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| **Section:** | Prescription Drugs | **Effective Date:** | October 1, 2023 |
| **Subsection:** | Topical Products | **Original Policy Date:** | October 22, 2021 |
| **Subject:** | Opzelura | **Page:** | 1 of 9 |

***Last Review Date:*** September 8, 2023

# Opzelura

## Description

### Opzelura (ruxolitinib)

**Background**
Opzelura (ruxolitinib) is indicated for the topical treatment of mild to moderate atopic dermatitis and nonsegmental vitiligo. Atopic dermatitis, a chronic inflammatory skin disease, is often referred to as "eczema," which is a general term for the several types of inflammation of the skin. Atopic dermatitis is the most common of the many types of eczema and onset typically begins in childhood and can last through adulthood. The cause of atopic dermatitis is a combination of genetic, immune and environmental factors. Opzelura is a topical Janus kinase (JAK) inhibitor. Janus kinases (JAK1 and JAK2) are involved in a signaling cascade that recruits signal transducers and activators of transcription (STATs) to the nucleus leading to modulation of gene expression for many pathways including immune function (1).

**Regulatory Status**
FDA-approved indications: Opzelura is a Janus kinase (JAK) inhibitor indicated for (1):

- the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adult and pediatric patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.
- the topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older.

Limitations of Use:
Use of Opzelura in combination with therapeutic biologics, other JAK inhibitors, or potent immunosuppressants such as azathioprine or cyclosporine is not recommended (1).

Opzelura has a boxed warning regarding serious infections. Serious infections have occurred in patients receiving oral JAK inhibitors and serious lower respiratory tract infections were reported by patients using topical ruxolitinib. Use in active, serious infection should be avoided. Risks and benefits should be carefully considered before using in patients with a history of or at an increased risk for: chronic or recurrent infection, opportunistic infection, or tuberculosis. All patients should be closely monitored for development of infection and treatment interrupted and permanently discontinued as appropriate (1).

Opzelura also carries boxed warnings for mortality and major adverse cardiovascular events (MACE). A higher risk of all-cause mortality, including sudden cardiovascular death was observed in clinical trials of oral JAK inhibitors. Additionally, these clinical trials recorded MACE, which includes fatal cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke. The risks and benefits of treatment with Opzelura should be carefully considered before prior to initiating or continuing treatment (1).

The last boxed warnings are regarding malignancies and thrombosis. Lymphoma and other malignancies have been observed in patients treated with oral Janus kinase inhibitors. Non-melanoma skin cancers, including basal cell and squamous cell have occurred in patients treated with Opzelura. Thrombosis, including pulmonary embolism, deep venous thrombosis, and arterial thrombosis have occurred in patients treated with oral JAK inhibitors used to treat inflammatory conditions (1).

Opzelura has a maximum dose of 60 grams (one tube) per week. The manufacturer notes that it expects typical use to be 3-4 tubes of medication per year (1-2).

The safety and effectiveness of Opzelura in patients less than 12 years of age have not been established (1).

**Related policies**
Eucrisa

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Opzelura may be considered **medically necessary** if the conditions indicated below are met.

Opzelura may be considered **investigational** for all other indications.

## Prior-Approval Requirements

**Age** 12 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Mild to moderate atopic dermatitis (eczema)
   a. 18 years of age or older
      i. Inadequate treatment response, intolerance, or contraindication to **ONE** medication in **EACH** of the following categories:
         1) Topical calcineurin inhibitor (see Appendix I)
         2) **High** potency topical corticosteroid (see Appendix II)
      ii. Prescriber agrees that treatment will be stopped when signs and symptoms resolve **OR** that the patient will be treated for no longer than 8 weeks at a time

   b. 12 to 17 years of age
      i. Inadequate treatment response, intolerance, or contraindication to **ONE** medication in **EACH** of the following categories:
         1) Topical calcineurin inhibitor (see Appendix I)
         2) A topical corticosteroid (see Appendix II)
      ii. Prescriber agrees that treatment will be stopped when signs and symptoms resolve **OR** that the patient will be treated for no longer than 8 weeks at a time

   c. Documented baseline evaluation of the condition using **ONE** of the following scoring tools:
      i. Investigator's Static Global Assessment (ISGA) score
      *(*e.g., *https://www.eczemacouncil.org/assets/docs/Validated-Investigator-Global-Assessment-Scale_vIGA-AD_2017.pdf)*
      ii. Eczema Area and Severity Index (EASI)
      (e.g., *https://dermnetnz.org/topics/easi-score/*)

iii. Patient-Oriented Eczema Measure (POEM)
*(*e.g., *https://jamanetwork.com/data/Journals/DERM/11776/dea40003f1.png)*
iv. Scoring Atopic Dermatitis (SCORAD) index
(e.g., *https://dermnetnz.org/topics/scorad/)*

2. Nonsegmental vitiligo
   a. Inadequate treatment response, intolerance, or contraindication to **ONE** medication in **EACH** of the following categories:
      i. Topical calcineurin inhibitor (see Appendix I)
      ii. A topical corticosteroid (see Appendix II)

   b. Other causes of depigmentation (e.g., tinea versicolor, albinism, age spots, melasma, piebaldism, hypopigmented mycosis, pityriasis alba, etc.) have been ruled out

**AND ALL** of the following for **ALL** indications:
   a. Patient is **NOT** immunocompromised
   b. Prescriber agrees to evaluate patient for latent and active TB infections prior to and during treatment with Opzelura therapy, as appropriate
   c. **NO** active bacterial, invasive fungal, viral, or other opportunistic infections
   d. **NOT** used in combination with potent immunosuppressants, such as azathioprine or cyclosporine
   e. Prescriber has assessed the patient's risk factors for malignancy and major adverse cardiovascular events (MACE) (e.g., advanced age, smoking history, etc.) and determined that treatment with Opzelura therapy is appropriate
   f. **NO** dual therapy with Eucrisa (crisaborole)

## Prior – Approval *Renewal* Requirements

**Age** 12 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Atopic dermatitis (eczema)
   a. Documented improvement using **ONE** of the following scores:
      i. ISGA – decrease from baseline by at least 2 points

(e.g., *https://www.eczemacouncil.org/assets/docs/Validated-Investigator-Global-Assessment-Scale_vIGA-AD_2017.pdf*)

ii. EASI – decrease from baseline by at least 75%
(e.g., *https://dermnetnz.org/topics/easi-score/*)

iii. POEM – decrease from baseline by at least 3 points
(e.g., *https://jamanetwork.com/data/Journals/DERM/11776/dea40003f1.png*)

iv. SCORAD – decrease from baseline by at least 50%
(e.g., *https://dermnetnz.org/topics/scorad/*)

b. Prescriber agrees that treatment will be stopped when signs and symptoms resolve **OR** that the patient will be treated for no longer than 8 weeks at a time

2. Nonsegmental vitiligo
   a. Condition has improved or stabilized

**AND ALL** of the following for **ALL** indications:

a. Patient is **NOT** immunocompromised
b. **NO** active bacterial, invasive fungal, viral, or other opportunistic infections
c. **NOT** used in combination with potent immunosuppressants, such as azathioprine or cyclosporine
d. Prescriber has assessed the patient's risk factors for malignancy and major adverse cardiovascular events (MACE) (e.g., advanced age, smoking history, etc.) and determined that treatment with Opzelura therapy is appropriate
e. **NO** dual therapy with Eucrisa (crisaborole)

## Policy Guidelines

### Pre – PA Allowance

None

### Prior - Approval Limits

**Atopic dermatitis**

| | |
|---|---|
| **Quantity** | 4 tubes |
| **Duration** | 12 months |

**Nonsegmental vitiligo**

| | |
|---|---|
| **Quantity** | 12 tubes |
| **Duration** | 12 months |

## Prior – Approval *Renewal* Limits

Same as above

## Rationale

**Summary**

Opzelura (ruxolitinib) is a topical JAK inhibitor indicated for the treatment of mild to moderate atopic dermatitis and nonsegmental vitiligo in patients 12 years of age and older. Opzelura carries boxed warnings regarding infection, mortality, malignancy, MACE, and thrombosis. Patients should be carefully evaluated for risks of benefits of treatment before initiating or continuing therapy. The safety and effectiveness of Opzelura in patients less than 12 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Opzelura while maintaining optimal therapeutic outcomes.

**References**

1. Opzelura [package insert]. Wilmington, DE: Incyte Corporation.; January 2023.
2. Opzelura (ruxolitinib) cream FDA Approval Call; Incyte Manufacturer Website; https://s21.q4cdn.com/114423841/files/doc_presentations/2021/Rux-Cream-approval-call_v31_no-notes.pdf; September 22, 2021.

## Policy History

| Date | Action |
|---|---|
| October 2021 | Addition to PA |
| December 2021 | Annual review |
| July 2022 | Per PI update – addition of vitiligo to criteria noting that it is excluded from coverage |
| September 2022 | Annual review |
| October 2022 | Per FEP revised TB requirement to “Prescriber agrees to evaluate patient for latent and active TB infections prior to and during treatment with Opzelura therapy, as appropriate” |
| December 2022 | Annual review |
| January 2023 | Changed Appendix 2 and moved fluradrenolide tape to very high potency |
| March 2023 | Annual review |

| | |
|---|---|
| September 2023 | Annual review and reference update. Per SME, added indication of nonsegmental vitiligo |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 8, 2023 and is effective on October 1, 2023.**

## Appendix 1

| Relative Potency of Topical Calcineurin Inhibitors | | |
|---|---|---|
| **Drug** | **Dosage Form** | **Strength** |
| ***Medium Potency*** | | |
| Tacrolimus | Ointment | 0.1% |
| ***Low Potency*** | | |
| Tacrolimus | Ointment | 0.03% |
| Pimecrolimus | Cream | 1% |

## Appendix 2

| Relative Potency of Selected Topical Corticosteroids | | |
|---|---|---|
| **Drug** | **Dosage Form** | **Strength** |
| ***Very high Potency*** | | |
| Augmented betamethasone dipropionate | Ointment, Gel | 0.05% |
| Clobetasol propionate | Cream, Ointment | 0.05% |
| Diflorasone diacetate | Ointment | 0.05% |
| Flurandrenolide | Tape | 4 mcg/cm2 |
| Halobetasol propionate | Cream, Ointment | 0.05% |
| ***High Potency*** | | |
| Amcinonide | Cream, Lotion, Ointment | 0.1% |
| Augmented betamethasone dipropionate | Cream, Lotion | 0.05% |
| Betamethasone dipropionate | Cream, Ointment | 0.05% |
| Betamethasone valerate | Ointment | 0.1% |
| Desoximetasone | Cream, Ointment | 0.25% |
| | Gel | 0.05% |
| Diflorasone diacetate | Cream, Ointment (emollient base) | 0.05% |
| Fluocinonide | Cream, Ointment, Gel | 0.05% |
| Halcinonide | Cream, Ointment | 0.1% |
| Triamcinolone acetonide | Cream, Ointment | 0.5% |
| ***Medium Potency*** | | |
| Betamethasone dipropionate | Lotion | 0.05% |

| | | |
|---|---|---|
| Betamethasone valerate | Cream | 0.1% |
| Clocortolone pivalate | Cream | 0.1% |
| Desoximetasone | Cream | 0.05% |
| Fluocinolone acetonide | Cream, Ointment | 0.025% |
| Flurandrenolide | Cream, Ointment, Lotion | 0.05% |
| Fluticasone propionate | Cream | 0.05% |
| | Ointment | 0.005% |
| Hydrocortisone butyrate | Ointment, Solution | 0.1% |
| Hydrocortisone valerate | Cream, Ointment | 0.2% |
| Mometasone furoate | Cream, Ointment, Lotion | 0.1% |
| Prednicarbate | Cream, Ointment | 0.1% |
| Triamcinolone acetonide | Cream, Ointment, Lotion | 0.025% |
| | Cream, Ointment, Lotion | 0.1% |
| ***Low Potency*** | | |
| Alclometasone dipropionate | Cream, Ointment | 0.05% |
| Desonide | Cream | 0.05% |
| Fluocinolone acetonide | Cream, Solution | 0.01% |
| Hydrocortisone | Lotion | 0.25% |
| | Cream, Ointment, Lotion, Aerosol | 0.5% |
| | Cream, Ointment, Lotion, Solution | 1% |
| | Cream, Ointment, Lotion | 2.5% |
| Hydrocortisone acetate | Cream, Ointment | 0.5% |
| | Cream, Ointment | 1% |