Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-2596

Drug Class Literature Scan: Medications for Vitiligo

Date of Review: June 2022

Date of Last Review: N/A
Literature Search: 1946 - 03/21/2022

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

Conclusions:

- The objective of a 2015 Cochrane review was to update a 2010 review that assessed the effects of therapeutic interventions used in the management of vitiligo.[1] This review identified evidence from individual studies to support existing therapies for vitiligo, but the usefulness of the findings is limited by the different designs, outcome measurements and lack of quality of life measures.[1] There is moderate evidence for the use of topical corticosteroids (TCS), although long-term use is likely to lead to adverse effects.[1] When used as monotherapy, it may be preferable to use super potent TCS preparations to give a better chance of therapeutic response, but close monitoring for adverse effects is necessary.[1] The topical calcineurin inhibitor (TCI), tacrolimus, seems to be a reasonable alternative to topical corticosteroids, particularly on anatomical sites where there may be a higher risk of adverse effects with TCS.[1]
- In 2021, the British Association of Dermatologists (BAD) updated a 2008 guideline for the management of vitiligo for implementation in the United Kingdom National Health Service.[2] First-line treatments consist of topical treatments TCS and TCI.[2] Commonly prescribed TCS include betamethasone dipropionate, clobetasol dipropionate and fluticasone.[2] Tacrolimus, as monotherapy or in combination with phototherapy, is just as effective as TCS therapy but has a safer side-effect profile.[2] Second-line treatments consist of phototherapy (narrow band ultra violet B rays [NB-UVB] or psoralen and UVA [PUVA]) and systemic steroid treatment.[2] Third-line treatments consist of surgical grafting techniques.[2] Despite the autoimmune nature of vitiligo, there is insufficient evidence to support the use of immunosuppressive therapies in managing vitiligo.[2]
- In January 2022, the Oregon HERC revised Guideline Note 21 to broaden coverage of severe inflammatory skin disease.[3] Inflammatory skin conditions in this guideline include: psoriasis, atopic dermatitis, lichen planus, darier disease, pityriasis ruba pilaris, discoid lupus, and vitiligo. Severe forms of these conditions are funded on line 426 and are defined as having functional impairment AND one or more of the following:
    A) At least 10% of body surface area (BSA) involved
    B) Hand, foot, face, or mucous membrane involvement

Recommendations:

- Revise prior authorization (PA) criteria for “Topical Agents for Inflammatory Skin Diseases” to reflect most recent Oregon Health Effectiveness Review Committee (HERC) guidance described in Guideline Note 21.
- After review of costs of topical steroids in Executive Session, betamethasone-propylene glycol cream, clobetasol propionate solution, desoximetasone cream, and hydrocortisone cream products were changed to preferred.

Author: Deanna Moretz, PharmD, BCPS

Summary of Current Policy

- In January 2022, the Oregon HERC revised Guideline Note 21 to broaden coverage of severe inflammatory skin disease.[3] Inflammatory skin conditions in this guideline include: psoriasis, atopic dermatitis, lichen planus, darier disease, pityriasis ruba pilaris, discoid lupus, and vitiligo. Severe forms of these conditions are funded on line 426 and are defined as having functional impairment AND one or more of the following:
    - At least 10% of body surface area (BSA) involved
    - Hand, foot, face, or mucous membrane involvement

  The definition of functional impairment, is defined as an assessment of severe disease using the Dermatology Life Quality Index (DLQI) (score $\geq$ 11), Children's Dermatology Life Quality Index (CDLQI) (score $\geq$ 13), or severe score on another validated tool.[3] If inflammatory skin conditions do not meet the criteria stipulated in Guideline Note 21, they are not funded by HERC and are included on lines 482, 504, 532, 541, and 656. The revised 2022 Guideline Note 21 is included in **Appendix 4.**
- Topical calcineurin inhibitors, tacrolimus 0.03% ointment, tacrolimus 0.1% ointment, and pimecrolimus 1% cream are designated as preferred agents on the Preferred Drug List (PDL). The Pharmacy and Therapeutics Committee reviewed topical steroids at the July 2017 meeting. No new comparative evidence was identified since the last review to support a difference in safety or efficacy among equipotent topical corticosteroids. At least one agent in each of the potency categories is designated as preferred on the PDL. A list of preferred topical agents for inflammatory skin conditions is included in **Appendix 1**.

Background:

Vitiligo, a chronic autoimmune skin disorder disease, is the most frequent cause of depigmentation worldwide, with an estimated prevalence of 1%.[4] It usually begins after birth and, although it can develop in childhood, the average age of onset is about 20 years.[5] This disorder can be psychologically devastating and stigmatizing, especially in dark skinned individuals.[4] Vitiligo is clinically characterised by the development of white macules due to the loss of functioning melanocytes in the skin or hair, or both.[4] Two forms of the disease are recognized: segmental vitiligo (SV) and non-segmental vitiligo (NSV).[6] Non-segmental vitiligo, the most common form of vitiligo, is characterized by symmetrical and bilateral white patches.[4] Non-segmental vitiligo develops at all ages, but usually occurs in young people between the ages of 10 years and 30 years.[4] The most commonly affected sites are the fingers, wrists, axillae, groin, mouth, eyes and genitalia.[7] Different NSV clinical subtypes have been described, including generalized, mucosal, acrofacial, and universal, all with a bilateral distribution.[4] In contrast, SV is less common than NSV and usually has asymmetrical, one-sided or band-shaped distribution.[4] Segmental vitiligo accounts for 5–16% of overall vitiligo cases.[4] Segmental vitiligo tends to occur at a young age, before age 30 years in 87% of cases and before age 10 years in 41% of cases.[4]

Vitiligo is classified as an autoimmune disease.[8] Recent evidence points towards an overlapping inflammatory pathogenesis for both SV and NSV.[8] Both types seem to involve a multistep process, which involves initial release of proinflammatory cytokines and neuropeptides elicited by external or internal injury, with subsequent vascular dilatation and immune response.[8] Many studies support the association of vitiligo with thyroid disorders and other associated autoimmune diseases, such as rheumatoid arthritis, psoriasis, adult-onset diabetes mellitus, Addison's disease, pernicious anemia, alopecia areata, and systemic lupus erythematosus.[4] Almost one-third of people with vitiligo have a positive family history of the disease.[4] Several corresponding relevant genes associated with both vitiligo and other pigmentary, autoimmune and autoinflammatory disorders have now been identified.[8] They are involved in immune regulation, melanogenesis and apoptosis.[8]

The diagnosis of vitiligo is generally straightforward, made clinically based upon the finding of acquired, amelanotic, nonscaly, chalky-white macules with distinct margins in a typical distribution: periorificial, lips and tips of distal extremities, penis, segmental and areas of friction.[8] The diagnosis of vitiligo does not usually

require confirmatory laboratory tests.[8] A skin biopsy or other tests are not necessary except to exclude other disorders.[8] The diagnosis of vitiligo may be facilitated by the use of a Wood's lamp, a hand-held ultraviolet (UV) irradiation device that emits ultraviolet A rays (UVA).[8] It helps identify focal melanocyte loss and detect areas of depigmentation that may not be visible to the naked eye, particularly in pale skin.[8] Under the Wood's light, the vitiligo lesions emit a bright blue-white fluorescence and appear sharply demarcated.[8]

Treatment of vitiligo aims to halt disease spread and facilitate repigmentation.[9] Choice of treatment depends on several factors including: the subtype of the disease, the extent, distribution and activity of disease as well as the patient's age, phototype, effect on quality of life and motivation for treatment.[8] The face, neck, trunk and mid-extremities respond best to therapy, while the lips and distal extremities are more resistant.[8] The 2021 BAD Guidelines recommend that first-line treatment consist of high potency or very high potency TCS or topical tacrolimus.[2] Commonly prescribed TCS include betamethasone dipropionate, betamethasone valerate, clobetasol dipropionate and fluticasone propionate.[2] Use of the TCS or tacrolimus ointment, to treat vitiligo is off-label.[10] Topical tacrolimus, as monotherapy or in combination with phototherapy, is just as effective as TCS therapy but has a safer side-effect profile.[2] Second-line treatments consist of phototherapy NB-UVB or psoralen PUVA and systemic steroid treatment.[2] Third-line treatment consists of surgical grafting techniques.[2] Despite the autoimmune nature of vitiligo, there is insufficient evidence to support the use of immunosuppressive therapies in managing vitiligo.[2] Phototherapy has been a mainstay of treatment for vitiligo for several years.[5] Phototherapy is typically administered three times per week and is more effective if commenced early on in the disease.[11] It is used as first-line therapy in extensive disease. It can be used in combination with TCS or topical tacrolimus.[2]

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), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, 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.

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

New Systematic Reviews:
<u>2015 Cochrane: Interventions for Vitiligo</u>
The objective of a 2015 Cochrane review was to update a 2010 review that assessed the effects of therapeutic interventions used in the management of vitiligo.[1] The literature search was conducted through October 2013.[1] The 2015 update identified 39 new randomized controlled trials (RCTs) which added to the 57 RCTs in the previous review makes a total of 96 studies, totaling 4512 participants.[1] Most of the studies (72%) were small and had fewer than 50 participants.[1] Narrowband UVB light was used in 35 RCTs, either alone or in combination with other therapies.[1] Eighteen studies evaluated surgical management and 31 studies compared active treatment versus placebo.[1] Half of the studies lasted longer than six months.[1] Only 7 studies assessed children.[1] Most of the studies included subjects with NSV, only 1 RCT included participants with SV.[1] Most of the studies were conducted in Asia or Australia (n=49) followed by Europe (n=27), the Americas (n=14), and Africa (n=6).[1] Only 5 studies met the criteria for a well-designed trial.[1] Poor design, the number and complexity of the treatments and the fact that many of the studies assessed individual vitiligo patches in the same participant, made comparison of the studies difficult.[1]

Primary outcomes included: quality of life using a validated tool (e.g. DLQI), percentage of repigmentation (success rate defined as 75% or greater repigmentation), and adverse effects.[1] Nine studies assessed quality of life and showed no significant improvement between comparators.[1] Approximately half of the studies assessed repigmentation.[1] Only 3 RCTs reported a statistically significant result for 75% or greater repigmentation with the following results: topical corticosteroids were better than PUVA-sol (psoralen with sunlight) (RR 4.70, 95% CI 1.14 to 19.39, one study, N = 45); hydrocortisone plus laser light was better than laser light alone (RR 2.57, 95% CI 1.20 to 5.50, one study, N = 84); and oral minipulse of prednisolone (OMP) plus NB-UVB was better than OMP alone (RR 7.41, 95% CI 1.03 to 53.26, one study, N = 47).[1] None of the studies reported the long-term benefit of the treatment (i.e. two years sustained repigmentation).[1] The maximum follow-up time, reported in only one study, was one year post-treatment.[1]

Studies assessing topical preparations, in particular TCS, reported the most adverse effects.[1] Most studies examining TCS reported adverse effects including folliculitis, burning, mild pruritus, dryness, mild erythema, atrophy, telangiectasia and acneiform lesions.[1] In studies combining phototherapy and TCS, it was difficult to ascertain which treatment caused these effects.[1] In a meta-analysis comparing NB-UVB to PUVA, the NB-UVB group reported less observations of nausea in three studies (RR 0.13, 95% CI 0.02 to 0.69; I^2 = 0% three studies, N = 156) and erythema in two studies (RR 0.73, 95% CI 0.55 to 0.98; I^2 = 0%, two studies, N = 106), but no itching in two studies (RR 0.57, 95% CI 0.20 to 1.60; I^2 = 0%, two studies, N = 106).[1]

This review identified evidence from individual studies to support existing therapies for vitiligo, but the usefulness of the findings is limited by the different study designs, outcome measurements, and lack of quality of life measures.[1] There is moderate evidence for the use of TCS, although long-term use is likely to lead to adverse effects.[1] When used as monotherapy, it may be preferable to use super potent TCS preparations to provide optimal therapeutic response, but close monitoring for adverse effects is necessary.[1] The TCI, tacrolimus ointment, seems to be a reasonable alternative to TCS, particularly on anatomical sites where there may be a higher risk of adverse effects with TCS.[1] There is a need for follow-up studies to assess permanence of repigmentation as well as high-quality randomized trials using standardized measures and which also address quality of life.[1]

After review, 5 systematic reviews were excluded due to poor quality, wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).[12-16]

New Guidelines:

British Association of Dermatologists

In 2021, BAD updated a 2008 guideline for the management of vitiligo for implementation in the United Kingdom National Health Service.[2] The National Institute for Health and Care Excellence (NICE) accredited the process used by BAD to produce the clinical guidelines.[2] A literature search was conducted through May 2019 to identify key articles on vitiligo.[2] Nearly all the evidence supporting BAD recommendations relate to studies in adults.[2] There is very little published evidence for treatment interventions in children aged under 12 years.[2] Young children are more at risk from skin atrophy from TCS treatment, especially on delicate areas such as the face.[2] Nonsteroid options such as tacrolimus should be considered first line alongside potent TCS in children.[2] Topical potent and very potent steroids are more likely to have a systemic effect due to the increased surface-area-to-volume ratio in young children, and caution should be exercised regarding their use, especially in generalized widespread disease.[2]

Treatment recommendations for adults with vitiligo are as follows:

Topical Therapies

- Offer a potent or very potent TCS once daily, to minimize potential side-effects, to people with vitiligo as the first-line treatment, avoiding the periocular area. (Strong Recommendation)[2]

- Consider topical tacrolimus 0.1% ointment twice daily in people with facial vitiligo as an alternative to potent or very potent topical corticosteroids. (Weak Recommendation)[2]
- Consider topical tacrolimus 0.1% ointment twice daily under occlusion on photoexposed areas only in people with nonfacial vitiligo as an alternative to potent or very potent TCS. (Weak Recommendation)[2]
- There is insufficient evidence to recommend topical vitamin D analogs (i.e. calcipotriene) in people with vitiligo.[2]

Systemic Therapies

- Consider oral betamethasone 0.1 mg/kg twice weekly on two consecutive days for 3 months followed by tapering of the dose by 1 mg per month for a further 3 months in combination with NB-UVB in people with rapidly progressive vitiligo to arrest activity of the disease, after careful consideration of the risks and benefits. (Weak Recommendation)[2]
- Do not offer azathioprine in combination with PUVA (or NB-UVB) to people with vitiligo, due to the risk of malignancy. (Strong Recommendation)[2]
- There is insufficient evidence to recommend any currently available systemic treatments as monotherapy for people with stable vitiligo.[2]
- There is insufficient evidence to recommend minocycline, methotrexate or tofacitinib for people with vitiligo.[2]

Light and Laser Therapy

- Offer NB-UVB (whole body or localized, e.g. home based handheld) as first-line phototherapy to people with vitiligo who have an inadequate response to topical therapy and/or who have extensive or progressive disease. (Strong Recommendation)[2]
- Consider excimer laser or light in people with localized vitiligo in combination with TCIs (more evidence for tacrolimus). (Weak Recommendation)[2]
- There is insufficient evidence to recommend combination treatment of potent or very potent TCS with NB-UVB plus CO_2 laser for people with vitiligo.[2]

A patient management algorithm was developed to be used in conjunction with the summary of recommendations and supporting information provided in the BAD publication.[2]

First line treatment:

- Offer a potent or very potent TCS once daily.[2]
- Consider topical tacrolimus 0.1% ointment twice daily in people with facial vitiligo especially the periocular region.[2]
- Consider topical tacrolimus 0.1% ointment twice daily under occlusion on photoexposed areas only in people with nonfacial vitiligo.[2]
- Consider an intermittent regimen, e.g. alternating weeks of once-daily application of potent or very potent TCS with or without topical tacrolimus for areas with thinner skin.[2]

Second line treatment:

- Offer NB-UVB (whole-body or localized) with or without TCS or topical calcineurin inhibitors.[2]
- For rapidly progressing disease, consider oral betamethasone 0.1 mg/kg twice weekly on two consecutive days for 3 months followed by tapering of the dose by 1 mg per month for a further 3 months in combination with NB-UVB.[2]

Third line treatment:

- Consider excimer laser/light with TCIs for localized vitiligo.[2]
- Consider cellular grafting for stable segmental or nonsegmental vitiligo.[2]

After review, 3 guidelines were excluded due to poor quality.[17-19]

References:

1. Whitton ME, Pinart M, Batchelor J, et al. Interventions for vitiligo. *Cochrane Database Syst Rev.* 2015(2):Cd003263.
2. Eleftheriadou V, Atkar R, Batchelor J, et al. British Association of Dermatologists guidelines for the management of people with vitiligo 2021. *The British journal of dermatology.* 2022;186(1):18-29.
3. Oregon Health Evidence Review Commission. Coverage Guidance and Reports. http://www.oregon.gov/oha/hpa/csi-herc/pages/index.aspx. Accessed March 1, 2022.
4. Ezzedine K, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. *Lancet (London, England).* 2015;386(9988):74-84.
5. Gawkrodger DJ, Ormerod AD, Shaw L, et al. Vitiligo: concise evidence based guidelines on diagnosis and management. *Postgraduate medical journal.* 2010;86(1018):466-471.
6. Ezzedine K, Lim HW, Suzuki T, et al. Revised classification/nomenclature of vitiligo and related issues: the Vitiligo Global Issues Consensus Conference. *Pigment Cell Melanoma Res.* 2012;25(3):E1-13.
7. Gawkrodger DJ, Ormerod AD, Shaw L, et al. Guideline for the diagnosis and management of vitiligo. *The British journal of dermatology.* 2008;159(5):1051-1076.
8. Bergqvist C, Ezzedine K. Vitiligo: A Review. *Dermatology (Basel, Switzerland).* 2020;236(6):571-592.
9. Searle T, Al-Niaimi F, Ali FR. Vitiligo: an update on systemic treatments. *Clin Exp Dermatol.* 2021;46(2):248-258.
10. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at http://www.micromedexsolutions.com. Accessed March 22, 2022.
11. Daniel BS, Wittal R. Vitiligo treatment update. *Australas J Dermatol.* 2015;56(2):85-92.
12. de Menezes AF, Oliveira de Carvalho F, Barreto RS, et al. Pharmacologic Treatment of Vitiligo in Children and Adolescents: A Systematic Review. *Pediatric dermatology.* 2017;34(1):13-24.
13. Dang YP, Li Q, Shi F, Yuan XY, Liu W. Effect of topical calcineurin inhibitors as monotherapy or combined with phototherapy for vitiligo treatment: a meta-analysis. *Dermatologic Therapy.* 2016;29(2):126-133.
14. Bae JM, Hong BY, Lee JH, Lee JH, Kim GM. The efficacy of 308-nm excimer laser/light (EL) and topical agent combination therapy versus EL monotherapy for vitiligo: A systematic review and meta-analysis of randomized controlled trials (RCTs). *J Am Acad Dermatol.* 2016;74(5):907-915.
15. Chang HC, Hsu YP, Huang YC. The effectiveness of topical calcineurin inhibitors compared with topical corticosteroids in the treatment of vitiligo: A systematic review and meta-analysis. *J Am Acad Dermatol.* 2020;82(1):243-245.
16. Phan K, Phan S, Shumack S, Gupta M. Repigmentation in vitiligo using janus kinase (JAK) inhibitors with phototherapy: systematic review and Meta-analysis. *The Journal of dermatological treatment.* 2022;33(1):173-177.
17. Taieb A, Alomar A, Böhm M, et al. Guidelines for the management of vitiligo: the European Dermatology Forum consensus. *The British journal of dermatology.* 2013;168(1):5-19.
18. Oiso N, Suzuki T, Wataya-Kaneda M, et al. *J Dermatol.* 2013;40(5):344-354.
19. Böhm M, Schunter JA, Fritz K, et al. S1 Guideline: Diagnosis and therapy of vitiligo. *J Dtsch Dermatol Ges.* 2022;20(3):365-378.
20. Abdel Latif AA, Ibrahim SM. Monochromatic excimer light versus combination of topical steroid with vitamin D3 analogue in the treatment of nonsegmental vitiligo: a randomized blinded comparative study. *Dermatologic Therapy.* 2015;28(6):383-389.

Appendix 1: Current Preferred Drug List

Topical Products for Atopic Dermatitis

Generic	Brand	Route	Form	PDL
pimecrolimus	ELIDEL	TOPICAL	CREAM (G)	Y
pimecrolimus	PIMECROLIMUS	TOPICAL	CREAM (G)	Y
tacrolimus	PROTOPIC	TOPICAL	OINT. (G)	Y
tacrolimus	TACROLIMUS	TOPICAL	OINT. (G)	Y
crisaborole	EUCRISA	TOPICAL	OINT. (G)	N
ruxolitinib phosphate	OPZELURA	TOPICAL	CREAM (G)	N

Topical Steroids

Generic	Brand	Route	Form	PDL
alclometasone dipropionate	ALCLOMETASONE DIPROPIONATE	TOPICAL	CREAM (G)	Y
alclometasone dipropionate	ALCLOMETASONE DIPROPIONATE	TOPICAL	OINT. (G)	Y
betamethasone dipropionate	BETAMETHASONE DIPROPIONATE	TOPICAL	CREAM (G)	Y
betamethasone dipropionate	ALPHATREX	TOPICAL	LOTION	Y
betamethasone dipropionate	BETAMETHASONE DIPROPIONATE	TOPICAL	LOTION	Y
betamethasone dipropionate	ALPHATREX	TOPICAL	OINT. (G)	Y
betamethasone dipropionate	BETAMETHASONE DIPROPIONATE	TOPICAL	OINT. (G)	Y
betamethasone valerate	BETAMETHASONE VALERATE	TOPICAL	CREAM (G)	Y
betamethasone valerate	BETATREX	TOPICAL	CREAM (G)	Y
betamethasone valerate	BETAMETHASONE VALERATE	TOPICAL	OINT. (G)	Y
betamethasone valerate	BETATREX	TOPICAL	OINT. (G)	Y
clobetasol propionate	CLOBETASOL PROPIONATE	TOPICAL	CREAM (G)	Y
clobetasol propionate	CLOBETASOL PROPIONATE	TOPICAL	OINT. (G)	Y
desonide	DESONIDE	TOPICAL	CREAM (G)	Y
desonide	DESOWEN	TOPICAL	CREAM (G)	Y
desonide	TRIDESILON	TOPICAL	CREAM (G)	Y
desonide	DESONIDE	TOPICAL	OINT. (G)	Y
desonide	TRIDESILON	TOPICAL	OINT. (G)	Y
fluocinolone acetonide	FLUOCINOLONE ACETONIDE	TOPICAL	CREAM (G)	Y
fluocinolone acetonide	SYNALAR	TOPICAL	CREAM (G)	Y
fluocinolone acetonide	FLUOCINOLONE ACETONIDE	TOPICAL	SOLUTION	Y
fluocinolone acetonide	SYNALAR	TOPICAL	SOLUTION	Y
fluocinonide	FLUOCINONIDE	TOPICAL	CREAM (G)	Y

fluocinonide	VANOS	TOPICAL	CREAM (G)	Y
fluocinonide	FLUOCINONIDE	TOPICAL	SOLUTION	Y
fluocinonide/emollient base	FLUOCINONIDE-E	TOPICAL	CREAM (G)	Y
hydrocortisone	ANTI-ITCH	TOPICAL	CREAM (G)	Y
hydrocortisone	HYDROCORTISONE	TOPICAL	CREAM (G)	Y
hydrocortisone	HYDROCORTISONE	TOPICAL	CREAM (G)	Y
hydrocortisone	HYCORT	TOPICAL	OINT. (G)	Y
hydrocortisone	HYDROCORTISONE	TOPICAL	OINT. (G)	Y
hydrocortisone	HYDROCORTISONE	TOPICAL	OINT. (G)	Y
hydrocortisone acetate	HYDROCORTISONE ACETATE	TOPICAL	CREAM (G)	Y
hydrocortisone butyrate	HYDROCORTISONE BUTYRATE	TOPICAL	SOLUTION	Y
triamcinolone acetonide	TRIAMCINOLONE ACETONIDE	TOPICAL	CREAM (G)	Y
triamcinolone acetonide	TRIAMCINOLONE ACETONIDE	TOPICAL	OINT. (G)	Y
triamcinolone acetonide	TRIANEX	TOPICAL	OINT. (G)	Y
amcinonide	AMCINONIDE	TOPICAL	CREAM (G)	N
betamethasone dipropionate	DIPROSONE	TOPICAL	AEROSOL	N
betamethasone dipropionate	BETAMETHASONE DIPROP AUGMENTED	TOPICAL	GEL (GRAM)	N
betamethasone valerate	BETAMETHASONE VALERATE	TOPICAL	FOAM	N
betamethasone valerate	LUXIQ	TOPICAL	FOAM	N
betamethasone valerate	BETAMETHASONE VALERATE	TOPICAL	LOTION	N
betamethasone/propylene glyc	BETAMETHASONE DIPROP AUGMENTED	TOPICAL	CREAM (G)	N
betamethasone/propylene glyc	BETAMETHASONE DIPROP AUGMENTED	TOPICAL	LOTION	N
betamethasone/propylene glyc	BETAMETHASONE DIPROP AUGMENTED	TOPICAL	OINT. (G)	N
betamethasone/propylene glyc	DIPROLENE	TOPICAL	OINT. (G)	N
clobetasol propionate	CLOBETASOL PROPIONATE	TOPICAL	FOAM	N
clobetasol propionate	OLUX	TOPICAL	FOAM	N
clobetasol propionate	CLOBETASOL PROPIONATE	TOPICAL	GEL (GRAM)	N
clobetasol propionate	IMPEKLO	TOPICAL	LOT MD PMP	N
clobetasol propionate	CLOBETASOL PROPIONATE	TOPICAL	LOTION	N
clobetasol propionate	CLOBETASOL PROPIONATE	TOPICAL	SHAMPOO	N
clobetasol propionate	CLOBEX	TOPICAL	SHAMPOO	N
clobetasol propionate	CLODAN	TOPICAL	SHAMPOO	N
clobetasol propionate	CLOBETASOL PROPIONATE	TOPICAL	SOLUTION	N
clobetasol propionate	CLOBETASOL PROPIONATE	TOPICAL	SPRAY	N
clobetasol propionate	CLOBEX	TOPICAL	SPRAY	N
clobetasol propionate/emoll	CLOBETASOL EMOLLIENT	TOPICAL	CREAM (G)	N
clobetasol propionate/emoll	CLOBETASOL EMOLLIENT	TOPICAL	FOAM	N
clobetasol propionate/emoll	CLOBETASOL EMULSION	TOPICAL	FOAM	N
clobetasol propionate/emoll	OLUX-E	TOPICAL	FOAM	N

clobetasol propionate/emoll	TOVET EMOLLIENT	TOPICAL	FOAM	N
clobetasol/emollient no.65	TOVET KIT	TOPICAL	COMBO. PKG	N
clobetasol/skin cleanser no.28	CLODAN	TOPICAL	KT SHM CLN	N
clocortolone pivalate	CLOCORTOLONE PIVALATE	TOPICAL	CREAM (G)	N
clocortolone pivalate	CLODERM	TOPICAL	CREAM (G)	N
desonide	DESONIDE	TOPICAL	LOTION	N
desoximetasone	DESOXIMETASONE	TOPICAL	CREAM (G)	N
desoximetasone	TOPICORT	TOPICAL	CREAM (G)	N
desoximetasone	DESOXIMETASONE	TOPICAL	GEL (GRAM)	N
desoximetasone	TOPICORT	TOPICAL	GEL (GRAM)	N
desoximetasone	DESOXIMETASONE	TOPICAL	OINT. (G)	N
desoximetasone	TOPICORT	TOPICAL	OINT. (G)	N
desoximetasone	DESOXIMETASONE	TOPICAL	SPRAY	N
desoximetasone	TOPICORT	TOPICAL	SPRAY	N
diflorasone diacet/emollient	APEXICON E	TOPICAL	CREAM (G)	N
diflorasone diacetate	DIFLORASONE DIACETATE	TOPICAL	CREAM (G)	N
diflorasone diacetate	PSORCON	TOPICAL	CREAM (G)	N
diflorasone diacetate	DIFLORASONE DIACETATE	TOPICAL	OINT. (G)	N
fluocinolone acetonide	DERMA-SMOOTHE-FS	TOPICAL	OIL	N
fluocinolone acetonide	FLUOCINOLONE ACETONIDE	TOPICAL	OIL	N
fluocinolone acetonide	FLUOCINOLONE ACETONIDE	TOPICAL	OINT. (G)	N
fluocinolone acetonide	SYNALAR	TOPICAL	OINT. (G)	N
fluocinolone acetonide	CAPEX SHAMPOO	TOPICAL	SHAMPOO	N
fluocinolone/emol comb no.65	SYNALAR	TOPICAL	CMB ONT CR	N
fluocinolone/emol comb no.65	SYNALAR	TOPICAL	CREAM (G)	N
fluocinolone/shower cap	DERMA-SMOOTHE-FS	TOPICAL	OIL	N
fluocinolone/shower cap	FLUOCINOLONE ACETONIDE	TOPICAL	OIL	N
fluocinolone/skin clnsr28	SYNALAR TS	TOPICAL	KIT	N
fluocinonide	FLUOCINONIDE	TOPICAL	GEL (GRAM)	N
fluocinonide	FLUOCINONIDE	TOPICAL	OINT. (G)	N
flurandrenolide	FLURANDRENOLIDE	TOPICAL	CREAM (G)	N
flurandrenolide	FLURANDRENOLIDE	TOPICAL	LOTION	N
flurandrenolide	CORDRAN	TOPICAL	MED. TAPE	N
flurandrenolide	FLURANDRENOLIDE	TOPICAL	OINT. (G)	N
fluticasone propionate	FLUTICASONE PROPIONATE	TOPICAL	CREAM (G)	N
fluticasone propionate	BESER	TOPICAL	LOTION	N
fluticasone propionate	FLUTICASONE PROPIONATE	TOPICAL	LOTION	N
fluticasone propionate	FLUTICASONE PROPIONATE	TOPICAL	OINT. (G)	N
fluticasone/emollient no.65	BESER KIT	TOPICAL	KT LOTN CE	N

halcinonide	HALCINONIDE	TOPICAL	CREAM (G)	N
halcinonide	HALOG	TOPICAL	CREAM (G)	N
halcinonide	HALOG	TOPICAL	OINT. (G)	N
halcinonide	HALOG	TOPICAL	SOLUTION	N
halobetasol propionate	HALOBETASOL PROPIONATE	TOPICAL	CREAM (G)	N
halobetasol propionate	ULTRAVATE	TOPICAL	CREAM (G)	N
halobetasol propionate	HALOBETASOL PROPIONATE	TOPICAL	FOAM	N
halobetasol propionate	LEXETTE	TOPICAL	FOAM	N
halobetasol propionate	BRYHALI	TOPICAL	LOTION	N
halobetasol propionate	ULTRAVATE	TOPICAL	LOTION	N
halobetasol propionate	HALOBETASOL PROPIONATE	TOPICAL	OINT. (G)	N
halobetasol propionate	ULTRAVATE	TOPICAL	OINT. (G)	N
halobetasol/lactic acid	ULTRAVATE X	TOPICAL	CMB ONT CR	N
halobetasol/lactic acid	ULTRAVATE X	TOPICAL	COMBO. PKG	N
hydrocortisone	HYDROCORTISONE	TOPICAL	CREAM (G)	N
hydrocortisone	HYDROCORTISONE	TOPICAL	CREAM PACK	N
hydrocortisone	CETACORT	TOPICAL	LOTION	N
hydrocortisone	HYDROCORTISONE	TOPICAL	LOTION	N
hydrocortisone	HYDROCORTISONE	TOPICAL	LOTION	N
hydrocortisone	SCALP CORT	TOPICAL	LOTION	N
hydrocortisone	SCALP	TOPICAL	SOLUTION	N
hydrocortisone	SCALPICIN	TOPICAL	SOLUTION	N
hydrocortisone	TEXACORT	TOPICAL	SOLUTION	N
hydrocortisone	HYDROCORTISONE	TOPICAL	SPRAY	N
hydrocortisone acet/aloe vera	HYDROCORTISONE ACETATE W/ALOE	TOPICAL	CREAM (G)	N
hydrocortisone acet/aloe vera	HYDROCORTISONE W/ALOE	TOPICAL	CREAM (G)	N
hydrocortisone acet/aloe vera	HYDROCORTISONE ACETATE W/ALOE	TOPICAL	OINT. (G)	N
hydrocortisone acet/aloe vera	HYDROCORTISONE W/ALOE	TOPICAL	OINT. (G)	N
hydrocortisone acet/aloe vera	HYDROCORTISONE W/ALOE	TOPICAL	PACKET	N
hydrocortisone acetate	MICORT-HC	TOPICAL	CRM/PE APP	N
hydrocortisone acetate	HYDROCORTISONE	TOPICAL	OINT. (G)	N
hydrocortisone acetate	HYDROCORTISONE ACETATE	TOPICAL	OINT. (G)	N
hydrocortisone butyrate	HYDROCORTISONE BUTYRATE	TOPICAL	CREAM (G)	N
hydrocortisone butyrate	HYDROCORTISONE BUTYRATE	TOPICAL	LOTION	N
hydrocortisone butyrate	LOCOID	TOPICAL	LOTION	N
hydrocortisone butyrate	HYDROCORTISONE BUTYRATE	TOPICAL	OINT. (G)	N
hydrocortisone butyrate/emoll	HYDROCORTISONE BUTYRATE	TOPICAL	CREAM (G)	N
hydrocortisone butyrate/emoll	LOCOID LIPOCREAM	TOPICAL	CREAM (G)	N
hydrocortisone probutate	PANDEL	TOPICAL	CREAM (G)	N

hydrocortisone valerate	HYDROCORTISONE VALERATE	TOPICAL	CREAM (G)	N
hydrocortisone valerate	HYDROCORTISONE VALERATE	TOPICAL	OINT. (G)	N
hydrocortisone/aloe vera	ANTI-ITCH WITH ALOE	TOPICAL	CREAM (G)	N
hydrocortisone/aloe vera	HYDROCORTISONE PLUS	TOPICAL	CREAM (G)	N
hydrocortisone/aloe vera	HYDROCORTISONE W/ALOE	TOPICAL	CREAM (G)	N
hydrocortisone/aloe vera	HYDROCORTISONE-ALOE	TOPICAL	CREAM (G)	N
hydrocortisone/aloe vera	HYDROCORTISONE W/ALOE	TOPICAL	OINT. (G)	N
hydrocortisone/skin cleanser25	AQUA GLYCOLIC HC	TOPICAL	COMBO. PKG	N
mometasone furoate	MOMETASONE FUROATE	TOPICAL	CREAM (G)	N
mometasone furoate	MOMETASONE FUROATE	TOPICAL	OINT. (G)	N
mometasone furoate	MOMETASONE FUROATE	TOPICAL	SOLUTION	N
neomycin sulfate/fluocinolone	NEO-SYNALAR	TOPICAL	CREAM (G)	N
neomycin/fluocinolone/emoll 65	NEO-SYNALAR	TOPICAL	CREAM (G)	N
prednicarbate	PREDNICARBATE	TOPICAL	CREAM (G)	N
prednicarbate	PREDNICARBATE	TOPICAL	OINT. (G)	N
triamcinolone acetonide	KENALOG	TOPICAL	AEROSOL	N
triamcinolone acetonide	TRIAMCINOLONE ACETONIDE	TOPICAL	AEROSOL	N
triamcinolone acetonide	KENALOG	TOPICAL	LOTION	N
triamcinolone acetonide	TRIAMCINOLONE ACETONIDE	TOPICAL	LOTION	N
hydrocortisone	ANUSOL-HC	TOPICAL	CRM/PE APP	
hydrocortisone	HYDROCORTISONE	TOPICAL	CRM/PE APP	
hydrocortisone	PROCTO-MED HC	TOPICAL	CRM/PE APP	
hydrocortisone	PROCTOSOL-HC	TOPICAL	CRM/PE APP	
hydrocortisone	PROCTOZONE-HC	TOPICAL	CRM/PE APP	
neomycin sulfate/hydrocort	NEOMYCIN W/HYDROCORTISONE	TOPICAL	OINT. (G)	

Appendix 2: New Comparative Clinical Trials

A total of 44 citations were manually reviewed from the initial literature search. After further review, 43 citations were excluded because of wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical). The remaining 2 trials are summarized in the table below. Full abstracts are included in **Appendix 3**.

Table 1. Description of Randomized Comparative Clinical Trials.

Study	Comparison	Population	Primary Outcome	Results	Notes/Limitations
Abdel L, et al[20] DB, RCT	1. Topical calcipotriol and betamethasone ointment once daily 2. Monochromatic excimer light twice weekly Duration: 12 weeks	Subjects aged 6 to 64 yo with NSV Mean age: 35 yo N=44	Repigmentation grade after 12 weeks of treatment of 2 stable vitiligo lesions	Percentage of repigmentation 1. 63.75% 2. 65% Difference between treatments: P = 0.23 (NS)	• Small sample size • Method of randomization not described • 18% of patients (n=8) did not complete all treatment sessions for unknown reasons • Repigmentation assessment conducted via visual analysis by 2 independent clinicians
Abbreviations: CI = confidence interval; DB = double blind; N = number; NB-UVB = narrow band ultra violet B; NSV = non-segmental vitiligo; NR = not reported; RCT = randomized clinical trial; VASI = vitiligo and activity scoring index; yo = years old					

Appendix 3: Abstracts of Comparative Clinical Trials

Monochromatic Excimer Light Versus Combination Of Topical Steroid With Vitamin D3 Analogue In The Treatment Of Nonsegmental Vitiligo: A Randomized Blinded Comparative Study[20]

Vitiligo is a difficult disease to treat, socially stigmatizing its patients. Monochromatic excimer light (MEL) was developed for use in dermatology and adapted for the treatment of vitiligo. Comparing the efficacy of MEL versus topical combination therapy of vitamin D3 analogue and steroid in the treatment of nonsegmental vitiligo. Forty-four patients with localized and stable nonsegmental vitiligo participated in the present study. In each patient, two lesions were selected and divided randomly into two groups, group A was treated with daily topical combination of calcipotriol and betamethasone and group B was treated with biweekly sessions of MEL for 3 months. Efficacy based on repigmentation percentages were blindly evaluated by two independent physicians and patient's satisfaction. There was significant improvement in both treatment modalities at the end of the study, but without significant differences in both groups. There was a significant difference between both groups regarding the onset of repigmentation (p-value < 0.05), whereas group B showed early sign of repigmentation in first 4 weeks of treatment in 16 patients versus 7 patients in group A. Both treatment modalities offered encouraging results and both are promising lines for the treatment of vitiligo.

Appendix 4: Prioritized List Guideline Note

Extracted from the January 1, 2022 Prioritized List
Searchable Prioritized List 2022

GUIDELINE NOTE 21, SEVERE INFLAMMATORY SKIN DISEASE
Lines 426,482,504,532,541,656

Inflammatory skin conditions included in this guideline are:

A) Psoriasis
B) Atopic dermatitis
C) Lichen planus
D) Darier disease
E) Pityriasis rubra pilaris
F) Discoid lupus
G) Vitiligo

The conditions above are included on Line 426 if severe, defined as having functional impairment as indicated by Dermatology Life Quality Index (DLQI) ≥ 11 or Children's Dermatology Life Quality Index (CDLQI) ≥ 13 (or severe score on other validated tool) AND one or more of the following:

C) At least 10% of body surface area involved
D) Hand, foot, face, or mucous membrane involvement.

Otherwise, these conditions above are included on Lines 482, 504, 532, 541 and 656.
For severe psoriasis, first line agents include topical agents, phototherapy and methotrexate. Second line agents include other systemic agents and oral retinoids and should be limited to those who fail, or have contraindications to, or do not have access to first line agents. Biologics are included on this line only for the indication of severe plaque psoriasis; after documented failure of first line agents and failure of (or contraindications to) a second line agent.

For severe atopic dermatitis/eczema, first-line agents include topical moderate- to high- potency corticosteroids and narrowband UVB. Second line agents include topical calcineurin inhibitors (e.g. pimecrolimus, tacrolimus), topical phosphodiesterase (PDE)-4 inhibitors (e.g. crisaborole), and oral immunomodulatory therapy (e.g. cyclosporine, methotrexate, azathioprine, mycophenolate mofetil, or oral corticosteroids). Use of the topical second line agents (e.g. calcineurin inhibitors and phosphodiesterase (PDE)-4 inhibitors) should be limited to those who fail or have contraindications to first line agents. Biologic agents are included on this line for atopic dermatitis only after failure of or contraindications to at least one agent from each of the following three classes: 1) moderate to high potency topical corticosteroids, 2) topical calcineurin inhibitors or topical phosphodiesterase (PDE)-4 inhibitors, and 3) oral immunomodulator therapy.

ICD-10-CM Q82.8 (Other specified congenital malformations of skin) is included on Line 426 only for Darier disease.

Appendix 5: Medline Search Strategy

Ovid MEDLINE(R) without Revisions 1946 to March Week 2 2022, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations 1946 to March 18, 2022

1	exp Vitiligo/cl, dt, ep, ge, pp, th [Classification, Drug Therapy, Epidemiology, Genetics, Physiopathology, Therapy]	2853
2	Glucocorticoids/ or Dermatitis, Atopic/ or topical glucocorticoids.mp. or Anti-Inflammatory Agents/	173169
3	Calcineurin Inhibitors/tu [Therapeutic Use]	650
4	2 or 3	173687
5	1 and 4	179
6	limit 5 to (english language and humans)	165
7	limit 6 to (clinical trial, all or clinical trial, phase iii or clinical trial or comparative study or controlled clinical trial or guideline or meta-analysis or multicenter study or practice guideline or pragmatic clinical trial or randomized controlled trial or "systematic review")	44

Appendix 6: Key Inclusion Criteria

Population	Adults and Children
Intervention	Topical corticosteroids and topical calcineurin inhibitors
Comparator	Placebo
Outcomes	Extent of repigmentation
Timing	2-3 months
Setting	Outpatient

Topical Agents for Inflammatory Skin Diseases

Goal(s):

- Restrict dermatological drugs only for funded OHP diagnoses. Treatments are funded on the OHP for severe inflammatory skin diseases including: psoriasis, atopic dermatitis, lichen planus, Darier disease, pityriasis rubra pilaris, discoid lupus and vitiligo. Treatments for mild or moderate psoriasis, mild or moderate atopic dermatitis, lichen planus, Darier disease, pityriasis rubra pilaris, discoid lupus and vitiligo seborrheic dermatitis, keratoderma and other hypertrophic and atrophic conditions of skin are not funded.

Length of Authorization:

- From 6 to 12 months

Requires PA:

- Non-preferred antipsoriatics
- All atopic dermatitis drugs
- STC = 92 and HIC = L1A, L5F, L9D, T0A
- This PA does not apply to targeted immune modulators for psoriasis or atopic dermatitis which are subject to separate clinical PA criteria.

Covered Alternatives:

- Preferred alternatives listed at www.orpdl.org/drugs/

Table 1. FDA-approved ages for atopic dermatitis drugs

Drug	Minimum Age
Crisaborole	3 months
Pimecrolimus	2 years
Ruxolitinib	12 years
Tacrolimus 0.03%	2 years
Tacrolimus 0.1%	16 years

Approval Criteria		
1. What diagnosis is being treated?	Record ICD 10 code.	
2. Is the diagnosis for mild or moderate inflammatory skin conditions?	**Yes:** Pass to RPh; deny, not funded by the OHP.	**No:** Go to #3
3. Is the request for treatment of severe inflammatory skin disease? Severe disease is defined as:[1] • Having functional impairment as indicated by Dermatology Life Quality Index (DLQI) ≥ 11 or Children's Dermatology Life Quality Index (CDLQI) ≥ 13 (or severe score on other validated tool) AND one or more of the following: 1. At least 10% body surface area involved OR 2. Hand, foot, face, or mucous membrane involvement	**Yes:** Go to #4	**No:** Pass to RPh; deny, not funded by the OHP
4. Is the diagnosis psoriasis?	**Yes:** Go to #8	**No:** Go to #5
5. Is the diagnosis atopic dermatitis?	**Yes:** Go to #6	**No:** Go to #10
6. Does the patient meet the age requirements per the FDA label (Table 1)?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness

Approval Criteria		
7. Does the patient have a documented contraindication, intolerance or failed trials of at least 2 first line agents (i.e. topical corticosteroids, tacrolimus) indicated for the treatment of severe AD? *Note ruxolitinib, pimecrolimus and crisaborole are FDA approved to manage mild to moderate AD, while tacrolimus is FDA approved to manage moderate to severe AD.	**Yes:** Document drug and dates trialed, and intolerances or contraindications (if applicable): 1._____(dates) 2._____(dates) Approve for length of treatment; maximum 6 months.	**No:** Pass to RPh. Deny; medical appropriateness
8. Is the requested product preferred?	**Yes:** Approve for length of treatment; maximum 1 year.	**No:** Go to #9
9. 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.	**Yes:** Inform provider of preferred alternatives. Approve for length of treatment; maximum 1 year.	**No**: Approve for length of treatment; maximum 1 year.
10. RPH only: All other indications need to be evaluated as to whether they are funded by the OHP.*	**If funded, and clinic provides supporting literature:** Approve for 1 year.	**If not funded:** Deny, not funded by the OHP.

P&T/DUR Review: *6/22 (DM); 12/20; 10/20; 7/19; 5/19; 3/18; 9/17; 7/15; 1/15; 09/10; 9/09; 3/09; 5/07; 2/06*
Implementation: *7/1/22; 1/1/2021, 11/1/20; 8/19/19; 4/16/18; 10/15; 8/15; 9/13; 6/12; 9/10; 1/10; 7/09; 6/07; 9/06*

**The Health Evidence Review Commission has stipulated via Guideline Note 21 that mild and moderate uncomplicated inflammatory skin conditions including psoriasis, atopic dermatitis, lichen planus, Darier disease, pityriasis rubra pilaris, and discoid lupus are not funded. Uncomplicated is defined as no functional impairment; and/or involving less than 10% of body surface area and no involvement of the hand, foot, face or mucous membranes.*

Reference:

1.Oregon Health Evidence Review Commission. Coverage Guidance and Reports. http://www.oregon.gov/oha/hpa/csi-herc/pages/index.aspx *Accessed March 1, 2022.*