Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35, Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Month/Year of Review: January 2015
PDL Classes: Topical Psoriasis

Date of Last Review: January 2010
Source Document: Provider Synergies

Current Status of PDL Class:

- Preferred Agents: CALCIPOTRIENE CREAM AND SOLUTION, CALCIPOTRIENE/BETAMETHASONE (TACLONEX) OINTMENT, TAZAROTENE CREAM AND GEL (TAZORAC®)
- Non-preferred Agents: ANTHRALIN CREAM AND SHAMPOO, CALCITRIOL OINTMENT, CALCIPOTRIENE/BETAMETHASONE SUSPENSION (TACLONEX), CALCIPOTRIENE FOAM (SORILUX®)

PA criteria: Topical antipsoriatics are only covered for OHP diagnoses. Moderate and severe psoriasis treatments are covered. Treatments for mild psoriasis, seborrheic dermatitis, keroderma, and other hypertrophic and atrophic conditions of the skin are not covered. PA criteria are included in appendix 1.

Previous Conclusions and Recommendation:

- Evidence does not support a difference in efficacy/effectiveness
- Evidence does not support a difference in harms/adverse events
- Tazarotene carries a pregnancy category X rating. Consider PA for tazarotene in women of childbearing age.
- Consider including a representative of the steroid, retinol and vitamin d analogue classes and anthralin.

Conclusions and Recommendations:

- First line therapy for psoriasis remains traditional topical therapies, including corticosteroids, vitamin D and vitamin D analogues, dithranol (anthralin), and tar preparations.
- There is no evidence of a significant difference in efficacy/effectiveness or harms between the different vitamin D analogues.
- Combination therapy with a vitamin D analogue and corticosteroid has proved to be more effective than either component alone.
- Calcipotriene is recommended first line in childhood psoriasis.
- There is lower strength of evidence for the efficacy of anthralin and it should be used as alternative therapy after vitamin D analogues and/or corticosteroids.
- No further review or research needed. Evaluate comparative costs in executive session.

Methods:

A Medline OVID search was conducted with the following search terms: calcipotriene cream, calcipotriene/betamethasone, tazarotene, tazorac, anthralin, calcitriol ointment and psoriasis. The search was limited to English language articles of controlled trials conducted on humans published from 2010 to December 2014. The Cochrane Collection, Dynamed and Medline OVID were searched for high quality systematic reviews. The FDA website was searched for new drugs, indications, and safety alerts. Finally, a search for new or updated guidelines was conducted at the AHRQ National Guideline Clearinghouse (NGC).

New Systematic Reviews:

1. A 2013 Cochrane Collaboration systematic review evaluated topical treatments for chronic plaque psoriasis[1,2] The review included 177 randomized, controlled trials (RCTs) (n=34,808). Results demonstrated that most treatments were more effective than placebo, including vitamin-D analogues. The average effect was similar for calcipotriene, calcitriol and tacalcitol. Overall, there was no statistically significant difference between vitamin D analogues and

potent corticosteroids. A single trial of tazarotene improved psoriasis by 1 point more than placebo on a 6-point scale, which was a similar effect observed with vitamin-D analogues and potent corticosteroids. Combination therapy with a vitamin D analogue plus corticosteroid was more effective than either individual product used as monotherapy. Overall, vitamin D products generally performed better than coal tar, but studies found conflicting results when comparing vitamin D with dithranol (anthralin). [1,2]

The authors concluded that corticosteroids perform at least as well as vitamin D analogues and they are associated with a lower incidence of local adverse events. Data demonstrated that calcipotriene monotherapy was associated with a significantly higher rate of local adverse events than potent steroids. [1,2]

2. A systematic review by Hendriks, et al. also reviewed the efficacy and safety of first-line topical treatments for chronic plaque psoriasis.[3] A total of 45 studies were included in the analysis. Overall, the combination of steroids and vitamin D analogues is more effective than monotherapies. There was no significant difference between the combination of clobetasol with either calcipotriene ointment or calcitriol. Another systematic review confirmed that the combination of vitamin D analogues plus topical steroids is more effective than vitamin D analogues alone. [4]

3. A systematic review evaluated the effectiveness of the two-compound formulation calcipotriene and betamethasone in the treatment of moderately severe scalp psoriasis.[5] The combination gel was found to be significantly superior in the Investigator Global Assessment (IGA) compared to placebo (RR 2.99; 95% CI 1.25 to 7.16), calcipotriene (RR 1.84; 95%CI 1.84 to 3.27) and betamethasone monotherapy (RR 1.16; 95% CI 1.06 to 1.27). Compared to other topical treatments, the gel was associated with a similar or lower risk of overall adverse events, skin adverse events, and withdrawals due to adverse events.

4. A review on the efficacy and safety of treatment in childhood psoriasis was performed by de Jager, et al.[6] The levels of evidence were determined and an algorithm for the treatment of childhood psoriasis was proposed. The majority of the data in children are for calcipotriene. The authors concluded that calcipotriene is an effective, reasonably well-tolerated treatment option for childhood plaque psoriasis. As calcitriol was only studied in 18 patients, it was concluded that it seems to be an effective treatment of child psoriasis with mild side effects. A lower strength of evidence was given for dithranol (anthralin) and it was concluded to be an effective treatment in childhood psoriasis with a good margin of safety for short-term use. Based on a review of the evidence, the authors recommend that calcipotriene with or without topical corticosteroids is first line therapy, followed by dithranol (anthralin).[6]

Guidelines:

1. German guidelines for the treatment of psoriasis vulgaris were released in 2012.[8] The following recommendations are provided:
   - Dithranol (Anthralin) monotherapy may be recommended for induction therapy in hospitalized patients with mild to moderate plaque psoriasis (Level 2 evidence).
   - Monotherapy with dithranol may be considered for outpatient induction therapy in patients with mild or moderate plaque psoriasis (Level 2 evidence).
   - Topical use of tazarotene may be considered in the treatment of mild to moderate psoriasis (Level 2 evidence).
   - Vitamin D analogues are recommended for use in induction therapy for mild to moderate psoriasis (Level 1 evidence).
   - Combination therapy with vitamin D analogues and steroids is recommended in the first four weeks as induction therapy for mild to moderate psoriasis (Level 1 evidence).

2. Guidelines from the Scottish Intercollegiate Guidelines Network (SIGN) released updated guidelines on the diagnosis and management of psoriasis and psoriatic arthritis in adults in October 2010.[7] The following key recommendations on topical treatments are included:

- A vitamin D analogue is recommended for long term topical treatment of plaque psoriasis (Grade A Recommendation)
- If a vitamin D analogue is ineffective or not tolerated, then short contact dithranol (high-strength dithranol preparation for a shorter amount of time each day), coal tar solution, cream or lotion or tazarotene gel should be considered in appropriate patients (Grade B Recommendation)
- Short term intermittent use of a potent topical corticosteroid or a combined potent corticosteroid plus calcipotriene ointment is recommended to attain rapid improvement in plaque psoriasis (Grade A Recommendation)

Table 1 summarizes the efficacy and tolerability of commonly used topical treatments of psoriasis. [7]

Therapy	Efficacy	Suitability in inducing remission	Suitability as maintenance treatment	Patient acceptability
Coal tar	✓	✓	-	-
Corticosteroids [1]	✓✓✓✓	✓✓✓	✓	✓✓
Dithranol	✓✓	✓✓	-	- [2]
Tazarotene	✓✓	✓✓	✓✓	✓✓
Vitamin D analogues	✓✓✓	✓✓✓	✓✓✓	✓✓

3. The National Institute for Health and Clinical Excellence (NICE) also released clinical guidelines for the assessment and management of psoriasis in October 2012.[9,10] These recommendations are based on a systematic review of the best available evidence and consideration of cost effectiveness. The following recommendations are included:
   - Offer topical therapy as first line treatment to patients with psoriasis.
   - Offer phototherapy or systemic therapy as second-or third-line treatment options at the same time when topical therapy alone is unlikely to adequately control psoriasis.
   - When offering topical agents, take into account patient preference, cosmetic acceptability, and various formulations available.
   - Corticosteroids and/or vitamin D analogues are recommended first line, followed by tar preparations and dithranol.
   - For children or young people, calcipotriene or a corticosteroid is recommended.

New Formulations/Indications:
In October 2010, calcipotriene was approved in a new formulation, a 0.005% topical foam, for the treatment of mild to moderate plaque-type psoriasis. Approval was based on two 8-week, identically designed, randomized, double-blind, and vehicle-controlled phase 3 trials. These studies are summarized in Table 2.

In September 2012, the FDA expanded the indication for calipotriene (Sorilux®) foam to include the topical treatment of plaque psoriasis of the scalp in patients aged 18 years and older. Approval was based on a randomized, double-blind, vehicle controlled phase 3 study of patients with moderate scalp and body psoriasis.[11] A summary of this trial can be found in table 2. [12]

In August 2014, calcipotriene and betamethasone (Taclonex®) received FDA approval for plaque psoriasis of the scalp in patients aged 12 to 17 years.[13] It was previously only approved for adults 18 years of age and older. Approval was based on two unpublished, uncontrolled prospective clinical trials in 109 subjects with plaque psoriasis of the scalp. In one trial, 78 subjects with at least moderate scalp psoriasis were evaluated for safety. At the end of treatment, 66 (85%) had controlled disease according to the IGA disease severity and 6.4 % of patients had an adverse drug reaction. The second study included 31 subjects. Results were not available in clinicaltrials.gov for this clinical trial.

New FDA safety alerts:
None

New Trials:

Table 2: Summary of Relevant Randomized Controlled Trials

Study	Comparison	Population	Primary Outcome	Results	
Feldman, et al.[11] RCT, DB, PG, Phase 3b	Calcipotriene foam vs. vehicle foam (placebo)	12 years and older with plaque-type scalp psoriasis (n=363)	Proportion of subjects with an IGSA score of 0 (Clear) or 1 (almost clear) at week 8	<u>IGSA Score of 0 or 1:</u> Calc: 40.9% Pla: 24.2% P<0.001 NNT 6	
Feldman, et al.[12] 2 RCT, PG, DB	Calcipotriene 0.005% foam vs. vehicle foam (placebo)	12 years and older with plaque-type psoriasis	Treatment success (IGSA score of 0 or 1 and a minimum improvement in ISGA score of at least 2 grades from baseline)	<u>Tx Success (Study 1)</u> Calc: 14% Pla: 7% P=0.058	<u>Tx Success (Study 1)</u> Calc: 27% Pla: 16% P=0.016
Menter, et al.[14] RCT, DB	Calcipotriene/betamethasone vs. individual components vs. vehicle control	18 years and older with mild to moderate psoriasis vulgaris (n=1152)	Achieving controlled disease (clear or almost clear on IGA scale and minimum 2-poing change in scale)	<u>Controlled Disease at week 8:</u> Cal/Bet: 29% Bet: 21.5% Cal: 14.6% Pla: 6.3% P<0.008 for Cal/Bet vs. Pla and individual components	

RCT = randomized controlled trial, DB = double blind, PG = parallel group, IGSA = Investigator's Static Global Assessment , IGA = Investigators' Global Assessment

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Topical Antipsoriasis Drugs

Goal(s):

- Cover topical antipsoriasis drugs only for covered OHP diagnoses. Moderate/Severe psoriasis treatments are covered on the OHP. Treatments for mild psoriasis (696.1-696.2, 696.8), seborrheic dermatitis (690.XX), keroderma (701.1-701.3) and other hypertrophic and atrophic conditions of skin (701.8, 701.9) are not covered.

Length of Authorization:

Up to 12 months

Requires PA:

- Non-preferred drugs
- TC = 92 and HIC = L1A, L5F, L9D, T0A

Covered Alternatives:

Preferred alternatives listed at www.orpdl.org

Approval Criteria		
1. What diagnosis is being treated?	Record ICD9 code.	
2. Is the diagnosis for seborrheic dermatitis (690.XX), keroderma (701.1-701.3) or other hypertrophic and atrophic conditions of skin (701.8, 701.9)?	**Yes:** PASS TO RPH - Deny (not covered by the OHP)	**No:** Go to #3
3. Is the diagnosis Psoriasis? (ICD-9: 696.1-696.2, 696.8)	**Yes:** Go to #4	**No:** Go to #6
4. Is the Psoriasis Moderate/Severe? Defined as: At least 10% body surface area involved or with functional impairment?	**Yes:** Go to #5	**No:** PASS TO RPH; Deny (not covered by the OHP)
5. Is the product requested a non-preferred biologic agent approved for plaque psoriasis?	**Yes:** Go to #6	**No:** Go to #7
6. Has the patient tried and not had an adequate response to standard systemic therapies, including cyclosporine or methotrexate or acitretin, or the person is intolerant of or has a contraindication to these treatments?	**Yes**: Approve for length of treatment; maximum 1 year.	**No:** PASS TO RPH; Deny (medical appropriateness)
7. Is the product requested preferred?	**Yes:** Approve for length of treatment; maximum 1 year.	**No:** Go to #8

Approval Criteria		
8. Will the prescriber consider a change to a preferred product? Message: Preferred products are evidence-based reviewed for comparative effectiveness & safety by the Pharmacy and Therapeutics (P&T) Committee. Reports are available at: http://pharmacy.oregonstate.edu/drug_policy/index.php	**Yes:** Inform provider of covered alternatives in class. http://www.oregon.gov/DHS/healthplan/tools_prov/pdl.shtml . Approve for length of treatment or 1year.	**No:** Approve for length of treatment; maximum 1 year.
9. RPH only: All other indications need to be evaluated as to whether they are above the line or below the line diagnosis.	**If above the line or clinic provides supporting literature:** approve for length of treatment.	**If below the line:** Deny, (not covered by the OHP).

P&T / DUR Action: *1/15 (MH), 09/10, 9/09, 3/09, 2/06, 5/07*
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