymphoma [55], chronic kidney disease-associated pruritus [56], circumscribed palmar hypokeratosis [57,58], confluent and reticulated papillomatosis [59-63], disseminated superficial actinic porokeratosis [64,65], dystrophic epidermolysis bullosa [66,67], epidermolytic ichthyosis [68], epidermolytic palmoplantar keratoderma [69], erosive pustular dermatosis of the frontal scalp [70], eruptive vellus hair cysts [71], erythema annulare centrifugum [72], extramammary Paget disease [73], focal acral hyperkeratosis [74], granular parakeratosis [75-77], Grover disease [78], hand-foot syndrome [79], hyperkeratosis lenticularis perstans [80], ichthyosis linearis circumflex of Netherto syndrome [81], inflammatory linear verrucous epidermal nevus [82-85], Kaposi sarcoma [86], keratosis lichenoides chronica [87,88], lichen amyloidosis [89], lichen striatus [90], linear atrophoderma of Moulin [91], morphea or linear scleroderma [92-94], nevoid hyperkeratosis [95,96], oral leukoplakia [97,98], peeling skin syndrome [99], pityriasis rubra pilaris [100], progressive symmetrical erythrokeratoderma [101], prurigo nodularis [102], scleroderma [103], Sjogren-Larsson syndrome [104,105], and warts [106,107], (**Table 2**).

## Conclusion

Topical calcipotriol is a safe and effective therapy in the treatment of a wide variety of diseases. It is probably underutilized as a steroid-sparing agent by most dermatologists. Dermatologists may want to consider calcipotriol as an alternative or adjuvant topical therapy prior to considering more aggressive treatments.

## Potential conflicts of interest

The authors declare no conflicts of interest.

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**Table 1**. *Dermatoses treated with topical calcipotriol.*

| Dermatosis | Study Type | No. enrolled in calcipotriol group(s)* | Treatment group(s) | Duration | Response# | References |
|---|---|---|---|---|---|---|
| Actinic keratosis | RCT, R/L comparison | 9 | Calcipotriol cream vs placebo cream | 12 weeks | Partial response with significant decrease in total AK no. between baseline and week 12 on calcipotriol treated side (P=0.028); no difference seen on placebo side (P=1.00). 5/8 patients had >25% decrease in total AK number by week 12 with calcipotriol compared to 3/8 with placebo. 3/8 had increase in total AK number on placebo side by week 12 | Seckin et al. 2009 [10] |
| | CCT | 13 | Calcipotriol cream alone vs ATRA + calcipotriol cream vs ATRA alone vs placebo cream | 6 weeks | No significant differences in clinical, histological, and immunohistochemistry parameters between calcipotriol alone, ATRA + calcipotriene, ATRA alone, and placebo | Smit et al. 2002 [11] |
| | RCT | 65 | 5-FU cream + calcipotriol oint. (1:1 mixture) vs 5-FU cream + Vaseline (1:1 mixture) | 4 days | 27% of participants had complete clearance of facial AKs in calcipotriol/5FU group compared to 0% in the Vaseline/5FU group (P<0.0001). Across all anatomical sites, 100% had reduction in AK counts in calcipotriol group while 65%-80% in control group (depending on anatomical site) had reduction in AK counts (P<0.01 for all sites) | Cunningham et al. 2017 [12] |
| | Prospective cohort study (Continuation of Cunningham et al. 2017) | 64§ | 5-FU cream + calcipotriol oint. (1:1 mixture) vs 5-FU cream + Vaseline (1:1 mixture) | 4 days | Partial response. Significantly fewer participants developed SCC on face and scalp within 3 years of calcipotriol/5FU therapy (2/30 [7%] versus 11/40 [28%] in control group; hazard ratio 0.215 [95% CI: 0.048–0.972], P=0.032) | Rosenberg et al. 2019 [13] |
| | Retrospective chart review | 175 | Cryotherapy (Group 1, N=50) vs cryotherapy followed by 1% 5-FU cream (Group 2, N=50) vs cryotherapy followed by 1% 5-FU cream and calcipotriene 0.005% foam (Group 3, N=50) vs cryotherapy followed by calcipotriene 0.005% foam (Group 4, N=25); all applied zinc healing cream as needed | Groups 2-4: 3-week cycles of topicals for 5 nights on face and 7 nights elsewhere, then no treatment for 2 weeks, cycles repeat for 300 days | At 101-200 days of treatment compared to Group 1, only Group 3 showed a statistically significant mean reduction in number of AKs (P=0.002). At 201-300 days of treatment compared to Group 1, Groups 2-4 showed statistically significant mean reductions in number of AKs with Group 3 showing the greatest reduction (-14.70, P=0.001) | Moore et al. 2021 [14] |

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| | | | and sunblock every morning for 3 weeks | | | |
| Alopecia areata | CCT, R/L comparison | 20 | Calcipotriol oint. applied to ½ of scalp; vehicle control applied to contralateral side | 4-26 weeks | No response in any subject | Berth-Jones & Hutchinson 1991 [18] |
| | Retrospective study | 48 | Topical calcipotriol cream | 12 weeks | Partial response. >60% of participants had 75%+ hair regrowth by week 12. 13/48 at week 12 had complete response | Cerman et al. 2015 [15] |
| | CT | 22 | Topical calcipotriol lotion | 12 weeks | Partial response in 13/22 patients. | Narang et al. 2017 [16] |
| | CT, R/L comparison | 35 | Calcipotriol oint. applied to ½ of scalp; Clobetasol propionate 0.05% oint. Applied to contralateral side | 24 weeks | Partial response. 69% of calcipotriol-treated areas had >75% hair regrowth at 24 weeks, no significant difference compared to clobetasol | Molinelli et al. 2020 [17] |
| | RCT | 50 | Mometasone 0.1% cream + calcipotriol oint. vs Mometasone alone | 24 weeks | Addition of calcipotriol nightly resulted in improved response (significant decrease in SALT score seen in combination therapy, P<0.001) | Alam et al. 2019 [19] |
| | RCT | 15 | Group 1: NB-UVB. Group 2: 0.005% Calcipotriol oint. Group 3: NB-UVB and calcipotriol oint. Group 4: Placebo oint. | 3 months | Partial response seen in all groups except placebo group | El Taieb et al. 2019 [20] |
| Chronic hand eczema | CT, R/L comparison | 13 | Calcipotriol oint. on one hand vs 0.25% Desoximetasone on other hand | 8 weeks | Partial response in 70% of subjects in both groups | Juntongjin & Pongprasert 2019 [21] |
| Lichen planus | CT | 16 | Topical calcipotriol oint. | 3 months | Complete resolution in 31.25% (5/16) and partial response in 25% (4/16) of the patients. No improvement was observed in 43.75% (7/16) | Bayramgurler et al. 2002 [22] |
| | CR | 1 | Topical calcipotriol oint. | 7 months | Complete resolution. | De Paola et al. 2014 [23] |
| | CT | 15 | Calcipotriol oint. vs 0.1% Betamethasone valerate | 12 weeks | Partial response. ≥ 75% of lesion flattening in 46.7% in calcipotriol group and 50.0% in betamethasone group. Resolution in 1/15 in calcipotriol group, 0/16 in betamethasone group | Theng et al. 2004 [24] |
| Extragenital lichen sclerosus | CR | 1 | Topical calcipotriol oint. | 12 weeks | Partial response clinically and on in vivo confocal laser scanning microscopy | Kreuter et al. 2002 [26] |
| Genital lichen sclerosus | CT | 23 | Topical calcipotriol oint. | 16 weeks | Partial response. Statistically significant improvement in symptoms seen in both men and women and in clinical signs seen in women | Gupta et al. 2005 [25] |

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| Seborrheic dermatitis | CT | 5 | Calcipotriol cream vs 0.005% Calcipotriol alcohol solution | 15 days | Partial response. 2/5 patients in the cream group and 4/5 in the alcohol solution group with partial or complete response within an average of 8 days | Kowalzick & Schlehaider 1998 [27] |
| | RCT | 19 | Calcipotriol cream + calcipotriol scalp solution vs vehicle controls | 4 weeks | Partial response in 1/19 in calcipotriol group. In placebo group, 6/20 had complete response and 2/20 had partial response | Berth-Jones & Adnitt 2001 [28] |
| | CT | 30 | Calcipotriol solution vs 0.1% betamethasone valerate solution | 4 or 8 weeks | Complete response in 4 weeks in 20/30 in betamethasone group vs 7/30 in calcipotriol group (3 more in calcipotriene cleared at 8 weeks). Betamethasone was statistically significantly superior | Basak & Ergin 2001 [29] |
| Seborrheic keratosis | CCT | 15 | Vanicream® vs Calcipotriol oint. vs 0.1% tazarotene vs 5% imiquimod vs cryosurgery | 4 months | No response in any subject with calcipotriol or imiquimod QD. 7/15 patients had complete response with BID tazarotene (QD application resulted in no improvement). Imiquimod BID had intolerable side effects in 5 patients.15/15 patients had complete response with cryosurgery | Herron et al. 2004 [30] |
| | CCT | 34 | 10% salicylic acid in petrolatum vs calcipotriol oint. vs tacalcitol oint. vs maxacalcitol oint. | 3-12 months | Partial response. Calcipotriol group: 12/34 lesions (35.3%) had >80% decrease in SK size. 17/34 (50%) patients had 40-80% decrease in SK size. 5/34 (14.7%) patients had a decrease <40% in SK size. Salicylic acid group: 0/30 had between 40-100% decrease in size. Tacalcitol group: 27/45 had 40-100% decrease in size. Maxacalcitol group: 33/37 had 40-100% decrease in size | Mitsuhashi et al. 2005 [31] |
| Vitiligo | CT | 18 | Topical calcipotriol cream or oint. | 4 months | Complete response in 3/14, partial response in 7/14, no response in 4/14 | Gargoom et al. 2004 [32] |
| | CCT, R/L comparison | 24 | Calcipotriol to one lesion compared to untreated lesion on contralateral side (vehicle unknown) | 3-6 months | Only partial repigmentation in 3/24 patients. No repigmentation was seen in 21/24. | Chiaverini et al. 2002 [33] |
| | CT | 22 | Calcipotriol oint. vs 0.05% Clobetasol oint. | 4 months | Partial response. 8/20 in clobetasol group had >75% repigmentation compared to 0/22 in calcipotriol group. 12/22 in calcipotriol had partial response and 10/22 had no response. Only 3/20 in clobetasol group had no response. Compared with clobetasol, calcipotriol was inferior | Kose et al. 2002 [34] |
| | RCT, R/L comparison | 27 | PUVA + calcipotriol cream vs PUVA + control vehicle | Not stated | Partial response. Combination with PUVA resulted in higher percentage of repigmentation compared to placebo (63% vs 15%) | Ermis et al. 2001 [35] |

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| | CCT, R/L comparison | 23 | PUVA + calcipotriol oint. vs PUVA | 15 weeks | Partial response. 12/23 (52%) showed >50% improvement in combination group vs 7/23 (30%) in PUVA only group (P=0.13) | Cherif et al. 2003 [36] |
| | CCT | 26 | 22/26 had calcipotriol cream only; 4/26 had calcipotriol cream + PUVA | 3-9 months | Partial response. 5/22 patients in monotherapy group had >90% improvement and 7/22 had 50-90% improvement. Partial response was seen in 3/4 patients receiving dual therapy (1/4 had no response) | Ameen et al. 2001 [37] |
| | RCT, R/L comparison | 19 | 0.6mg/kg 8-methoxypsoralen + sunlight plus Calcipotriol oint. to one side vs placebo oint. to other side | 18 months | Partial response. 13/17 had >75% improvement on calcipotriol side compared to 9/17 on placebo side. 3/17 had minimal or no response on calcipotriol side compared to 7/17 on placebo side | Parsad et al. 1998 [38] |
| | CT | 21 | PUVA + calcipotriol oint | 20 weeks | Partial response. 6/21 had >50% repigmentation and 6/21 had no response | Yalcin et al. 2001 [39] |
| | CCT, R/L comparison | 22 | Calcipotriol cream + PUVA vs PUVA alone | 36 weeks | No significant difference in response between PUVA+ calcipotriene vs PUVA alone | Baysal et al. 2003 [40] |
| | CCT, R/L comparison | 20 | NB-UVB only to R side vs NB-UVB + calcipotriol oint. to L side | Up to 15 months | Partial response. 8/17 had >66% response after 67–180 UVB treatments, 6/17 had 26-65% response after 40-160 UVB treatments, 3/17 had <25% response after 14-57 UVB treatments. 6/17 patients had greater response on dual therapy side at end of study period; 11/17 had similar responses on both sides | Kullavanijaya et al. 2004 [41] |
| | CCT, R/L comparison | 28 | NB-UVB only to L side vs NB-UVB + calcipotriol cream to R side | 6 months | Partial response. Average response rates (excluding hands and feet) of patients receiving NB-UVB +calcipotriol and NB-UVB alone were 51% ± 19.6 and 39% ± 18.9, respectively (P=0.0006) | Goktas et al. 2006 [42] |
| | RCT | 15 per group | Group 1: Topical calcipotriol, NB-UVB, and topical betamethasone. Group 2: NB-UVB and topical calcipotriol. Group 3: NB-UVB alone (vehicle unknown) | 6 months | Partial response. Improvement of 63.33% ± 7.55 in group 1, 60.67% ± 5.75 in group 2, and 46.67% ± 7.98 in group 3. No statistically significant difference between groups 1 and 2, and groups 2 and 3, but there was a statistically significant difference between groups 1 and 3 (P=0.0048) | Akdeniz et al. 2014 [43] |
| | RCT, R/L comparison | 27 | NB-UVB + calcipotriol oint. vs NB-UVB alone | 24 weeks | Mean percent repigmentation was 51.4% for dual therapy vs 49.0% for monotherapy (P=0.557). Response not significantly different between NB-UVB and NB-UVB plus calcipotriol | Khullar et al. 2015 [44] |

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| | RCT | 15 (40 in total enrolled) | 13 treated with calcipotriol oint. + NB-UVB and 24 with NB-UVB alone | 10 weeks | Mean repigmentation of 41.6% ± 19.4 with NB-UVB alone and 45.01% ± 19.15 with dual therapy (P>0.05). Both treatments were effective (P<0.001) but neither was superior (P>0.05). 10/24 had ≥50% repigmentation after 10 weeks with NB-UVB alone. 6/13 had ≥50% repigmentation with dual therapy after 10 weeks | Arca et al. 2006 [45] |
| | CCT, R/L comparison | 20 | NB-UVB + calcipotriol cream to one side vs NB-UVB only to other side | 6-12 months | >50% repigmentation seen in 11/20 with NB-UVB monotherapy. Compared to dual therapy, no significance difference in response (P>0.05) | Ada et al. 2005 [46] |
| | CCT, four-quarter comparison | 10 | NB-UVB to upper body vs BB-UVB to lower body. Calcipotriol oint. applied to R side of body vs placebo oint. to L side | 12 months | NB-UVB therapy was effective in the treatment of vitiligo; BB-UVB had no effect. Combination with calcipotriol was not superior to NB-UVB monotherapy | Hartmann et al. 2005 [47] |
| | CCT, R/L comparison | 20 | NB-UVB + calcipotriol cream to R side vs NB-UVB only to L side | 20 weeks | Both sides had significant decrease in VIDA score 6 months after treatment compared to pretreatment. No significant difference in final clinical response between treatment arms | Gamil et al. 2010 [48] |
| | CT, R/L comparison | 13 | Group 1: 308nm excimer lamp + calcipotriol oint. x 12 weeks followed by 12 weeks of calcipotriol only. Group 2: 308nm excimer lamp + clobetasol oint. x 12 weeks followed by 12 weeks of clobetasol oint. only | 24 weeks | No significant difference found between treatments | Juntongjin & Sangganjana-vanich 2021 [49] |
| | RCT, R/L comparison | 10 | 308nm xenon chloride excimer laser therapy + calcipotriol oint. vs laser only | 8 weeks | 8/9 patients showed evidence of repigmentation on both sides after 8 weeks. Mean pigmentation rate was 22% ± 10.17 with laser only vs 23% ± 8.50 with dual therapy (P=0.51) | Goldinger et al. 2007 [50] |

*Reported number of patients in this column reflects number of patients who were enrolled in the study and received calcipotriol. This number may differ from number reported in results column, which reflects the number of patients who completed the study and who were included in the studies' analyses.
[§]64 completed the 4-day treatment. After exclusions and losing to follow-up, 41 had 1-year follow-up, 40 had 2-year follow up, 39 had 3-year follow-up. Outcomes in treatment arm for face and scalp were available for 30 patients at 3-years.
[#]Ratios indicate number of patients, such that 10 of 20 patients is written as 10/20.
5-FU, 5-fluorouracil; AK, actinic keratosis; AKs, actinic keratoses; ATRA, all trans retinoic acid; BB-UVB, broad-band ultraviolet B phototherapy; BID, twice daily; CCT, controlled clinical trial; CR, case report; CT, clinical trial; L, Left; NB-UVB, narrow-band ultraviolet B phototherapy; No., number; oint., ointment; PUVA, psoralen ultraviolet A phototherapy; QD, once daily; R, right; RCT, randomized controlled trial; SALT score, Severity of Alopecia Tool; SK, seborrheic keratosis; VIDA, vitiligo disease activity; vs, versus.

**Table 2**. *Additional dermatoses treated with topical calcipotriol.*

| Dermatosis | Study Type | No. enrolled in calcipotriol group(s)* | Treatment Group(s) | Duration | Response# | References |
|---|---|---|---|---|---|---|
| Acanthosis nigricans | CR | 1 | Topical calcipotriol cream | 3 months | Partial response | Bohm et al. 2002 [53] |
| | CR | 1 | Topical calcipotriol oint. | 8 weeks | Complete resolution by end of 4 weeks | Gregoriou et al. 2008 [54] |
| Bullous congenital ichthyosiform erythroderma (epidermolytic ichthyosis) | CR | 1 | Calcipotriol oint. on L leg vs 0.03% tretinoin oint. on R leg vs oint. w/ 10% urea, 5% lactic acid, 5% glycerol on R arm vs oint. w/ 10% urea and 10% sodium chloride on L arm | 3 years | Partial response. Most pronounced reduction of scaling and itching was with calcipotriol after 3-week trial period of each drug. Only calcipotriol was continued for 3 years with continued improvement in pruritus, scaling, and tenderness | Bogenrieder et al. 2003 [68] |
| Clear cell acanthoma | CR | 1 | Topical calcipotriol cream | 2 months | Complete resolution with mild residual pigmentation | Scanni & Pellacani 2014 [52] |
| Circumscribed plantar hypokeratosis | CR | 1 | Topical calcipotriol oint. | 2 months | Complete response | Batalla & de la Torre 2013 [57] |
| | CR | 1 | Topical calcipotriol oint. | 4.5 years | Complete response | Urbina et al. 2005 [58] |
| Chronic kidney disease associated pruritus | CCT | 13 | Calcipotriol solution vs vehicle | 4 weeks | Partial response. Validated modified pruritus assessment score and visual analogue scale were significantly decreased after 4 weeks of calcipotriol compared to vehicle, $P<0.05$. 7/10 in calcipotriol group had >50% improvement in scale compared to baseline as opposed to 1/10 in vehicle group | Jung et al. 2015 [56] |
| Confluent and reticulated papillomatosis | CR | 1 | Topical calcipotriol oint. | 3 weeks | Partial response | Carrozzo et al. 2000 [60] |
| | CR | 1 | Topical calcipotriol cream | 4 weeks | Complete resolution | Gregoriou et al. 2008 [63] |
| | CR | 1 | Topical calcipotriol oint. | 4 weeks | Partial response | Kurkcuoglu & Celebi 1995 [62] |
| | CR | 1 | Topical calcipotriol (vehicle unknown) | 8 weeks | Moderate improvement but recurrence after | Basak et al. 2001 [59] |
| | CR | 1 | Topical calcipotriol oint. | 4 weeks | Complete resolution | Gulec et al. 1999 [61] |
| Cutaneous T-cell lymphoma | CR | 1 | Topical calcipotriol (vehicle unknown) | Not stated | Partial response with plaque regression and inhibition of the proliferation of malignant cells | Scott-Mackie et al. 1993 [55] |
| Disseminated superficial actinic porokeratosis | CR | 1 | Topical calcipotriol cream | 3 months | Complete resolution | Bakardzhiev et al. 2012 [64] |
| | CS | 3 | Topical calcipotriol (vehicle unknown) | 6 to 8 weeks | Partial response with 50 to 75% improvement | Harrison & Stollery 1994 [65] |

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| Dystrophic epidermolysis bullosa | CR | 1 | Topical calcipotriol oint. | 1 month | Decreased itch and pain and complete wound closure observed within 2 weeks. Improved microbial diversity as measured by shotgun sequencing within 14 days and completely eradicated Staphylococcus Aureus colonization by 28 days | Guttmann-Gruber et al. 2018 [66] |
| | RCT | 12 | Calcipotriol oint. vs placebo | 4 weeks | Partial response. 6 patients in final analysis Significant reduction in wound area at day 14 in calcipotriol group compared to placebo (88.4% vs 65.5% reduction, P<0.006) | Guttmann-Gruber et al. 2021 [67] |
| Epidermolytic acanthoma | CR | 1 | Topical calcipotriol oint. | 2 months | Partial response with calcipotriol ointment. Some papules present without superficial keratotic material | Batalla et al. 2013 [51] |
| Epidermolytic palmoplantar keratoderma | CR | 1 | Topical calcipotriol oint. | 4 months | Partial response with markedly improved hyperkeratosis | Lucker et al. 1994 [69] |
| Erosive pustular dermatosis of the frontal scalp | CR | 1 | Topical calcipotriol cream | 2 months | Complete response. No signs of recurrence at 12 months after stopping treatment | Boffa 2003 [70] |
| Eruptive vellus hair cyst | CR | 1 | Topical calcipotriol cream | 2 months | Partial response with complete resolution of some cysts and flattening of the remaining lesions | Erkek et al. 2009 [71] |
| Erythema annulare centrifugum | CR | 1 | Topical calcipotriol oint. | 3 months | Complete response | Gniadecki 2002 [72] |
| Extramammary Paget disease-refractory | CS | 3 | 5-FU cream + calcipotriol cream (1:1 ratio) | 8-10 months | Partial response clinically noted in 3/3 cases with histopathological disease regression confirmed in 2/3 cases | Molina et al. 2019 [73] |
| Focal acral hyperkeratosis | CR | 1 | Topical calcipotriol (vehicle unknown) | 8 weeks | Partial response | Ballambat & Pai 2007 [74] |
| Granular parakeratosis | CR | 1 | Topical calcipotriol (vehicle unknown) | 3 days | Complete resolution | Urbina et al. 2012 [77] |
| | CR | 1 | Calcipotriol to R axilla (vehicle unknown), 12% ammonium lactate to L axilla | 1 month | Complete resolution in R axilla after 1 month of therapy. L axilla lesions resolved after 2 months of ammonium lactate. No recurrence at 9-month follow-up in either axilla | Contreras et al. 2003 [75] |
| | CR | 1 | Topical calcipotriol cream | 2 weeks | Complete resolution in axilla but not abdomen. Mild recurrences since while still using calcipotriol cream | Samrao et al. 2010 [76] |
| Hand-foot syndrome (associated with sorafenib) | CR | 1 | Topical calcipotriol cream | 2 weeks | Complete response | Demirkan et al. 2017 [79] |

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| Hyperkeratosis lenticularis perstans (Flegel disease) | CR | 1 | Topical calcipotriol oint. | 3 months | Complete response | Bayramgurler et al. 2002 [80] |
| Ichthyosis linearis circumflexa of Netherton syndrome | CR | 1 | Topical calcipotriol oint. | 3 weeks | Near complete response with recurrence upon stopping therapy | Godic & Dragos 2004 [81] |
| Inflammatory linear verrucous epidermal nevus | CR | 1 | Topical calcipotriol oint. | 8 weeks | Complete resolution | Bohm et al. 1999 [82] |
| | CR | 1 | Topical calcipotriol oint. | 12 weeks | Partial response with flattening of lesions and improvement in pruritis | Micali et al. 1995 [83] |
| | CS | 2 | Topical calcipotriol oint. | 4-7 weeks | Partial response. Decreased pruritis in both. One had significant improvement but recurrence with stopping. Second had resolution with residual inflammatory pigment alteration | Zvulunov et al. 1997 [84] |
| | CR | 1 | Topical calcipotriol (vehicle unknown) | 6 months | No response | Balci et al. 2012 [85] |
| Kaposi sarcoma | CT | 8 | Topical calcipotriol oint. | 2-104 weeks with median of 4 weeks | Partial response. 4/8 demonstrated 50% or greater reduction in their lesions after 3, 4, 10, and 13 weeks. 4/8 had no response | Masood et al. 2000 [86] |
| Keratosis lichenoides chronica | CR | 1 | Topical calcipotriol oint. | 4 months | Partial response | Grunwald et al. 1997 [87] |
| | CR | 1 | Topical calcipotriol oint. | 3 months | Partial response | Chang et al. 2000 [88] |
| Lichen amyloidosis | CT, R/L comp. | 16 | 50 µg/g Calcipotriol oint. vs 0.1% Betamethasone 17-valerate oint. | 12 weeks | Both sides demonstrated significant reduction in hyperpigmentation from baseline. Calcipotriol side demonstrated improvement in roughness from baseline. No statistically significant difference between calcipotriol and betamethasone for all weeks with regard to both treatment responses | Khoo et al. 1999 [89] |
| Lichen striatus | CR | 1 | Topical calcipotriol oint. | 6 months | Complete response | Ciconte & Bekhor 2007 [90] |
| Linear atrophoderma of moulin | CR | 1 | Topical calcipotriol (vehicle unknown) | 3 months | Partial response | Wongkietkachorn et al. 2013 [91] |
| Morphea or linear scleroderma | In vitro study | 6 | Topical calcipotriol (vehicle unknown) | Not stated | Results indicated that calcipotriol inhibited the proliferation of scleroderma fibroblasts with up to 4 to 20-fold inhibition in 2 patients while the other 4 patient samples all had inhibition but to a lesser extent | Bottomley et al. 1995 [103] |
| | CT | 12 | Topical calcipotriol oint. | 3 months | Partial response with statistically significant improvement in hyperpigmentation, induration, erythema, and telangiectasia after 3 months of therapy | Cunningham et al. 1998 [92] |

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| | CR | 1 | Topical calcipotriol oint. | 3 months | Partial response | Koeger et al. 1999 [93] |
| | CR | 1 | Topical calcipotriol oint. | 9 months | Complete response | Tay 2003 [94] |
| Nevoid hyperkeratosis | CR | 1 | Topical calcipotriol oint. | 2 months | Partial response with significant improvement in hyperkeratosis and verrucous thickening | Sengul et al. 2006 [95] |
| | CR | 2 | Topical calcipotriol oint. | 1 & 2 months then intermittently | Partial response in hyperpigmentation and hyperkeratosis | Bayramgurler et al. 2002 [96] |
| Oral leukoplakia | CT | 20 | Topical calcipotriol in adhesive vehicle (carboxymethyl-cellulose) vs topical tretinoin cream | 5 weeks | 80% of patients in both study arms showed complete clinical resolution of lesions. Resolution persisted in 14/20 (calcipotriol) and 16/20 (tretinoin) (P<0.05, t-test) of the responder patients | Femiano et al. 2001 [97] |
| | RCT | 20 | Calcipotriol gel vs tretinoin cream | 4 weeks | Partial response. 11/20 had moderate to complete response with calcipotriol compared to 8/20 in tretinoin group | Ghalwash et al. 2017 [98] |
| Peeling skin syndrome | CR | 1 | Topical calcipotriol oint. | 4 months | Partial response with improvement in peeling and erythema | Mizuno et al. 2006 [99] |
| Pityriasis rubra pilaris | CS | 3 | Topical calcipotriol oint. | 5 & 8 weeks, 10 months | Complete response in 2/3 cases. Partial response in 1/3 with atypical adult-onset pityriasis rubra pilaris | Van de Kerkhof & Steijlen 1994 [100] |
| Progressive symmetrical erythro-keratoderma | CR | 1 | Topical calcipotriol oint. | 15 days | Complete response but recurrence upon cessation of treatment | Bilgin et al. 2011 [101] |
| Prurigo nodularis | CT, R/L comp. | 10 | Calcipotriol oint. vs 0.1% Betamethasone valerate oint. | 8 weeks | Partial response. 9 completed study. After 8 weeks of therapy, number of nodules decreased by 49% with calcipotriol compared to 18% with betamethasone (P=0.02). Size of nodules decreased by 56% with calcipotriol compared to 25% with betamethasone (P=0.02) | Wong & Goh 2000 [102] |
| Sjogren-Larsson syndrome | CR | 1 | Topical calcipotriol (vehicle unknown) | not stated | Progressive disappearance of scaly lesions without relapse | Fernández-Vozmediano et al. 2003 [105] |
| | CS | 2 | Topical calcipotriol oint. | 12 weeks | Near complete disappearance of roughness and scale | Lucker et al. 1995 [104] |
| Transient acantholytic dermatosis (Grover disease) | CR | 1 | Topical calcipotriol oint. | 3 weeks | Partial response | Mota et al. 1998 [78] |
| Warts | CR | 1 | Topical calcipotriol cream | 2 months | Complete resolution with residual pigmentation | Labandeira et al. 2005 [107] |
| | CR | 1 | Topical calcipotriol oint. | 8 weeks | Complete response of verruca plana | Elmas et al. 2020 [106] |

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which reflects the number of patients who completed the study and who were included in the studies' analyses.
[#]Ratios indicate number of patients, such that 10 of 20 patients is written as 10/20.
5-FU, 5-fluorouracil; comp., comparison; CR, case report; CS, case series; CT, clinical trial; CCT, controlled clinical trial; comp, comparison, L, Left; No., number; oint., ointment; R, right; RCT, randomized controlled trial; vs, versus.