PRIOR AUTHORIZATION POLICY

POLICY: Dermatology – Opzelura Prior Authorization Policy
- Opzelura® (ruxolitinib 1.5% cream – Incyte)

REVIEW DATE: 09/04/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Opzelura, a Janus kinase (JAK) inhibitor, is indicated for the following uses:[1]
- **Atopic dermatitis**, for the topical short-term and non-continuous treatment of mild to moderate disease in patients ≥ 12 years of age whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.
- **Nonsegmental vitiligo**, for the topical treatment of patients ≥ 12 years of age.

Limitation of Use: Use of Opzelura in combination with therapeutic biologics, other JAK inhibitors, or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

For atopic dermatitis, Opzelura is applied twice daily to affected areas of up to 20% body surface area (BSA). Patients should stop using Opzelura when signs and symptoms of atopic dermatitis (e.g., itch, rash, and redness) resolve. If signs and symptoms do not improve within 8 weeks, patients should be re-evaluated by their healthcare provider.

For vitiligo, Opzelura is applied twice daily to affected areas of up to 10% BSA.[1] Patients may require more than 24 weeks of treatment to achieve a satisfactory

response. If the patient does not find the repigmentation meaningful after 24 weeks of therapy, the patient should be re-evaluated by their healthcare provider.

Clinical Efficacy

Atopic Dermatitis

Two pivotal Opzelura studies enrolled patients ≥ 12 years of age with a diagnosis of atopic dermatitis present for ≥ 2 years, affecting 3% to 20% of their BSA.[1,2] Patients were also required to have an Investigator's Global Assessment (IGA) score of 2 or 3. While prior treatment was not a requirement for study enrollment, 90% of patients had received prior therapies for atopic dermatitis, including low-, medium-, and high-potency topical corticosteroids (49.6%, 42.4%, and 32.7% of patients, respectively), as well as topical calcineurin inhibitors (e.g., tacrolimus 0.03% and 0.1% ointment and pimecrolimus 1% cream [Elidel®, generic]) [21.5% of patients]. At Week 8, Opzelura cream was found to be more effective in achieving IGA treatment success, defined as an IGA score of 0 (clear) or 1 (almost clear) with a ≥ 2-grade improvement from baseline. A third, non-pivotal, Phase II trial of Opzelura cream in a similar patient population included a triamcinolone acetonide 0.1% cream comparator arm.[3] At Week 4, Opzelura 1.5% cream produced greater improvement in the Eczema Area and Severity Index score from baseline; however, the treatment difference vs. triamcinolone was not statistically significant.

Vitiligo

One Phase III Opzelura study enrolled patients ≥ 12 years of age with a diagnosis of non-segmental vitiligo and depigmented areas covering ≤ 10% of their BSA.[4] While prior treatment was not a requirement for study enrollment, 61% of patients had received prior topical therapies for vitiligo, including topical corticosteroids and topical calcineurin inhibitors. Efficacy was evaluated at Week 24.

Guidelines

Atopic Dermatitis Guidelines

In general, the American Academy of Dermatology Guidelines of Care for the Management of Atopic Dermatitis (2014) recommends moisturizers/emollients as first-line therapy, followed by topical corticosteroids, when appropriate.[5] Topical calcineurin inhibitors are recommended for the treatment of atopic dermatitis, particularly when use of topical corticosteroids is not appropriate due to safety concerns (e.g., young infants, treatment of sensitive areas such as the face, eyelids, or genitalia). Opzelura is recommended for the treatment of patients with mild to moderate atopic dermatitis. However, Opzelura should not be used on more than 20% of the patient's BSA to avoid potential adverse events.

Vitiligo Guidelines

Guidelines from the International Vitiligo Task Force (2023) recommend topical corticosteroids, topical calcineurin inhibitors, and Opzelura as treatment options in patients with vitiligo.[6] Most of the studies to support the use of topical corticosteroids used potent to very potent corticosteroids applied topically daily for 3 to 6 months. Intermittent/alternating treatment schemes have been found to reduce adverse effects from topical corticosteroids and may enable longer treatment periods. Topical corticosteroids should be used with caution on the eyelids, axilla, and inguinal

regions. Topical calcineurin inhibitors are often prescribed initially for up to 6 months. The guidelines note that topical corticosteroids and topical calcineurin inhibitors have not been found to be different in terms of efficacy; however, there are safety differences. These therapies may be used in combination. The guidelines do not compare the efficacy of Opzelura with that of the other topical therapies.

Safety

Opzelura carries a Boxed Warning regarding the risk of serious infections, mortality, malignancy and lymphoproliferative disorders, major adverse cardiac events, and thrombosis.[1] Other Warnings and Precautions include thrombocytopenia, anemia, neutropenia, and lipid elevations. Based on these risks, critical evaluation and monitoring of certain patients are recommended in the Opzelura prescribing information.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Opzelura cream. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Opzelura cream as well as the monitoring required for adverse events and long-term efficacy, approval requires Opzelura cream to be prescribed by or in consultation with a physician who specializes in the condition being treated.

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is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Atopic Dermatitis.** Approve for 8 weeks if the patient meets ALL of the following (A, B, C, D, E, and F):
   - **A)** Patient is ≥ 12 years of age; AND
   - **B)** According to the prescriber, patient has mild to moderate atopic dermatitis; AND
   - **C)** Patient has atopic dermatitis involvement estimated to affect ≤ 20% of the body surface area; AND
   - **D)** Patient meets ONE of the following (i or ii):
     - **i.** Patient meets ALL of the following (a, b, and c):
       - **a)** Patient has tried at least one medium-, medium-high, high-, and/or super-high-potency prescription topical corticosteroid; AND
         Note: Concomitant use of a topical corticosteroid with a topical calcineurin inhibitor would meet the requirement.

b) This topical corticosteroid was applied daily for at least 28 consecutive days; AND

c) According to the prescriber, inadequate efficacy was demonstrated with this topical corticosteroid therapy; OR

ii. Patient is treating atopic dermatitis affecting one of the following areas: face, eyes/eyelids, skin folds, and/or genitalia; AND

E) Patients meets ALL of the following (i, ii, and iii):

i. Patient has tried at least one topical calcineurin inhibitor; AND
Note: Examples of topical calcineurin inhibitors include tacrolimus ointment (Protopic, generic) and pimecrolimus cream (Elidel, generic). Concomitant use of a topical calcineurin inhibitor with a topical corticosteroid would meet the requirement.

ii. This topical calcineurin inhibitor was applied daily for at least 28 consecutive days; AND

iii. According to the prescriber, inadequate efficacy was demonstrated with this topical calcineurin inhibitor; AND

F) The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist.

2. Vitiligo. Approve for 6 months if the patient meets ALL of the following (A, B, C, D, E, and F):

A) Patient is ≥ 12 years of age; AND

B) Patient has nonsegmental vitiligo; AND

C) Patient has vitiligo involvement estimated to affect ≤ 10% of the body surface area; AND

D) Patient meets ONE of the following (i or ii):

i. Patient meets ALL of the following (a, b, and c):

a) Patient has tried at least one high-, and/or super-high-potency prescription topical corticosteroid; AND
Note: Concomitant use of a topical corticosteroid with a topical calcineurin inhibitor would meet the requirement.

b) The duration of this topical corticosteroid therapy was at least 12 weeks; AND
Note: Intermittent or continuous use of a topical corticosteroid for at least 12 weeks would meet the requirement.

c) According to the prescriber, inadequate efficacy was demonstrated with this topical corticosteroid therapy; OR

ii. Patient is treating vitiligo affecting one of the following areas: face, eyes/eyelids, skin folds, and/or genitalia; AND

E) Patients meets ALL of the following (i, ii, and iii):

i. Patient has tried at least one topical calcineurin inhibitor; AND
Note: Examples of topical calcineurin inhibitors include tacrolimus ointment (Protopic, generic) and pimecrolimus cream (Elidel, generic). Concomitant use of a topical calcineurin inhibitor with a topical corticosteroid would meet the requirement.

ii. This topical calcineurin inhibitor was applied daily for at least 12 weeks; AND

iii. According to the prescriber, inadequate efficacy was demonstrated with this topical calcineurin inhibitor; AND

F) The medication is prescribed by or in consultation with a dermatologist.

CONDITIONS NOT COVERED

- **Opzelura® (ruxolitinib 1.5% cream – Incyte)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Use with a Biologic or with other JAK inhibitors.** Use of Opzelura in combination with therapeutic biologics or other JAK inhibitors is not recommended (see Appendix for examples).[1] Use of biologics or other JAK inhibitors was prohibited during the Opzelura pivotal studies.[2] There are no data evaluating combination use of Opzelura with these therapies; therefore, safety and efficacy of these combinations are unknown.

2. **Concurrent use with Other Potent Immunosuppressants** (e.g., azathioprine, cyclosporine). Use of Opzelura in combination with potent immunosuppressants is not recommended.[1] Use of systemic immunosuppressants was prohibited during the Opzelura pivotal studies.[2] There are no data evaluating combination of Opzelura with these therapies; therefore, safety and efficacy of these combinations are unknown.

3. **Alopecia.** Opzelura is not indicated for the treatment of alopecia.[1] A Phase II study involving patients with alopecia areata did not find any significant improvement in hair regrowth with Opzelura 1.5% cream compared with vehicle.[7] Additional data are needed to establish the efficacy and safety of Opzelura in patients with alopecia.

4. **Plaque Psoriasis.** Opzelura is not indicated for the treatment of plaque psoriasis.[1] There are very limited Phase II data regarding the use of Opzelura in patients with plaque psoriasis.[8,9] Additional data are needed to establish the efficacy and safety of Opzelura in patients with plaque psoriasis.

REFERENCES

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6. Seneschal J, Speekaert R, Taieb A, et al. Worldwide expert recommendations for the diagnosis and management of vitiligo: position statement from the International Vitiligo Task Force—Part 2: specific treatment recommendations. *J Eur Acad Dermatol Venereol*. 2023;37(11):2185-2195. .
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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	08/16/2023
Annual Revision	No criteria changes. The Appendix was updated to include the following biologic agents: Zymfentra (infliximab-dyyb subcutaneous [SC] injection), Omvoh™ (mirikizumab-mrkz SC and IV injection), Leqselvi™ (deuruxolitinib tablets), Litfulo™ (ritlecitinib capsules), Nemluvio® (nemlizumab-ilto SC injection), Zeposia® (ozanimod tablets), Velsipity® (etrasimod tablets), and biosimilars to Actemra.	09/04/2024

APPENDIX

Table 1. Examples of Other Therapeutic Biologics and Other JAK Inhibitors.

Product	Mechanism of Action
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF
Tocilizumab Products (Actemra® IV, biosimilar; Actemra SC, biosimilar)	Inhibition of IL-6
Kevzara® (sarilumab SC injection)	Inhibition of IL-6
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody
Kineret® (anakinra SC injection)	Inhibition of IL-1
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23
Siliq® (brodalumab SC injection)	Inhibition of IL-17
Cosentyx® (secukinumab SC injection)	Inhibition of IL-17A
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A
Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23
Omvoh™ (mirikizumab-mrkz SC injection, mirikizumab IV injection)	Inhibition of IL-23
Skyrizi® (risankizumab-rzaa SC injection)	Inhibition of IL-23
Tremfya® (guselkumab SC injection)	Inhibition of IL-23
Entyvio® (vedolizumab IV infusion)	Integrin receptor antagonist
Otezla® (apremilast tablets)	Inhibition of PDE4
Sotyktu™ (deucravacitinib tablets)	Inhibition of TYK2
Inrebic® (fedratinib tablets)	Inhibition of JAK pathways
Jakafi® (ruxolitinib tablets)	Inhibition of JAK pathways
Leqselvi™ (deuruxolitinib tablets)	Inhibition of JAK pathways
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways
Cibinqo® (abrocitinib tablets)	Inhibition of JAK pathways
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways
Xeljanz® (tofacitinib tablets, oral solution)	Inhibition of JAK pathways
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways
Litfulo™ (ritlecitinib capsules)	Inhibition of kinases
Xolair® (omalizumab SC injection)	IgE antagonist
Dupixent® (dupilumab SC injection)	IL-4 receptor antagonist
Cinqair® (reslizumab IV injection)	IL-5 antagonist
Nucala® (mepolizumab SC injection)	IL-5 antagonist
Fasenra® (benralizumab SC injection)	IL-5 receptor antagonist
Adbry® (tralokinumab-ldrm SC injection)	IL-13 antagonist
Nemluvio® (nemlizumab-ilto SC injection)	IL-31 receptor antagonist
Zeposia® (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator
Velsipity® (etrasimod tablets)	Sphingosine 1 phosphate receptor modulator
Tezspire® (tezepelumab-ekko SC injection)	TSLP blocker

JAK – Janus kinase; SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous; IL – Interleukin; PDE4 – Phosphodiesterase 4; TYK2 – Tyrosine kinase 2; IgE – Immunoglobulin E; TSLP – Thymic stromal lymphopoietin.