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Coverage Policy Number **IP0369**

Topical Ruxolitinib

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Related Coverage Resources

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Overview

This policy supports medical necessity review for **Opzelura®** (ruxolitinib) 1.5% cream.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Topical ruxolitinib (Opzelura) is considered medically necessary when ONE of the following is met:

1. **Mild to Moderate Atopic Dermatitis.** Individual meets **ALL** of the following criteria:
   A. Age 12 years or older
   B. Has atopic dermatitis involvement estimated to affect 20% or less of the body surface area (BSA)
   C. Documentation of **ONE** of the following:

i. Failure to **ONE** prescription topical corticosteroid (medium-potency or higher) applied for at least 14 consecutive days, unless contraindicated or intolerant
ii. Treating atopic dermatitis affecting one of the following areas: face, eyes/eyelids, skin folds, and/or genitalia

D. Documentation of failure to **ONE** topical calcineurin inhibitor (for example, tacrolimus ointment, pimecrolimus cream) applied for 6 consecutive weeks, unless contraindicated or intolerant
E. Medication is prescribed by, or in consultation with, an allergist, immunologist, or dermatologist

Concomitant use of a topical calcineurin inhibitor and topical corticosteroid would meet requirements [C] and [D].

2. **Nonsegmental Vitiligo.** Individual meets **ALL** of the following criteria:
   A. Age 12 years or older
   B. Has vitiligo involvement estimated to affect 10% or less of the body surface area (BSA)
   C. Documentation of **ONE** of the following:
      i. Failure to ONE prescription topical corticosteroid (medium potency or higher) applied for at least 12 weeks, unless contraindicated or intolerant
      ii. Treating vitiligo affecting one of the following areas: face, eyes/eyelids, skin folds, and/or genitalia
   D. Documentation of failure to ONE topical calcineurin inhibitor (for example, tacrolimus ointment, pimecrolimus cream) applied for at least 12 weeks, unless contraindicated or intolerant
   E. Medication is prescribed by, or in consultation with, a dermatologist

   Concomitant use of a topical calcineurin inhibitor with a topical corticosteroid would meet requirements [C] and [D].

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of topical ruxolitinib (Opzelura) is considered medically necessary for **ALL** covered diagnoses when the above medical necessity criteria are met AND there is documentation of beneficial response.

Examples of beneficial response to therapy include:
1. **Mild to Moderate Atopic Dermatitis**: improvement in estimated body surface area affected, erythema, induration/papulation/edema, excoriations, lichenification

2. **Nonsegmental Vitiligo**: repigmentation, improvement in Vitiligo Activity Scoring Index (VASI)

Authorization Duration

Initial approval duration:
1. Atopic Dermatitis: up to 6 months
2. Vitiligo: up to 6 months

Reauthorization approval duration:
1. Atopic Dermatitis: up to 6 months
2. Vitiligo: up to 6 months

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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.[9] 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.[10,11] Additional data are needed to establish the efficacy and safety of Opzelura in patients with plaque psoriasis.

Background

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-examined 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 (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.[3] A third, non-pivotal, Phase II trial of Opzelura cream in a similar patient population included a triamcinolone acetonide 0.1% cream comparator arm.[4] 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.[5] 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.[6] Topical calcineurin inhibitors (i.e., tacrolimus 0.03% and 0.1% ointment [Protopic®, generic] and pimecrolimus 1% cream [Elidel®, generic]) 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 British Association of Dermatologists for the management of vitiligo (2021) do not address Opzelura.[7] A potent or very potent topical corticosteroid therapy should be offered to patients. As an alternative to topical corticosteroids, topical tacrolimus, a calcineurin inhibitor, may be considered. These therapies may also be used in combination as part of an intermittent therapy regimen. In general, efficacy of a topical corticosteroid or topical calcineurin inhibitor may not be evident for 8 to 12 weeks.[8]

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 is recommended in the Opzelura prescribing information.

Appendix A
Table 1. Examples of Other Therapeutic Biologics and Other JAK Inhibitors.*, [12]

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
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	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
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
Inrebic® (fedratinib tablets)	Inhibition of JAK pathways
Jakafi® (ruxolitinib tablets)	Inhibition of JAK pathways
Olumiant® (baricitinib 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
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

* Not an all-inclusive list of indications; SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous; IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; IgE – Immunoglobulin E.

Table 2. Topical Corticosteroids, Classified According to Potency (Adapted from Facts/Comparisons).[12]

Potency/Group	Examples
Super-high potency (Group 1)	augmented betamethasone dipropionate 0.05% gel, lotion, ointment; clobetasol propionate 0.05% cream, cream (emollient base), foam aerosol, gel, lotion, ointment, shampoo, solution (scalp), spray aerosol; fluocinonide 0.1% cream; flurandrenolide 4 mcg/cm^2 tape; halobetasol propionate 0.05% cream, lotion, ointment.
High potency (Group 2)	amcinonide 0.1% ointment; betamethasone dipropionate 0.05% cream (augmented), ointment; clobetasol propionate 0.025% cream; desoximetasone 0.25% cream, ointment, spray; desoximetasone 0.05% gel; diflorasone diacetate 0.05% cream (emollient), ointment; fluocinonide 0.05% cream, gel, ointment, solution; halcinonide 0.1% cream, ointment; halobetasol propionate 0.01% lotion.
Medium-High potency (Group 3)	amcinonide 0.1% cream, lotion; betamethasone dipropionate 0.05% cream (hydrophilic emollient); betamethasone valerate 0.1% ointment; betamethasone valerate 0.12% foam; desoximetasone 0.05% cream; diflorasone diacetate 0.05% cream; fluocinonide 0.05% cream (aqueous emollient); fluticasone propionate 0.005% ointment; mometasone furoate 0.1% ointment; triamcinolone acetonide 0.5% cream, ointment.
Medium potency (Group 4)	betamethasone propionate 0.05% spray; clocortolone pivalate 0.1% cream; fluocinolone acetonide 0.025% ointment; flurandrenolide 0.05% ointment; hydrocortisone valerate 0.2% ointment; mometasone furoate 0.1% cream, lotion, ointment, solution; triamcinolone acetonide 0.1% cream, ointment; triamcinolone acetonide 0.05% ointment; triamcinolone acetonide 0.2 mg aerosol spray.
Lower-mid potency (Group 5)	betamethasone dipropionate 0.05% lotion; betamethasone valerate 0.1% cream; desonide 0.05% gel, ointment; fluocinolone acetonide 0.025% cream; flurandrenolide 0.05% cream, lotion; fluticasone propionate 0.05% cream, lotion; hydrocortisone butyrate 0.1% cream, lotion, ointment, solution; hydrocortisone probutate 0.1% cream; hydrocortisone valerate 0.2% cream; prednicarbate 0.1% cream (emollient), ointment; triamcinolone acetonide 0.1% lotion; triamcinolone acetonide 0.025% ointment.
Low potency (Group 6)	aclometasone dipropionate 0.05% cream, ointment; betamethasone valerate 0.1% lotion; desonide 0.05% cream, foam, lotion; fluocinolone acetonide 0.01% cream, oil, shampoo, solution; triamcinolone acetonide 0.025% cream, lotion.
Least potent (Group 7)	hydrocortisone 2.5% cream, ointment, solution; hydrocortisone 2% lotion; hydrocortisone 1% cream, gel, lotion, ointment, solution, spray; hydrocortisone 0.5% cream, ointment; hydrocortisone acetate 2.5% cream; hydrocortisone acetate 2% lotion.

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