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Drug Class Literature Scan: Topical Steroids

Date of Review: September 2017

Date of Last Review: March 2015
Literature Search: 3/1/2015– 6/9/2017

Current Status of PDL Class:
See **Appendix 1**.

Conclusions:
- Since the last review additional evidence has become available with the publication of 2 systematic reviews and 1 CADTH Rapid Response Report. There are also 2 new topical steroid formulations.
- There is no new comparative evidence since the last review to support a difference in safety or efficacy among equipotent topical corticosteroids.
- There is insufficient evidence that the betamethasone valerate foam formulation provides any clinical benefit over other formulations currently available.

Recommendations:
- No further review or research needed.
- After evaluation of comparative costs in executive session, no PDL changes were recommended.

Previous Conclusions:
- Evidence does not support a difference in efficacy/effectiveness.
- Evidence does not support a difference in harms/adverse events.
- At least one agent in each of the potency categories should be preferred.

Previous Recommendations:
- No further review or research needed. Evaluate comparative costs in executive session.

Methods:
A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. A summary of the clinical trials is available in **Appendix 2** with abstracts presented in **Appendix 3**. The Medline search strategy used for this literature scan is available in **Appendix 4**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), the Cochrane Collaboration, National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, BMJ Clinical Evidence, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high

quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts. Finally, the AHRQ National Guideline Clearinghouse (NGC) was searched for updated and recent evidence-based guidelines.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials (RCTs) will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:

A 2016 Cochrane Collaboration systematic review evaluated topical treatments for scalp psoriasis.[1] Comparisons in safety and efficacy were made between very high, high, and medium-potency topical steroids, vitamin D3 analogues, corticosteroid plus vitamin D combination products, corticosteroid plus salicylic acid combination products, tar-based preparations, anthralin, salicylic acid monotherapy, and ciclopirox olamine, and calcineurin inhibitors. Fifty-nine randomized controlled trials in 11,561 participants were included. Data on age of participants were available in 38 of the studies (n=9051) with a mean age of 45.2 years. Follow-up lasted for a median duration of 2.4 weeks (range: 1-8 weeks). Primary outcomes included either lesion clearance or clinical response as measured by the 5-point Investigator's Global Assessment (IGA) scale, quality of life improvements, and adverse events leading to treatment withdrawal. The IGA scale ranges from 0 or 1 (clear) to 5 (severe disease). Investigators used the proportion of patients with at least a 2 point IGA point reduction from baseline to define clearance or clinical response to therapy in clinical trials.

Between topical steroid preparations, there was no difference found in lesion clearance or clinical response between the very high potency steroid clobetasol propionate and high potency steroid comparator betamethasone dipropionate.[1] Likewise, high potency steroids betamethasone and fluocinolone acetonide 0.025% were unable to demonstrate a significant difference in lesion clearance or response when compared to treatment with medium potency hydrocortisone 17-butyrate 0.1%.[1] Among high potency steroids, one study (n=203) of moderate quality demonstrated a higher proportion of participants achieved scalp lesion clearance with mometasone furoate than betamethasone valerate 0.1% (RR 1.84; 95% Confidence Interval (CI) 1.09 to 3.11; ARR = 14%; Number Needed to Treat (NNT) = 8), as measured by a 2-point IGA reduction. However, there was insufficient information on allocation concealment, participant and personnel blinding, and outcome assessment blinding which resulted in a unclear to high risk of bias.[1] Data from 4 studies (n=2180) demonstrated that topical steroids improved psoriatic lesion clearance in 29% of patients compared to 16% of patients on calcitriol (Relative Risk (RR) 1.82; 95% CI 1.52 to 2.18; Absolute Risk Reduction (ARR) = 13%; NNT = 8).[1] Three of the 4 studies had unclear blinding of the outcome assessment and all four studies had unclear allocation concealment which resulted in the quality of evidence downgraded to moderate risk of bias by the authors.[1] Combinations of topical steroids plus vitamin D was more effective than vitamin D alone (RR 2.28; 95% CI 1.87 to 2.78; ARR = 19%, NNT = 6; high quality evidence).[1] In three studies (n=1827), overall treatment response favored corticosteroids over vitamin D (RR 2.09; 95% CI 1.80 to 2.41; ARR = 28%, NNT=4; high quality evidence).[1] Treatment of scalp psoriasis with vitamin D appeared to increase study withdrawals due to adverse events when compared with corticosteroids (5% vs. 1%, respectively; four studies, n=2291; ARI = 4%, NNH = 25) although no study reported the nature of the adverse event requiring withdrawal.[1] There was insufficient evidence to assess efficacy and safety of additional topical agents such as salicylic acid, tar, or anthralin-based treatments.

A 2015 Cochrane Collaboration systematic review update compared the effects of topical corticosteroids on pregnancy outcomes in pregnant women.[2] Fourteen observational studies (n=1,601,515) were included in the review of multiple steroid agents with variable potency.[1] Primary outcomes assessed included congenital abnormalities, orofacial clefts, preterm delivery, or low birth weight. The majority of studies failed to find topical steroid use associated with significant increased risk of adverse pregnancy outcomes regardless of potency. Although 3 cohort studies showed an increased risk of low birth weight in

women exposed to potent or very potent topical steroids, pooled data from 47,651 patients found no associated risk [RR 1.58, 95% CI 0.96 to 2.58].[2] Based on variations within the 4 cohort studies and due to 1 study without reports of potent or very potent steroid use, the overall quality of evidence was graded by the authors as low to very low.[2]

A 2015 CADTH Rapid Response Report reviewed the clinical effectiveness of betamethasone valerate (BMV) 0.12% foam compared to BMV topical 0.1% lotion and calcipotriol for scalp psoriasis treatment.[3] The reviewers identified two studies which met inclusion criteria. The clinical measures used to assess primary outcomes were the psoriasis physical signs Sum score and the Investigator's/Physician's Global Assessment (PGA) score. The Sum score assigns a numeric value for physical characteristics of psoriasis as measured by erythema (0-4), scaling (0-4), and induration (0-4) and the total value correlates moderately well with disease severity.[4] The Investigator's/Physician's Global Assessment (IGA/PGA) Score is a reliable assessment tool which commonly exists as a 5, 6, or 7-point ordinal scale which ranges from a lower score of "clear" to a higher score indicative of "very severe psoriasis." In one study (n=241), the Sum score at 28 days was significantly lower for BMV 0.12% foam than of standard treatment, which included BMV 0.1% lotion and calcipotriol (Mean Sum Score BMV foam: 1.5 [95% CI: 1.3 – 1.7] vs. Standard treatment: 3.1 [95% CI: 2.8 – 3.4]) from a baseline value of 7.6 (95% CI: 7.3 – 7.9).[3] The same study demonstrated that BMV foam treatment resulted in a greater proportion of participants with cleared or almost cleared scalp psoriasis compared to standard treatment of corticosteroids plus calcipotriol (88% vs. 66%, p<0.001) as measured by IGA score reductions.[3] A different study demonstrated that a greater proportion of patients were completely or almost completely cleared of disease at 28 days with BMV 0.12% foam compared to BMV lotion or placebo lotion (72 % vs. 47% vs. 21% respectively, p<0.05) as measured by reductions in a 7-point IGA score[3,4] No significant differences were observed in pruritus scores between BMV foam and BMV lotion.

Guidelines:
No new guidelines identified.

New Formulations:
Ultravate® (halobetasol propionate lotion 0.05%) was FDA approved in November 2015 for the topical treatment of moderate plaque psoriasis in patients 18 years of age and older.[5] Approval was based on two identical unpublished, randomized, double-blind, vehicle-controlled studies (n=443) with moderate to severe plaque psoriasis involving 2-12% of body surface area (BSA).[6] Treatment success was defined by the proportion of patients cleared or almost cleared of scaling, erythema and plaque elevation at 2 weeks as determined by a 2-point reduction from baseline in the 5-point Investigator Global Assessment (IGA) score.[6] Overall treatment success for the first trial was 49/110 (44.5%) versus 7/111 (6.3%) (p<0.001, NNT=3) with the second trial showing similar success (49/110 [44.5%] vs. 8/112 [7.1%], p<0.001, NNT=3).[6] The most common adverse reactions were telangiectasia (1.1%) and skin atrophy (1.5%).[6]

In January, 2016 the FDA approved a 0.05% topical spray formulation of betamethasone dipropionate (Sernivo®) for the treatment of adults 18 years or older with mild to moderate plaque psoriasis.[7] Approval for the spray was based on two unpublished, multi-center, double-blind trials in subjects randomized to either Sernivo® Spray (n=352) or placebo vehicle spray (n=180) applied twice daily for 4 weeks.[7] Treatment success was defined by a two-point reduction in IGA score from a baseline of 3 (moderate) to 0 or 1 (clear or almost clear).[7] In both studies at 29 days, treatment success was achieved by a higher proportion of betamethasone diopropionate spray subjects than those on placebo (42.7% vs 11.7% and 34.5% vs 13.6%, P < .001, NNT=4 and 5, respectively).[7] Adverse reactions included pruritus (6%), burning and/or stinging (4.5%), and pain (2.3%).[7]

FDA Safety Alerts:
None identified.

References:

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2. Chi C-C, Wang S-H, Wojnarowska F, Kirtschig G, Davies E, Bennett C. Safety of topical corticosteroids in pregnancy. In: Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd; 2015. http://onlinelibrary.wiley.com.liboff.ohsu.edu/doi/10.1002/14651858.CD007346.pub3/abstract. Accessed April 7, 2017.
3. Betamethasone for Adults with Scalp Psoriasis: A Review of the Clinical and Cost-Effectiveness | CADTH.ca. https://www.cadth.ca/betamethasone-adults-scalp-psoriasis-review-clinical-and-cost-effectiveness-0. Accessed May 30, 2017.
4. Spuls PI, Lecluse LLA, Poulsen M-LNF, Bos JD, Stern RS, Nijsten T. How Good Are Clinical Severity and Outcome Measures for Psoriasis?: Quantitative Evaluation in a Systematic Review. Journal of Investigative Dermatology. 2010;130(4):933-943. doi:10.1038/jid.2009.391. Accessed June 9, 2017.
5. Ultravate® (halobetasol propionate lotion 0.05%) Prescribing Information. Ranbaxy Laboratories, Inc., Jacksonville, FL 32257. Nov 2015 http://www.ultravatelotion.com/pdf/ultravatelotionpi.pdf. Accessed May 4, 2017.
6. CDER Evaluation of Ultravate® https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/208183Orig1s000MedR.pdf Accessed May 4, 2017.
7. Sernivo® (betamethasone dipropionate) Prescribing Information. DPT Laboratories, Ltd., San Antonio, TX 78215. Feb 2016 http://sernivo.com/documents/sernivo-pi.pdf. Accessed April 27, 2017.

Appendix 1: Current Preferred Drug List

Generic Name	Brand Name	Form	PDL Status
ALCLOMETASONE DIPROPIONATE	ALCLOMETASONE DIPROPIONATE	CREAM (G)	Y
ALCLOMETASONE DIPROPIONATE	ALCLOMETASONE DIPROPIONATE	OINT. (G)	Y
BETAMETHASONE DIPROPIONATE	BETAMETHASONE DIPROPIONATE	CREAM (G)	Y
BETAMETHASONE DIPROPIONATE	BETAMETHASONE DIPROPIONATE	LOTION	Y
BETAMETHASONE DIPROPIONATE	BETAMETHASONE DIPROPIONATE	OINT. (G)	Y
BETAMETHASONE VALERATE	BETAMETHASONE VALERATE	CREAM (G)	Y
BETAMETHASONE VALERATE	BETAMETHASONE VALERATE	OINT. (G)	Y
CLOBETASOL PROPIONATE	CLOBETASOL PROPIONATE	CREAM (G)	Y
CLOBETASOL PROPIONATE	TEMOVATE	CREAM (G)	Y
CLOBETASOL PROPIONATE	CLOBETASOL PROPIONATE	OINT. (G)	Y
CLOBETASOL PROPIONATE	TEMOVATE	OINT. (G)	Y
DESONIDE	DESONIDE	CREAM (G)	Y
DESONIDE	DESONIDE	OINT. (G)	Y
FLUOCINOLONE ACETONIDE	SYNALAR	CREAM (G)	Y
FLUOCINOLONE ACETONIDE	FLUOCINOLONE ACETONIDE	CREAM (G)	Y
FLUOCINOLONE ACETONIDE	FLUOCINOLONE ACETONIDE	SOLUTION	Y
FLUOCINOLONE ACETONIDE	SYNALAR	SOLUTION	Y
FLUOCINONIDE	FLUOCINONIDE	CREAM (G)	Y
FLUOCINONIDE	VANOS	CREAM (G)	Y
FLUOCINONIDE	FLUOCINONIDE	SOLUTION	Y
FLUOCINONIDE/EMOLLIENT BASE	FLUOCINONIDE-E	CREAM (G)	Y
HYDROCORTISONE	ANTI-ITCH	CREAM (G)	Y
HYDROCORTISONE	PROCTOCORT	CREAM (G)	Y
HYDROCORTISONE	CORTIZONE-5	CREAM (G)	Y
HYDROCORTISONE	PREPARATION H	CREAM (G)	Y
HYDROCORTISONE	NOBLE FORMULA HC	CREAM (G)	Y
HYDROCORTISONE	NEOSPORIN	CREAM (G)	Y
HYDROCORTISONE	HYDROCREAM	CREAM (G)	Y
HYDROCORTISONE	ECZEMA ANTI-ITCH	CREAM (G)	Y
HYDROCORTISONE	CORTIZONE-10 PLUS	CREAM (G)	Y
HYDROCORTISONE	CORTIZONE-10	CREAM (G)	Y
HYDROCORTISONE	CORTIZONE FOR KIDS	CREAM (G)	Y
HYDROCORTISONE	CORTISONE	CREAM (G)	Y
HYDROCORTISONE	CORTAID	CREAM (G)	Y
HYDROCORTISONE	ANTI-ITCH	CREAM (G)	Y
HYDROCORTISONE	HYDROCORT	CREAM (G)	Y
HYDROCORTISONE	RECORT PLUS	CREAM (G)	Y
HYDROCORTISONE	SOOTHING CARE	CREAM (G)	Y

HYDROCORTISONE	HYDROCORTISONE	CREAM (G)	Y
HYDROCORTISONE	HYDROCORTISONE	OINT. (G)	Y
HYDROCORTISONE	HYDROCORTISONE ACETATE	OINT. (G)	Y
HYDROCORTISONE	HYDROCORTISONE	OINT. (G)	Y
HYDROCORTISONE	HYDROCORT	OINT. (G)	Y
HYDROCORTISONE	CORTIZONE-10	OINT. (G)	Y
HYDROCORTISONE	ANTI-ITCH	OINT. (G)	Y
HYDROCORTISONE ACETATE	HYDROCORTISONE ACETATE	CREAM (G)	Y
HYDROCORTISONE ACETATE	DERMAREST DRICORT	CREAM (G)	Y
HYDROCORTISONE BUTYRATE	HYDROCORTISONE BUTYRATE	SOLUTION	Y
TRIAMCINOLONE ACETONIDE	TRIAMCINOLONE ACETONIDE	CREAM (G)	Y
TRIAMCINOLONE ACETONIDE	TRIAMCINOLONE ACETONIDE	OINT. (G)	Y
TRIAMCINOLONE ACETONIDE	TRIANEX	OINT. (G)	Y
AMCINONIDE	AMCINONIDE	CREAM (G)	N
AMCINONIDE	AMCINONIDE	LOTION	N
AMCINONIDE	AMCINONIDE	OINT. (G)	N
BETAMETHASONE DIPROPIONATE	BETAMETHASONE DIPROPIONATE	GEL (GRAM)	N
BETAMETHASONE DIPROPIONATE	SERNIVO	SPRAY/PUMP	N
BETAMETHASONE VALERATE	BETAMETHASONE VALERATE	FOAM	N
BETAMETHASONE VALERATE	LUXIQ	FOAM	N
BETAMETHASONE VALERATE	BETAMETHASONE VALERATE	LOTION	N
BETAMETHASONE/PROPYLENE GLYC	DIPROLENE AF	CREAM (G)	N
BETAMETHASONE/PROPYLENE GLYC	BETAMETHASONE DIPROPIONATE	CREAM (G)	N
BETAMETHASONE/PROPYLENE GLYC	DIPROLENE	LOTION	N
BETAMETHASONE/PROPYLENE GLYC	BETAMETHASONE DIPROPIONATE	LOTION	N
BETAMETHASONE/PROPYLENE GLYC	DIPROLENE	OINT. (G)	N
BETAMETHASONE/PROPYLENE GLYC	BETAMETHASONE DIPROPIONATE	OINT. (G)	N
CLOBETASOL PROPIONATE	CLOBETASOL PROPIONATE	FOAM	N
CLOBETASOL PROPIONATE	OLUX	FOAM	N
CLOBETASOL PROPIONATE	CLOBETASOL PROPIONATE	GEL (GRAM)	N
CLOBETASOL PROPIONATE	CLOBEX	LOTION	N
CLOBETASOL PROPIONATE	CLOBETASOL PROPIONATE	LOTION	N
CLOBETASOL PROPIONATE	CLOBETASOL PROPIONATE	SHAMPOO	N
CLOBETASOL PROPIONATE	CLOBEX	SHAMPOO	N
CLOBETASOL PROPIONATE	CLODAN	SHAMPOO	N
CLOBETASOL PROPIONATE	CLOBETASOL PROPIONATE	SOLUTION	N
CLOBETASOL PROPIONATE	CLOBETASOL PROPIONATE	SPRAY	N
CLOBETASOL PROPIONATE	CLOBEX	SPRAY	N
CLOBETASOL PROPIONATE/EMOLL	CLOBETASOL EMOLLIENT	CREAM (G)	N
CLOBETASOL PROPIONATE/EMOLL	CLOBETASOL EMULSION	FOAM	N
CLOBETASOL PROPIONATE/EMOLL	OLUX-E	FOAM	N
CLOBETASOL PROPIONATE/EMOLL	CLOBETASOL EMOLLIENT	FOAM	N
CLOBETASOL/SKIN CLEANSER #28	CLODAN	KT SHM CLN	N
CLOCORTOLONE PIVALATE	CLOCORTOLONE PIVALATE	CREAM (G)	N
CLOCORTOLONE PIVALATE	CLODERM	CREAM (G)	N

DESONIDE	DESONATE	GEL (GRAM)	N
DESONIDE	DESONIDE	LOTION	N
DESOXIMETASONE	TOPICORT	CREAM (G)	N
DESOXIMETASONE	DESOXIMETASONE	CREAM (G)	N
DESOXIMETASONE	TOPICORT	GEL (GRAM)	N
DESOXIMETASONE	DESOXIMETASONE	GEL (GRAM)	N
DESOXIMETASONE	DESOXIMETASONE	OINT. (G)	N
DESOXIMETASONE	TOPICORT	OINT. (G)	N
DESOXIMETASONE	TOPICORT	SPRAY	N
DIFLORASONE DIACETATE	DIFLORASONE DIACETATE	CREAM (G)	N
DIFLORASONE DIACETATE	PSORCON	CREAM (G)	N
DIFLORASONE DIACETATE	DIFLORASONE DIACETATE	OINT. (G)	N
DIFLORASONE DIACETATE/EMOLL	APEXICON E	CREAM (G)	N
FLUOCINOLONE ACETONIDE	FLUOCINOLONE ACETONIDE	OIL	N
FLUOCINOLONE ACETONIDE	DERMA-SMOOTHE-FS	OIL	N
FLUOCINOLONE ACETONIDE	FLUOCINOLONE ACETONIDE	OINT. (G)	N
FLUOCINOLONE ACETONIDE	SYNALAR	OINT. (G)	N
FLUOCINOLONE ACETONIDE	CAPEX SHAMPOO	SHAMPOO	N
FLUOCINOLONE/EMOL CMB#65	SYNALAR	CMB ONT CR	N
FLUOCINOLONE/EMOL CMB#65	SYNALAR	CREAM (G)	N
FLUOCINOLONE/SHOWER CAP	FLUOCINOLONE ACETONIDE	OIL	N
FLUOCINOLONE/SHOWER CAP	DERMA-SMOOTHE-FS	OIL	N
FLUOCINOLONE/SKIN CLNSR28	SYNALAR TS	KIT	N
FLUOCINONIDE	FLUOCINONIDE	GEL (GRAM)	N
FLUOCINONIDE	FLUOCINONIDE	OINT. (G)	N
FLURANDRENOLIDE	FLURANDRENOLIDE	CREAM (G)	N
FLURANDRENOLIDE	FLURANDRENOLIDE	LOTION	N
FLUTICASONE PROPIONATE	FLUTICASONE PROPIONATE	CREAM (G)	N
FLUTICASONE PROPIONATE	FLUTICASONE PROPIONATE	LOTION	N
FLUTICASONE PROPIONATE	CUTIVATE	LOTION	N
FLUTICASONE PROPIONATE	FLUTICASONE PROPIONATE	OINT. (G)	N
HALCINONIDE	HALOG	CREAM (G)	N
HALCINONIDE	HALOG	OINT. (G)	N
HALOBETASOL PROPIONATE	HALOBETASOL PROPIONATE	CREAM (G)	N
HALOBETASOL PROPIONATE	ULTRAVATE	CREAM (G)	N
HALOBETASOL PROPIONATE	ULTRAVATE	LOTION	N
HALOBETASOL PROPIONATE	HALOBETASOL PROPIONATE	OINT. (G)	N
HALOBETASOL PROPIONATE	ULTRAVATE	OINT. (G)	N
HALOBETASOL/LACTIC ACID	ULTRAVATE X	CMB ONT CR	N
HALOBETASOL/LACTIC ACID	ULTRAVATE X	COMBO. PKG	N
HC/MINERAL OIL/PETROLAT,WHT	HYDROCORTISONE	OINT. (G)	N
HYDROCORTISONE	ANUSOL-HC	CREAM (G)	N
HYDROCORTISONE	HYDRO SKIN	LOTION	N
HYDROCORTISONE	HYDROCORTISONE	LOTION	N
HYDROCORTISONE	SCALPICIN	SOLUTION	N

HYDROCORTISONE	TEXACORT	SOLUTION	N
HYDROCORTISONE ACETATE	MICORT-HC	CRM/PE APP	N
HYDROCORTISONE BUTYRATE	HYDROCORTISONE BUTYRATE	CREAM (G)	N
HYDROCORTISONE BUTYRATE	HYDROCORTISONE BUTYRATE	OINT. (G)	N
HYDROCORTISONE BUTYRATE/EMOLL	HYDROCORTISONE BUTYRATE	CREAM (G)	N
HYDROCORTISONE PROBUTATE	PANDEL	CREAM (G)	N
HYDROCORTISONE VALERATE	HYDROCORTISONE VALERATE	CREAM (G)	N
HYDROCORTISONE VALERATE	HYDROCORTISONE VALERATE	OINT. (G)	N
HYDROCORTISONE/ALOE VERA	HYDROCORTISONE PLUS	CREAM (G)	N
HYDROCORTISONE/ALOE VERA	HYDROCORTISONE-ALOE	CREAM (G)	N
HYDROCORTISONE/ALOE VERA	HYDROSKIN	CREAM (G)	N
MOMETASONE FUROATE	MOMETASONE FUROATE	CREAM (G)	N
MOMETASONE FUROATE	ELOCON	CREAM (G)	N
MOMETASONE FUROATE	MOMETASONE FUROATE	OINT. (G)	N
MOMETASONE FUROATE	ELOCON	OINT. (G)	N
MOMETASONE FUROATE	MOMETASONE FUROATE	SOLUTION	N
NEOMYCIN SULFATE/FLUOCINOLONE	NEO-SYNALAR	CREAM (G)	N
NEOMYCIN/BACITRA/POLYMYXIN/HC	CORTISPORIN	OINT. (G)	N
NEOMYCIN/FLUOCINOLONE/EMOL #65	NEO-SYNALAR	CREAM (G)	N
PREDNICARBATE	DERMATOP	CREAM (G)	N
PREDNICARBATE	PREDNICARBATE	CREAM (G)	N
PREDNICARBATE	PREDNICARBATE	OINT. (G)	N
PREDNICARBATE	DERMATOP	OINT. (G)	N
TRIAMCINOLONE ACETONIDE	KENALOG	AEROSOL	N
TRIAMCINOLONE ACETONIDE	TRIAMCINOLONE ACETONIDE	AEROSOL	N
TRIAMCINOLONE ACETONIDE	TRIAMCINOLONE ACETONIDE	LOTION	N
HYDROCORTISONE	PROCTOSOL-HC	CRM/PE APP	
HYDROCORTISONE	PROCTOZONE-HC	CRM/PE APP	
HYDROCORTISONE	PROCTO-PAK	CRM/PE APP	
HYDROCORTISONE	HYDROCORTISONE	CRM/PE APP	
HYDROCORTISONE	PROCTO-MED HC	CRM/PE APP	
HYDROCORTISONE ACETATE	MICORT-HC	CRM/PE APP	
NEOMYCIN/POLYMYXIN B SULF/HC	CORTISPORIN	CREAM (G)	

Appendix 2: New Comparative Clinical Trials

A total of 70 citations were manually reviewed from the initial literature search. After further review, all citations were excluded because of wrong study design (eg, observational), comparator (eg, no control or placebo-controlled), or outcome studied (eg, non-clinical).

Appendix 3: Medline Search Strategy

Ovid MEDLINE(R) without Revisions 1996 to June Week 2 2017

1	aclometasone.mp.1
2	Betamethasone Valerate/ or Betamethasone/ or betamethasone.mp.3158
3	clobetasol.mp. or Clobetasol/1019
4	Fluocinolone Acetonide/ or fluocinolone.mp.444
5	hydrocortisone.mp. or Hydrocortisone/ 29324
6	Triamcinolone Acetonide/ or Triamcinolone/ or triamcinolone.mp.5132
7	fluocortolone.mp. or Fluocortolone/55
8	diflorasone.mp. 16
9	flurandrenolide.mp. or Flurandrenolone/9
10	halobetasol.mp.28
11	prednicarbate.mp.77
12	amcinonide.mp.10
13	clocortolone.mp.8
14	desoximetasone.mp. or Desoximetasone/34
15	Fluticasone/ or fluticasone.mp.3512
16	administration, topical.mp. or Administration, Topical/21895
17	topical corticosteroid.mp.1075
18	topical corticosteroids.mp.2269
19	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 41494
20	16 or 17 or 18 23982
21	19 and 20 1931
22	limit 21 to (english language and humans and (clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or guideline or meta analysis or practice guideline or randomized controlled trial or systematic reviews) and last 3 years) 70