

**Month/Year of Review:** March 2013

**PDL Classes:** Topical Steroids

**Date of Last Review:** October 2009

**Source Document:** Provider Synergies

**Current Status of PDL Class:**

- Preferred Agents: ALCLOMETASONE CREAM/OINTMENT, BETAMETHASONE CREAM/LOTION/OINTMENT, CLOBETASOL CREAM/OINTMENT, DESONIDE CREAM/OINTMENT, FLUOCINOLONE CREAM/SOLUTION, FLUOCINOLONE ACETONIDE, HYDROCORTISONE CREAM/OINTMENT/SOLUTION, TRIAMCINOLONE CREAM/OINTMENT
- Non Preferred Agents: MOMETASONE, DESOXIMETASONE, HALOBETASOL, PREDNICARBATE (DERMATOP), FLURANDRENOLIDE (CORDAN), CLOCORTOLONE (CLODERM), AMCINONIDE, HALCINONIDE (HALOG)

**Previous Recommendations:**

- Evidence does not support a difference in efficacy/effectiveness
- Evidence does not support a difference in harm/adverse events
- Consider covering at least one representative from each potency group

**Methods:**

A Medline OVID search was conducted with the following search terms: alclometasone, desonide, fluocinolone, hydrocortisone, hydrocortisone valerate, hydrocortisone butyrate, betamethasone dipropionate, betamethasone valerate, fluticasone, mometasone, prednicarbate, amcinonide, desoximetasone, diflorasone, triamcinolone, halobetasol, clobetasol, skin disorder, atopic dermatitis, hyperkeratotic dermatosis, eczema, pruritus ani, vitiligo, allergic disorder, skin disease, collagen disease, plaque psoriasis, and scalp psoriasis. The search was limited to English language articles of controlled trials conducted on humans published from 2009 to January week 2 2013.

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), the American Academy of Dermatology (AAD), and the UK's National Institute of Clinical Excellence (NICE).

**New Trials:**

A total of 120 citations resulted from the initial MEDLINE search. Articles were excluded due to the wrong study design (observational), comparator (placebo or not a steroid), or outcome (non-clinical). After a review of titles and abstracts for inclusion, three relevant head-to-head clinical trials were identified and are discussed below. Please see Appendix 1 for the full abstracts.

All three trials compared topical corticosteroids for treating psoriasis. All were small or very small trials of low quality without defined methods (allocation, blinding) and poorly described results.

Queille-Roussel<sup>1</sup> et al conducted a small (n=24), within-subject randomized, intraindividual comparison trial. Five topical treatments (calcipotriol ointment, calcipotriol cream, calcipotriol + betamethasone cream, calcipotriol + betamethasone gel, and calcipotriol + hydrocortisone ointment) and an ointment vehicle control were applied simultaneously to a predetermined site on individuals; each individual had six test sites total on their trunk, legs, or arms. Success was measured by response and scaled from 0 to 5 with clearer skin having lower scores. Calcipotriol + betamethasone ointment and gel were more effective at improving plaques (p<0.001) than all other compounds, but were not significantly different from one another (p= 0.23). The calcipotriol ointment and hydrocortisone ointment were more

effective than the calcipotriol cream and placebo ( $p < 0.001$ ) but had no statistical difference between one another ( $p = 0.053$ ).

Lee<sup>2</sup> et al also compared steroids on intraindividual sites. Five psoriasis patients were given fluocinonide, clobetasol, halobetasol cream, and placebo ointment on a site on either the upper or lower extremity for 12 days. All treatments saw improvement, with 80% of treated areas classified as “clear or almost clear” compared with zero for placebo. There was no statistical difference between steroid treatments.

Mentor<sup>3</sup> et al conducted a trial comparing clobetasol spray with betamethasone plus calcipotriene ointment in 93 patients with psoriasis over a four week treatment period. Patients were randomized to either the spray or ointment. Plaque changes were measured by investigators and graded on a scale. After four weeks no statistical difference was seen between the numbers of patients judged to have successful treatment (73% vs. 65%;  $p > 0.05$ ).

**New drugs:**

None

**New Formulations/Indications:**

None

**New FDA safety alerts:**

No new safety alerts were found, but safety labeling changes were added to topical flurandrenolide<sup>4</sup> warning of increased absorption when used in pediatric patients and for adult patients when applied to the groin, hands or face.

**New Systematic Reviews:**

No new or updated, relevant systematic reviews were identified.

**Guidelines:**

The 2009 updated version for psoriasis<sup>5</sup> treatment from the American Academy of Dermatology was reviewed; as was the psoriasis guidance<sup>6</sup> from the UK’s National Institute for Clinical Excellence. No changes regarding the use of steroids were found.

**Recommendations:**

- No further research or review needed at this time.
- Evaluate comparative costs in executive session.

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## References:

1. Queille-Roussel C, Hoffmann V, Ganslandt C, Hansen KK. Comparison of the Antipsoriatic Effect and Tolerability of Calcipotriol-Containing Products in the Treatment of Psoriasis Vulgaris Using a Modified Psoriasis Plaque Test. *Clinical Drug Investigation*. 2012;32(9):613–619.
2. Lee CS, Koo J. The efficacy of three class I topical synthetic corticosteroids, fluocinonide 0.1% cream, clobetasol 0.05% cream and halobetasol 0.05% cream: a Scholtz-Dumas bioassay comparison. *J Drugs Dermatol*. 2009;8(8):751–755.
3. Menter A, Abramovits W, Colón LE, Johnson LA, Gottschalk RW. Comparing clobetasol propionate 0.05% spray to calcipotriene 0.005% betamethasone dipropionate 0.064% ointment for the treatment of moderate to severe plaque psoriasis. *J Drugs Dermatol*. 2009;8(1):52–57.
4. Safety Information > Cordran (flurandrenolide, USP) Lotion. Available at: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm266733.htm>. Accessed January 23, 2013.
5. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. *Journal of the American Academy of Dermatology*. 2009;60(4):643–659.
6. NICE. Psoriasis: The assessment and management of psoriasis CG153. *National Institute for Health and Clinical Excellence*. 2012. Available at: <http://publications.nice.org.uk/psoriasis-cg153>. Accessed January 24, 2013.

## Appendix 1

### Randomized Control Trials

**Queille-Roussel C, Hoffmann V, Ganslandt C, Hansen KK. Comparison of the Antipsoriatic Effect and Tolerability of Calcipotriol-Containing Products in the Treatment of Psoriasis Vulgaris Using a Modified Psoriasis Plaque Test. *Clinical Drug Investigation*. 2012; 32(9):613–619.**

**BACKGROUND AND OBJECTIVE:** In 1972, Dumas and Scholtz developed the psoriasis plaque test to evaluate the potency of local corticosteroids. Through further modification of this method, the efficacy between antipsoriatic products can be differentiated. This method allowed for the simultaneous application of several products to different test sites in the same psoriasis patient. The objective of this current study was to compare the antipsoriatic effect of six topical products using a modified version of the original psoriasis plaque test with emphasis on the predictive capacity of this model. Validation of the use of immunohistochemical and histological scoring of biopsy material, in conjunction with clinical scoring, in the prediction of antipsoriatic effects was an additional objective. **METHODS:** This study was a single-centre, investigator-blinded, within-subject randomized, active- and vehicle-controlled, intraindividual comparison of six topical products in patients with psoriasis vulgaris. The products evaluated were calcipotriol ointment (50 µg/g); calcipotriol cream (50 µg/g); two-compound ointment (calcipotriol 50 µg/g; betamethasone dipropionate 0.5 mg/g); two-compound gel (calcipotriol 50 µg/g; betamethasone dipropionate 0.5 mg/g) [all in their marketed formulations]; an investigational ointment (calcipotriol 25 µg/g; hydrocortisone 10 mg/g); and a vehicle control. Psoriasis patients (≥18 years of age; n = 24) received simultaneous topical application of each of the products 6 days a week for a period of 21 days, at different test sites located on psoriasis plaques. Clinical assessment of the test sites was completed twice a week. Test site biopsies were taken at the final visit for histological analysis. The primary endpoint was the absolute change in total clinical score (TCS; erythema, scaling and infiltration) from baseline. **RESULTS:** For all products, the change in TCS correlated well with changes in histological and immunohistochemical values. The two-compound ointment and the two-compound gel both resulted in a large and significant reduction in TCS. Calcipotriol ointment and the calcipotriol/hydrocortisone ointment were less effective, although they were still more effective than the calcipotriol cream and the ointment vehicle. **CONCLUSION:** This study has demonstrated that the modified psoriasis plaque test can provide a relatively quick and effective method to evaluate the antipsoriatic effect of several topical treatments in small cohorts and that, by combining clinical scoring and histological assessment, a more accurate prediction of the antipsoriatic effect can be made. The two-compound formulations (ointment and gel) had a comparable antipsoriatic effect, which was superior to the other products tested. Furthermore, these data indicate that the gel formulation could provide an alternative effective treatment option to the well-established two-compound ointment for psoriasis patients.

**Lee CS, Koo J. The efficacy of three class I topical synthetic corticosteroids, fluocinonide 0.1% cream, clobetasol 0.05% cream and halobetasol 0.05% cream: a Scholtz-Dumas bioassay comparison. *J Drugs Dermatol*. 2009; 8(8):751–755.**

**BACKGROUND:** This study compared the efficacy of a novel, topical class I synthetic, 0.10% fluocinonide corticosteroid with two other class I corticosteroids and placebo for the treatment of plaque psoriasis. **METHODS:** A 0.5 gram dose of fluocinonide 0.1% cream, clobetasol propionate 0.05% cream, halobetasol propionate 0.05% cream, and placebo ointment were applied to test sites on one psoriatic plaque per patient (n=5). Test sites were outlined according to the Scholtz-Dumas bioassay. Test sites were assessed by a blinded evaluator (1 = psoriasis worsened to 5 = psoriasis clear or almost clear), cleaned and medications were reapplied on days 3, 5, 7, 10 and 12. **RESULTS & CONCLUSION:** The three class I corticosteroid products were comparably effective, numerically and statistically, in clearing the psoriatic plaques. Upon completion of treatment, 60-80% of active-treated sites were clear or almost clear of psoriasis compared to zero with the placebo.

**Menter A, Abramovits W, Colón LE, Johnson LA, Gottschalk RW. Comparing clobetasol propionate 0.05% spray to calcipotriene 0.005% betamethasone dipropionate 0.064% ointment for the treatment of moderate to severe plaque psoriasis. *J Drugs Dermatol*. 2009; 8(1):52–57.**

Topical corticosteroids are widely used in the treatment of psoriasis. This study was conducted to compare the efficacy and safety of clobetasol propionate (CP) 0.005% spray to calcipotriene 0.005%-betamethasone dipropionate 0.064% (C-BD) ointment in patients with moderate to severe plaque psoriasis. Assessments were made at baseline, week 2, week 4 (end of treatment) and week 8 (4 weeks post treatment). An assessment for Overall Disease Severity (ODS) found that 75% of CP spray-treated patients achieved a rating of clear or almost clear after 4 weeks of treatment compared to 45% of C-BD ointment-treated patients (P=.003). Adverse events were reported by less than one-third of patients from each treatment group (31% for CP spray and 33% for C-BD ointment).