

Therapeutic Class Overview

Topical Vitamin D Analogs and Combinations

Therapeutic Class

- Overview/Summary:** The focus of this review will be the topical vitamin D analogs and combination products. In general, these agents are Food and Drug Administration (FDA)-approved for the treatment of plaque psoriasis in adults. However, depending on the formulation, several products have been approved for use in children or for the treatment of plaque psoriasis.¹⁻⁸ There are currently two topical vitamin D analogs, calcipotriene and calcitriol. Calcitriol is the active form of vitamin D₃, cholecalciferol, which is synthesized in the body; calcipotriene is structurally similar to naturally occurring calcitriol. In addition, calcipotriene has been formulated in combination with betamethasone, a corticosteroid. The exact mechanism of action by which vitamin D analogs exert their effect for the treatment of plaque psoriasis is unknown. They are believed to involve the drug's ability to inhibit keratinocyte proliferation and stimulate keratinocyte differentiation.⁹

Psoriasis is a common chronic skin disorder typically characterized by erythematous papules and plaques with a silver scale, although other presentations occur. Most cases are not severe enough to affect general health and are treated in the outpatient setting.⁹ The options for treatment are topical or systemic and depend on the severity of the disease. Mild-to-moderate disease can often be managed with topical agents, while patients with moderate-to-severe disease may need systemic therapy. Moderate-to-severe disease is usually considered to affect more than 5 to 10% of the body. Topical therapy help provide symptomatic relief, minimize required doses of systemic medications (if being used) and may also be psychologically cathartic for some patients.⁹ Treatment options for mild-to-moderate disease include topical corticosteroids, emollients, tar, topical retinoids and the vitamin D analogs. Most often, a combination of topical corticosteroids and either calcipotriene, calcitriol or tazarotene are prescribed.⁹ Many patients find that certain medications are very messy or difficult to apply. For scalp psoriasis, many patients prefer lotions, solutions, gels, foams, or sprays as vehicles as opposed to creams and ointments.⁹

Table 1. Medications Included Within the Therapeutic Class Review¹⁻⁸

Generic Name (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/ Strength	Generic Availability
Single-Entity Agents			
Calcipotriene (Calcitrene ^{®*} , Dovonex ^{®*} , Sorilux [®])	Treatment of plaque psoriasis (cream, ointment, foam) , Treatment of plaque psoriasis of the scalp (foam, solution)	Cream: 0.005% Foam: 0.005% Ointment: 0.005% Solution: 0.005%	✓
Calcitriol (Vectical ^{®*})	Treatment of plaque psoriasis [†]	Ointment: 3 µg/g	✓
Combination Products			
Calcipotriene/ betamethasone (Enstilar [®] , Taclonex ^{®*} , Taclonex Scalp ^{®*})	Treatment of plaque psoriasis [‡] , treatment of plaque psoriasis of the scalp (suspension)	Foam: 0.005%/0.064% Ointment: 0.005%/0.064% Suspension: 0.005%/0.064%	✓

*Generic is available in at least one dosage form or strength.

Evidence-based Medicine

- Clinical trials have consistently demonstrated the safety and efficacy of the topical psoriasis agents, calcipotriene, calcitriol and tazarotene either alone or in combination.¹³⁻⁵⁴
- Calcipotriene monotherapy is an effective and safe treatment for the management of psoriasis and studies have evaluated its effectiveness versus placebo, coal tar and betamethasone.¹³⁻¹⁸
 - Calcipotriene was also found to be safe and effective for the treatment of scalp psoriasis.¹⁹⁻²¹
- The combination of calcipotriene and betamethasone was more effective than placebo or monotherapy with either agent alone at treating the signs and symptoms of psoriasis.²³⁻³⁶
 - The efficacy combination calcipotriene and betamethasone was also seen when treating patients who had a diagnosis of scalp psoriasis.³⁸⁻⁴¹
- Calcitriol has been shown to be an effective treatment option for patients with psoriasis.⁴²⁻⁴⁶
- There have been several head-to-head studies evaluating the safety and efficacy of these agents.⁴⁷⁻⁵⁴
 - When calcipotriene was compared to calcitriol as monotherapies or in combination with a corticosteroid, the results of trials regarding “superiority” are conflicting, but suggest that both agents are effective.⁴⁸⁻⁵¹
 - One study found that calcitriol is better tolerated than the calcipotriene, with perilesional erythema ($P < 0.001$), perilesional edema ($P < 0.02$) and stinging/burning ($P < 0.001$) all less severe with calcitriol than with calcipotriol.⁵¹
 - Tazarotene plus mometasone was compared to calcipotriene monotherapy and was shown to be not significantly different in the percentage of patients achieving complete or almost complete clearance at any time during eight weeks of treatment.⁵² Two other studies comparing calcipotriene to tazarotene showed similar results.^{53,54}

Key Points within the Medication Class

- According to Current Clinical Guidelines:
 - Potent corticosteroids are recommended as first-line treatment for mild/moderate plaque psoriasis they have well documented efficacy and well known safety profile.¹⁰⁻¹¹
 - For psoriasis not responsive to a potent steroid and treatment is required longer than four to eight weeks (depending on potency of steroid), topical vitamin D analogs, tazarotene and other agents such as coal tar can be used.
 - Special considerations need to be made depending on the location and severity of the disease. For areas of the face, flexures and genitals, which are highly sensitive to steroid atrophy, a short term of mild or moderate potency corticosteroids are recommended for a short period of time (two weeks maximum).¹⁰
 - For moderate to severe plaque psoriasis requiring systemic therapy, topical agents can be used as an adjunctive therapy to help with the signs and symptoms of the disease.¹²
- Other Key Facts:
 - Generic products are available for calcipotriene (cream, ointment, solution), calcitriol, and calcipotriene/betamethasone (ointment).

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