Halobetasol Propionate (ULTRAVATE) Lotion 0.05%, and Halobetasol Propionate Cream and Ointment

National Drug Monograph
October 2016
VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The purpose of VA PBM Services drug monographs is to provide a focused drug review for making formulary decisions. Updates will be made when new clinical data warrant additional formulary discussion. Documents will be placed in the Archive section when the information is deemed to be no longer current.

FDA Approval Information

Description/Mechanism of Action	Halobetasol propionate is a corticosteroid that plays a role in cellular signaling, immune function, inflammation, and protein regulation; however, the precise mechanism of action in plaque psoriasis is unknown. Halobetasol propionate has a trihalogenated chemical structure that is similar to that of clobetasol propionate. Halobetasol propionate lotion is a super-high potency corticosteroid product.
Indication(s) Under Review in This Document	Lotion: Topical treatment of plaque psoriasis in patients eighteen (18) years of age and older Cream and Ointment: Relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.
Dosage Form(s) Under Review	• The primary formulation under review is halobetasol propionate lotion 0.05%. Each gram of lotion contains 0.5 mg of halobetasol propionate. • Secondary formulations under review: Cream 0.05% and Ointment 0.05%
REMS	☐ **REMS** ☒ **No REMS** ☐ **Postmarketing Requirements** See Other Considerations for additional REMS information
Pregnancy Rating	Lotion: No data in pregnant women. Cream and Ointment: Category C

Executive Summary

Efficacy	• Halobetasol propionate lotion had a moderate to large effect size in achieving overall treatment success (NNTs of 2.6 and 2.7) in two major efficacy-safety trials. • Halobetasol propionate cream was similar in efficacy, incidence of adverse events and usability in comparison with either **clobetasol propionate cream** or **betamethasone dipropionate cream** in patients with acute atopic dermatitis. • In psoriasis, halobetasol propionate ointment was similar to or better than clobetasol propionate ointment in efficacy depending on the outcome measure, and similar in safety and usability. • Compared with **betamethasone dipropionate ointment** (a corticosteroid formulation of similar potency) halobetasol propionate ointment was numerically but not statistically better in efficacy, similar in adverse events and statistically better in usability.
Safety	• Prescribing information regarding safety of halobetasol lotion, cream and ointment were similar with a few exceptions.
Other Considerations	• Like the cream and ointment formulations, halobetasol propionate lotion is classified as a superpotent corticosteroid based on a vasoconstrictor assay in healthy subjects. • Similar blanching scores do not necessarily imply therapeutic equivalence.
Projected Place in Therapy	• In summary, the results of two unpublished trials of unclear quality showed that **halobetasol propionate lotion** had a moderate to large effect size in achieving overall treatment success relative to vehicle lotion in patients with psoriasis. While there is a lack of active-comparator trials, nonformulary betamethasone dipropionate augmented lotion would be the preferred treatment alternative to halobetasol propionate lotion given its similar potency rating and more favorable

	cost. • **Halobetasol propionate cream** is similar in efficacy and safety to, and less costly than, the two formulary products clobetasol propionate cream and the upper-medium potency betamethasone dipropionate cream, at least for treatment of acute atopic dermatitis. There is no evidence of the relative efficacy among the three cream products in the treatment of psoriasis. Betamethasone dipropionate cream 0.05% (unaugmented) may be used to treat localized psoriasis but may not be an equivalent therapeutic alternative to superpotent corticosteroids creams for this indication. • **Halobetasol propionate ointment** is similar in efficacy and safety to betamethasone dipropionate ointment, consistent with the similar high to super-high potency ratings of these products. Halobetasol propionate ointment is better in efficacy than the less potent betamethasone valerate ointment in localized psoriasis. The generic halobetasol propionate ointment offers potential cost savings over the formulary, superpotent corticosteroid products betamethasone dipropionate ointment and clobetasol dipropionate ointment. • Therapeutic interchanges between different corticosteroid products should require provider authorization and informed discussion with the patient to ensure treatment adherence.

Background

Purpose for Review	Recent FDA approval of the lotion. Review other halobetasol topical formulations for formulary consideration. Halobetasol lotion is a new formulation with randomized clinical trials to support its marketing application. The lotion is available under the trade name ULTRAVATE. Halobetasol cream and ointment are available as generics. The ULTRAVATE brand cream and ointment are still listed as approved by FDA but do not appear to be marketed. Issues to be determined: ✔ Does halobetasol lotion, cream or ointment offer efficacy advantages over available alternatives? ✔ Does halobetasol lotion, cream or ointment offer safety advantages over available alternatives? ✔ Are there subgroup response predictors for halobetasol lotion, cream or ointment?
Other Therapeutic Options	• Noncorticosteroid agents approved for topical treatment of plaque psoriasis include the formulary agents calcipotriene 0.005% cream and calcitriol ointment 3mcg/g and the nonformulary products calcipotriene and betamethasone dipropionate ointment and suspension, calcipotriene foam, ointment and solution (all 0.005%), and tazarotene cream, foam and gel (all 0.05% or 0.1%). • Tacrolimus ointment 0.03% or 0.1% and pimecrolimus cream 1% may be used off-label to treat psoriasis. • Alternative superpotent (Class 1) topical corticosteroids that are indicated **for the treatment of plaque psoriasis** (PPsO) or for the relief of inflammatory and pruritic manifestations of corticosteroid-response dermatoses (CRD) are shown in the table below. Since halobetasol lotion is the new branded product, halobetasol cream and ointment, available as branded and generic products, are also listed as alternatives.

Formulary Topical Corticosteroid Alternatives	Other Considerations
Betamethasone Dipropionate Ointment Eq 0.05% Base (generics)	Ointment: High to super-high potency (Class 1–2). Apply 1–2 times daily for up to 2 consecutive wks. Max. 50 g/wk. Avoid use on face, groin, or axillae.
Clobetasol Cream, Cream emollient, Ointment, Solution (scalp) (CORMAX, EMBELINE, EMBELINE E, generics)	Super high potency (Class 1)
Fluocinonide Cream 0.05%, 0.1%; Cream emulsified base 0.05%; Ointment 0.05%; Solution 0.05% (LIDEX, VANOS, generics)	Super high potency (Class 1)
Flurandrenolide Topical Tape 0.004 mg / cm^2 (CORDRAN)	Super high potency (Class 1). Occlusive dressing. Useful particularly for dry, scaling localized lesions. Not recommended for lesions exuding serum or in intertriginous areas. Dose: Once every 12–24 hours.

Nonformulary Topical Corticosteroid Alternatives	Other Considerations
Betamethasone Dipropionate Augmented Gel, **Augmented Lotion**, Augmented Ointment (DIPROLENE, generics)	Augmented Gel, Augmented Lotion, Augmented Ointment: Super high potency (Class 1) Dose: 1–2 times daily.
Clobetasol Propionate Foam, Gel, **Lotion**, Shampoo, Aerosol Spray (all 0.05%) (CLOBEX, EMBELINE, OLUX (scalp), OLUX E, generics)	Foam, Gel, Lotion: CRD Spray: PPsO up to 20% BSA. All formulations: Super high potency (Class 1)
Halobetasol Propionate Cream, Ointment (ULTRAVATE, generic) (all 0.05%)	Super high potency (Class 1) Dose: 1–2 times daily

Efficacy (FDA Approved Indications)

Literature Search Summary

For the new halobetasol lotion product, a literature search was performed on PubMed/Medline (1966 to May 2016) and the Cochrane Central Register of Controlled Trials (Issue 5 of 12, May 2016) using the search terms *halobetasol* and *lotion*. No relevant publications were found. No manufacturer's AMCP dossier was available. The FDA Medical Review[1] and prescribing information[2] for halobetasol lotion were also reviewed.

For halobetasol cream and ointment, a literature search was performed on PubMed/Medline and the Cochrane Central Register of Controlled Trials using the search terms *halobetasol* and *cream OR ointment.* Since halobetasol cream and ointment are established products, randomized clinical trials (RCTs) that compared active agents were preferred over placebo-only–controlled trials (PCTs). Therefore, one PCT that evaluated the cream formulation[3] and two PCTs, reported in one article that evaluated the ointment[4] are not summarized. One multicenter study (Lebwohl, Siskin [1996]), which compared concomitant therapy with calcipotriene ointment in the morning and halobetasol ointment in the evening with calcipotriene ointment monotherapy and halobetasol ointment monotherapy, was excluded because the paper did not indicate that it was an RCT[5]. A trial comparing calcipotriene ointment with placebo, each given in combination with halobetasol ointment, was also excluded.[6] Trials comparing halobetasol cream or ointment with a non-FDA–approved product were excluded. No FDA Medical Reviews for halobetasol cream and ointment were available. Prescribing information for halobetasol cream[7] and ointment[8] were reviewed.

Review of Efficacy

The clinical trials for the lotion and the active comparator trials for the cream and ointment formulations of halobetasol are summarized in Table 1.

Table 1 Summary of Clinical Trials

Trial	Design / Interventions	Population	Main Efficacy Results
Lotion 0.05%: All Randomized Trials			
1 (Unpublished)	MC DB VC RCT Major efficacy-safety trial HBPL vs. Vehicle Lotion twice daily for up to 14 d	Adults 18 yrs and older with moderate–severe PPsO involving 2%–12% of BSA N = 221	Overall Treatment Success: 49/110 (44.5%) vs. 7/111 (6.3%), calc. $p < 0.01$; NNT = 2.6
2 (Unpublished)	Same as study 1	Same as study 1 N = 222	Overall Treatment Success: 49/110 (44.5%) vs. 8/112 (7.1%), calc. $p < 0.01$; NNT = 2.7
Cream 0.05%: Active Comparator Studies			
Yawalkar and Schwerzmann (1991)[9]	Two MC DB RCTs PP HBPC 0.05% 2 x/d CBPC 0.05% 2 x/d and HBPC 0.05% 2 x/d BMDC 0.05% 2 x/d Without occlusion 14 d (max 4 x 30-g tubes)	Noninfected, acute, severe exacerbation of atopic dermatitis N = 63 / 68 and N = 58 / 59	Had onset of improvement w/in 3 d: 41% vs. 38% and 40% vs. 39% Success (healed / marked improvement): 89% vs. 93% and 88% vs. 90% Healing w/in 11 d: 19% vs. 21% and 16% vs. 22% AEs: 6% vs. 4% and 9% vs. 3% Cosmetic acceptability and ease of application "good" or "very good": 95.2% vs. 95.6% and 89.6% vs. 94.9%
Ointment 0.05%: Active Comparator Studies			
Goldberg (1991)[10]	MC DB RCT PP HBPO 0.05% 2x/d CBPO 0.05% 2x/d Without occlusion 28 d (max 7 x 30-g tubes) Pretreatment with 10% salicylic acid ointment 2x/d for 2–3 d to remove scales.	Severe, chronic localized PPsO up to 10% of BSA N = 134 S. Africa 47.8% male, aged 18–76 y	Had onset of improvement w/in 5 d: 72.1% vs. 72.8% Success (healed / marked improvement): 96% vs. 91% **No Disease / Mild Disease after 14 d: 86% vs. 70% (p = 0.023)** Early Healing (within 24 d): 69% vs. 56% Cosmetic acceptability and ease of application recorded as "very good": 90% vs. 80% AEs: 7% vs. 12%
Dhurat (2016)[11]	MC DB RCT Aim: To compare efficacy and tolerability of HBPO and CBPO in Indian patients. HBPO 0.05% 2 x/d CBPO 0.05% 2 x/d One-half FTU per dose Without occlusion 14 d	Chronic localized PPsO, or palmoplantar psoriasis, up to 10%–20% of BSA (size of selected lesion about 4–10 cm^2). N = 202 (103 HBPO, 99 CBPO) India BL patient characteristics NR	Mean reduction in local plaque severity index scores, BL to EOT: -4.2 ± 2.0 vs. -4.1 ± 2.3. **PGA at 14 d** **Almost total clearing: 32.0% vs. 19.2%** **Marked improvement: 50.5% vs. 47.5%** **P = 0.019 for tx diffs in PGA** **Cosmetic acceptability of Good to Very Good: 98% vs. 97% (p = 0.042)** **Ease of application:** **Good: 66% vs. 46.5%** **Very Good: 33% vs. 52.5%** **P = 0.019** Serum Cortisol (in 40% of patients), Δ from BL: NSD AEs: None occurred

Trial	Design / Interventions	Population	Main Efficacy Results
Datz and Yawalkar (1991)[12]	MC DB RCT PP Germany HBPO 0.05% 2 x/d CBPO 0.05% 2 x/d Without occlusion 21 d (max 5 x 30-g tubes)	Chronic localized atopic dermatitis or lichen simplex chronicus up to 20% of BSA N = 127 50% male, age (range, 18–79),	Had onset of improvement w/in 3 d: 24% vs. 28% Success (healed and marked improvement): 93.7% vs. 92.2% Healing: 65.1% vs. 54.7% (NSD) Healing w/in 17 d: 35% vs. 38% AEs: 5% vs. 2% Cosmetic acceptability and ease of application "very good" or "good": 94% vs. 97%
Blum and Yawalkar (1991)[13]	MC DB RCT HBPO 0.05% 2 x/d BMVO 0.1% 2 x/d Without occlusion 28 d (max 8 x 30-g tubes) Pretreatment with 10% salicylic acid ointment	Severe localized PPsO up to 20% of BSA N = 84 65% male, median age 42 y (range, 18–79 y)	Had onset of improvement within 5 d: 76% vs. 67% **Success (healed / marked improvement): 88.1% vs. 64.3% (p = 0.02)** AEs: 2% vs. 2% Cosmetic acceptability and ease of application "good" to "very good": 81% vs. 55%
Mensing (1991)[14]	MC DB RCT PP Low quality HBPO 0.05% 2 x/d BMDO 0.05% 2 x/d Without occlusion 28 d Average of 3 tubes per pt (allowed max of 8 x 30-g tubes) Pretreatment with 10% salicylic acid ointment	Severe, chronic localized PPsO up to 20% of BSA N = 104 51% male, median age 42 y (range, 18–76 y)	Had onset of improvement w/in 5 d: 71.7% vs. 72.6% Success (healed / marked improvement): 88.7% vs. 78.5% (NSD) Healing within 24 d: 40% vs. 25% (NSD) AEs: 8% vs. 4% **Cosmetic acceptability and ease of application "good" to "very good": 98.1% vs. 84.3% (p = 0.02)**
Gupta (2011)[15]	Cases were divided into 8 groups "randomly." Atypical outcome measure was used. Low-quality study. Compare topical therapies and NB-UVB in combination with methotrexate 7.5 mg p.o. weekly (x 8 wks) I: Salicylic acid oint 6% daily + MTX II: Tacrolimus oint 0.1% + MTX III: Crude coal tar oint + MTX IV: Tazarotene gel 0.1% + MTX V: HBPO + MTX VI: NB-UVB VII: NB-UVB + MTX VIII: Bland emollient + MTX	Outpatients with palmoplantar psoriasis N = 98	Good improvement (Erythema, scaling, induration and fissuring (ESIF) score > 50% improvement, palmar / plantar, and recurrence rates, % (N): I: 61.2 / 58.6 and 63.6% (11) II: 61.6 / 60.4 and 50.0% (4) III: 63.6 / 61.4 and 47.1% (17) IV: 64.4 / 62.2 and 33.3% (9) V: 66.9 / 64.8 and 70.0% (20) VI: 61.5 / 60.5 and 33.3% (12) VII: 68.1 / 64.8 and 17.6% (17) VIII: 60.6 / — and 37.5% (8) HBPO had highest rate of recurrence (70%) upon stopping tx. Adverse Events, %: I: 27.3% (irritation, burning) II: 25.0% (irritation, burning) III: 41.2% (irritation, burning, staining, contact dermatitis) IV: 66.7% (irritation, burning, erythema, exfoliation) V: 45.0% (atrophy, pustular psoriasis, acneiform eruption, Cushingoid faces) VI: 16.7% (erythema, stinging)

Trial	Design / Interventions	Population	Main Efficacy Results
			VII: 17.6% (erythema, irritation)

Bolded text = Statistically significant treatment difference ($p < 0.05$)
AE, Adverse event; BL, Baseline; BMDO, Betamethasone dipropionate ointment; BMVO, Betamethasone valerate ointment; CPTO, Calcipotriene ointment; CBPO, Clobetasol propionate ointment; DB, Double-blind; EOT, End of treatment; HBPL, Halobetasol propionate lotion; HBPO, Halobetasol propionate ointment; MC, Multicenter; PP, Per protocol analysis; RCT, Randomized clinical trial; VO, Vehicle ointment; VC, Vehicle-controlled

Halobetasol Lotion

- The FDA approval of halobetasol propionate lotion was based mainly on two major efficacy-safety trials (Table 1).[16]
- The primary efficacy measure (PEM) was *overall treatment success*, defined as cleared or almost cleared of all signs of psoriasis with at least a two-grade improvement from baseline.
- The efficacy results showed that halobetasol propionate lotion had a moderate to large effect size in achieving overall treatment success (NNTs of 2.6 and 2.7 in study 1 and study 2, respectively.)
- Secondary efficacy measures also showed that halobetasol lotion was significantly superior to vehicle control. NNTs for halobetasol lotion versus vehicle control for treatment success rate for each of the following symptoms are shown in Table 2.

Table 2 Numbers Needed to Treat for Secondary Efficacy Measures

Symptom	Trial 1	Trial 2
Scaling	2.2	2.0
Erythema	3.4	3.0
Plaque elevation	2.7	2.8

Halobetasol Cream: Active Comparator Trials

- Two small RCTs reported in one publication showed that halobetasol propionate cream was similar in efficacy, incidence of adverse events and usability in comparison with either **clobetasol propionate cream** or **betamethasone dipropionate cream** in patients with acute atopic dermatitis.[9]

Halobetasol Ointment: Active Comparator Trials

- Three trials compared halobetasol propionate ointment 0.05% with **clobetasol propionate ointment 0.05%:** one in patients with localized plaque psoriasis,[10] one in patients with localized plaque psoriasis or palmoplantar psoriasis[11] and one in patients with atopic dermatitis or lichen simplex chronicus.[12] In psoriasis, halobetasol propionate ointment was similar to or better than clobetasol propionate ointment in efficacy depending on the outcome measure, and similar in safety and usability (see Table 1). For atopic dermatitis or lichen simplex chronicus, the two corticosteroid products were similar in efficacy, safety and usability.
- Two trials compared halobetasol propionate ointment with either betamethasone valerate ointment 0.1%[13] or betamethasone dipropionate ointment 0.05%[14] in patients with localized plaque psoriasis. Compared with **betamethasone valerate ointment** (a less potent corticosteroid formulation), halobetasol propionate ointment was better in achieving treatment success, similar in the incidence of adverse events, and numerically better in usability. Compared with **betamethasone dipropionate ointment** (a corticosteroid formulation of similar potency) halobetasol propionate ointment was numerically but not statistically better in efficacy, similar in adverse events and statistically better in usability.
- In another study, the investigators divided 98 cases into eight groups "randomly" to assess various **topical therapies, including halobetasol propionate ointment, and narrowband ultraviolet B (NB-UVB) therapy with or without methotrexate** in patients with palmoplantar psoriasis.[15] Treatments were evaluated in terms of the percentage of patients with a "good" response, defined as > 50% improvement from baseline, and in recurrence rates. In the halobetasol propionate ointment plus oral methotrexate group, marked improvement was seen in 18 (90.0%) of 20 patients, with average response rates that were similar to those seen with the other therapies (66.9% for palms and 64.8% for soles). However, patients treated with halobetasol propionate ointment plus methotrexate experienced the highest rate of recurrence (70.0%) after stopping therapy. Local and systemic adverse effects were common (45%) given the relatively long duration (8 weeks) of potent corticosteroid therapy. No between-treatment statistical results were reported.

- The overall quality of evidence was low, primarily because almost all of the papers did not report withdrawal rates by treatment group and almost all studies performed efficacy and safety analyses on the per-protocol rather than the intent-to-treat population, which may have overestimated treatment effects.

Potential Off-Label Use

No published reports were found. The following potential off-label uses are based on indications for similar products and clinical judgment:

- PPsO of the scalp (lotion).
- Corticosteroid-responsive dermatoses other than PPsO.
- Subtypes of psoriasis other than PPsO.

Safety

Prescribing information regarding safety of halobetasol lotion, cream and ointment were similar with a few exceptions. For more detailed information, refer to the respective drug prescribing information.

Boxed Warning	• None
Contraindications	• Lotion: None • Cream, Ointment: Hypersensitivity to any components:
Warnings / Precautions	• Reversible hypothalamic-pituitary-adrenal (HPA) axis suppression • Systemic effects of topical corticosteroids may also include Cushing's syndrome, hyperglycemia and glucosuria • Systemic absorption may require evaluation for HPA axis suppression • Use of potent corticosteroids on large areas, for prolonged durations, under occlusive dressings, or on an altered skin barrier may increase systemic exposure. • Children may be more susceptible to systemic toxicity • Local adverse reactions with topical steroids may include atrophy, striae, irritation, acneiform eruptions, hypopigmentation, and allergic contact dermatitis. Adverse reactions may be more likely to occur with occlusive use or more potent corticosteroids. • Initiate appropriate therapy if concomitant skin infections develop. • Allergic contact dermatitis with corticosteroids is usually diagnosed by observing failure to heal rather than noting a clinical exacerbation. Consider appropriate patch testing. Discontinue therapy if allergic contact dermatitis is established. • Should not be used on the face, groin or in the axillae. • Cream, Ointment: Should not be used in the treatment of rosacea or perioral dermatitis.

Adverse Reactions

Common Adverse Reactions (≥ 1%)	Lotion: Telangiectasia, application site atrophy, and headache Cream: Stinging, burning or itching (4.4%); dry skin, erythema, skin atrophy, leukoderma, vesicle, rash. Ointment: Stinging or burning (1.6%); postulation, erythema, skin atrophy, leukoderma, acne, itching, secondary infection, telangiectasia, urticarial, dry skin, miliaria, paresthesia, rash.
Deaths / Serious Adverse Reactions	No data available.
Discontinuations Due to Adverse Reactions	No data available.

Drug Interactions

Drug-Drug Interactions	• None

Risk Evaluation

As of 6 June 2016

Sentinel Event Advisories	• None • Sources: ISMP, FDA, TJC
Look-alike / Sound-alike Error Potential	

NME Drug Name	Lexi-Comp	First DataBank	ISMP	Clinical Judgment
Halobetasol	None	None	None	Haloperidol Clobetasol
ULTRAVATE	CUTIVATE	None	None	ULTRACET ULTRAVIST UPTRAVI

Sources: Based on clinical judgment and an evaluation of LASA information from three data sources (Lexi-Comp, First Databank, and ISMP Confused Drug Name List)

Other Considerations

Therapeutic Equivalence with Other Superpotent Corticosteroids	• Like the cream and ointment formulations, halobetasol propionate lotion is classified as a superpotent corticosteroid based on a vasoconstrictor assay in healthy subjects. • Similar blanching scores do not necessarily imply therapeutic equivalence.

Dosing and Administration

- Apply a thin layer of halobetasol propionate lotion, cream or ointment to the affected skin twice daily for up to 2 weeks. Rub in gently.
- Discontinue therapy when control is achieved. If no improvement is seen within 2 weeks, reassessment of diagnosis may be necessary.
- Treatment beyond 2 weeks is not recommended and the total dosage should not exceed 50 grams (50 mL) per week because of the potential for the drug to suppress the HPA axis.
- Lotion: Do not use with occlusive dressings unless directed by a physician.
  Cream, Ointment: Should not be used with occlusive dressings. :
- For external use only.
- Avoid use on the face, scalp, groin, or axillae.
- Halobetasol propionate lotion is not for ophthalmic, oral, or intravaginal use.

Special Populations (Adults)

Elderly	• Lotion: Insufficient numbers of study patients to determine whether older subjects (≥ 65 years) respond differently from younger patients. • Cream, Ointment: No overall differences in safety or effectiveness were seen between older patients (≥ 61 years and ≥ 71 years) and younger patients.
Pregnancy	• No data in pregnant women. Teratogenic and embryotoxic in animals. (Cream, Ointment: Category C.)
Lactation	• No data on effects on breastfed infant or breastfeeding women. • It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable

	quantities in human milk. • Weigh risks versus benefits.
Renal Impairment	• No guidance in prescribing information.
Hepatic Impairment	• No guidance in prescribing information.
Pharmacogenetics/genomics	• No data.

Projected Place in Therapy

- The place in therapy of halobetasol lotion, cream or ointment is not specifically addressed in clinical practice guidelines.
  - The 2012 NICE treatment guideline recommends offering topical agents as first-line therapies to patients with plaque psoriasis, and offering second- or third-line therapies (phototherapy or systemic therapy) to use concomitantly with topical therapies when topical monotherapy is unlikely to adequately control psoriasis, such as for extensive disease (e.g., ≥10% BSA), moderate disease, or nail psoriasis.[17]
  - The 2012 S-3 German treatment guideline for plaque psoriasis recommends the use of class III corticosteroids and vitamin D_3 derivatives for induction therapy for patients with mild to moderate plaque psoriasis (Evidence Level 1).[18] The guideline also recommends combination therapy with vitamin D_3 derivatives and corticosteroids in the first 4 weeks as induction therapy for patients with mild to moderate plaque psoriasis (Evidence Level 1).
  - The 2015 best practice recommendations on the treatment of nail psoriasis by the Medical Board of the National Psoriasis Foundation indicate that high-potency topical corticosteroids with or without calcipotriene are initial treatment options.[19]
  - UpToDate states that corticosteroids are the mainstay of topical treatment for psoriasis and may be used as the sole initial therapy.[20] Keeping the treatment regimen simple (e.g., a single topical formulation, less frequent dosing) and tailoring the choice of vehicle to patient preferences may be beneficial in promoting treatment adherence, probably the key factor in determining treatment effectiveness. Calcipotriene in combination with class 1 topical corticosteroids can be used for short-term control then reduced to intermittent (weekend) use, with calcipotriene monotherapy given daily. Thick plaques on extensor surfaces are indications for potent corticosteroids (e.g., betamethasone 0.05% or clobetasol propionate 0.05%). The combination of a vitamin D analog plus corticosteroid seems to be slightly more effective than monotherapy with a potent corticosteroid for scalp psoriasis. Many patients prefer lotion, solution, gel, foam or spray formulations over thicker creams and ointments for psoriasis on the scalp.
  - The corticosteroid potency and vehicle should be selected according to lesion severity, location and characteristics, patient preference, and likelihood of patient adherence with therapy.[21]
- In summary, the results of two unpublished trials of unclear quality showed that **halobetasol propionate lotion** had a moderate to large effect size in achieving overall treatment success relative to vehicle lotion in patients with psoriasis. There are no superpotent corticosteroid lotions on VA National Formulary, and utilization of the nonformulary betamethasone dipropionate augmented lotion has been low. While there is a lack of active-comparator trials, nonformulary betamethasone dipropionate augmented lotion would be the preferred treatment alternative to halobetasol propionate lotion given its similar potency rating and more favorable cost.
- **Halobetasol propionate cream** is similar in efficacy and safety to, and less costly than, the two formulary products clobetasol propionate cream and the upper-medium potency betamethasone dipropionate cream, at least for treatment of acute atopic dermatitis. There is no evidence of the relative efficacy among the three cream products in the treatment of psoriasis. Halobetasol propionate cream, clobetasol propionate cream, fluocinonide cream 0.1% and fluocinonide emollient cream 0.05% may be therapeutically interchanged (with provider authorization) on the basis of their similar potencies and vehicles. Betamethasone dipropionate cream 0.05% (unaugmented) may be used to treat localized psoriasis but may not be an equivalent therapeutic alternative to superpotent corticosteroid creams for this indication.
- **Halobetasol propionate ointment** is similar in efficacy and safety to betamethasone dipropionate ointment, consistent with the similar high to super-high potency ratings of these products. Halobetasol propionate ointment is better in efficacy than the less potent betamethasone valerate ointment in localized psoriasis. The generic halobetasol propionate ointment formulation offers potential cost savings over the formulary, superpotent corticosteroid products betamethasone dipropionate ointment and clobetasol dipropionate ointment.

- Therapeutic interchanges between different corticosteroid products should require provider authorization and informed discussion with the patient to ensure treatment adherence.

References

[1] Center for Drug Evaluation and Research. Medical Review(s) of Halobetasol Propionate (ULTRAVATE) Lotion 0.05%. Food and Drug Administration. 22 October 2015. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/208183Orig1s000MedR.pdf .

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[3] Kantor I, Cook PR, Cullen SI, Willis I, Gibson JR, Stanfield JW. Double-blind bilateral paired comparison of 0.05% halobetasol propionate cream and its vehicle in patients with chronic atopic dermatitis and other eczematous dermatoses. J Am Acad Dermatol 1991;25 (6, Pt 2):1184–6.

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Appendix A: GRADEing the Evidence

Quality of Evidence	Description
High	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (2 consistent, higher-quality randomized controlled trials or multiple, consistent observational studies with no significant methodological flaws showing large effects).
Moderate	Evidence is sufficient to determine effects on health outcomes, but the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (1 higher-quality trial with > 100participants; 2 higher-quality trials with some inconsistency; 2 consistent, lower-quality trials; or multiple, consistent observational studies with no significant methodological flaws showing at least moderate effects) limits the strength of theevidence.
Low	Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality studies, important flaws in study design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

Please refer to Qaseem A, et al. The development of clinical practice guidelines and guidance statements of the American College of Physicians: Summary of Methods. Ann Intern Med 2010;153:194-199.