**Effective Date: 11/30/22**
**Last P&T Approval/Version:**
**Next Review Due By:**
**Policy Number: C24359-A**

# Opzelura (ruxolitinib) IL Medicaid Only

## PRODUCTS AFFECTED

Opzelura (ruxolitinib)

## COVERAGE POLICY

*Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.*
*This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines*

***Documentation Requirements:***
*Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive*

**DIAGNOSIS:**
Atopic Dermatitis, Vitiligo

**REQUIRED MEDICAL INFORMATION:**
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. ATOPIC DERMATITIS:
   1. Documented diagnosis of mild to moderate atopic dermatitis
      AND
   2. Documentation that the member experienced an inadequate treatment response (minimum 2-consecutive week trial), intolerance, or contraindication (e.g., areas involving the face, neck or intertriginous areas) to at least TWO formulary medium or high potency topical steroids (see Appendix)
      AND

3. Documentation that member experienced an inadequate treatment response (minimum of 6-week consecutive trial), intolerance or contraindication to ONE preferred/formulary topical calcineurin inhibitor (tacrolimus, pimecrolimus)
   AND
4. Prescriber attest member is non immunocompromised AND that Opzelura (ruxolitinib) will not be used concurrently with other therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine

B. VITILIGO:
1. Documentation that the member experienced an inadequate treatment response (minimum 2-week trial), intolerance, or contraindication (e.g., areas involving the face, neck or intertriginous areas) to at least TWO formulary topical steroids (see Appendix)
   AND
2. Documentation that member experience an inadequate treatment response (minimum of 6-week consecutive trial), intolerance or contraindication to ONE preferred/formulary topical calcineurin inhibitor (tacrolimus, pimecrolimus)
3. Prescriber attest member is non immunocompromised AND that Opzelura (ruxolitinib) will not be used concurrently with other therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine

**CONTINUATION OF THERAPY:**

A. ALL INDICATIONS:
1. Documentation of no intolerable adverse effects or drug toxicity
   AND
2. Documentation that member's condition has improved based upon the prescriber's assessment of disease control and clinical improvements while on therapy (e.g., reduction of affected BSA, improvements in severity of eczematous lesions, decrease in pruritus severity)

**DURATION OF APPROVAL:**

Initial authorization atopic dermatitis: 3 months, Continuation of Therapy: 6 months
Initial authorization vitiligo: 6 months, Continuation of Therapy 12 months

**PRESCRIBER REQUIREMENTS:**

Prescribed by or in consultation with a board-certified dermatologist, allergist/immunologist [If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

**AGE RESTRICTIONS:**

12 years of age and older

**QUANTITY:**

maximum of 60 grams/week, 240grams/month

**PLACE OF ADMINISTRATION:**

The recommendation is that topical medications in this policy will be for pharmacy benefit coverage and patient self-administered.

## DRUG INFORMATION

**ROUTE OF ADMINISTRATION:**

Topical

**DRUG CLASS:**

Atopic Dermatitis - Janus Kinase (JAK) Inhibitors

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

*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*

**COMPENDIAL APPROVED OFF-LABELED USES:**
None

## APPENDIX

### APPENDIX:

**Very High Potency**
Betamethasone dipropionate (augmented)
Clobetasol
Diflorasone diacetate ointment
Halobetasol

**High Potency**
Amcinonide
Betamethasone dipropionate
Desoximetasone gel, ointment, or cream 0.25% or more
Diflorasone diacetate cream
Fluocinolone cream 0.2% or more
Fluocinonide
Halcinonide
Triamcinolone 0.5% or more

**Medium Potency**
Beclomethasone
Betamethasone benzoate
Betamethasone valerate
Hydrocortisone acetate
Clobetasone
Clocortolone
Desoximetasone cream less than 0.25%
Diflucortolone
Fluocinolone ointment or topical solution or cream less than 0.2%
Flurandrenolide 0.025% or more
Fluticasone
Hydrocortisone butyrate
Hydrocortisone valerate Mometasone
Prednicarbate
Triamcinolone less than 0.5%

**Low Potency**
Alclometasone
Desonide
Dexamethasone
Flumethasone
Flurandrenolide less than 0.025%
Hydrocortisone

## BACKGROUND AND OTHER CONSIDERATIONS

**BACKGROUND:**
Atopic dermatitis (also known as atopic eczema) is a chronic, pruritic, inflammatory skin disease that is characterized by recurrent eczematous lesions. Clinical features of atopic dermatitis include skin dryness, erythema, oozing and crusting, lichenification with a hallmark of the condition being pruritus.
Originally regarded as a childhood disorder mediated by an imbalance towards a T-helper-2 response and exaggerated IgE responses to allergens, it is now recognized as a lifelong disposition with variable clinical manifestations and expressivity, in which defects of the epidermal barrier are central. Present prevention and treatment focus on restoration of epidermal barrier function, which is best achieved through the use of emollients. Topical corticosteroids are still the first-line therapy

for acute flares, but they are also used proactively along with topical calcineurin inhibitors to maintain remission. Non-specific immunosuppressive drugs are used in severe refractory cases.

Vitiligo is a chronic disease that targets melanocytes, causing skin depigmentation which leaves the skin looking white or pink in appearance. One major type of vitiligo is called NSV, which is thought to be an autoimmune disease and can be associated with the presence of other autoimmune diseases such as autoimmune thyroid disorders. Vitiligo shows a familial trait in about 20% of patients, but its heritability and the genes involved are poorly understood and environmental factors also play a role.

Topical ruxolitinib, a Janus kinase (JAK) inhibitor, is a new short-term therapy for atopic dermatitis (AD). In two randomized trials that enrolled over 1200 adolescents and adults with mild to moderate AD (<20 percent of body surface area affected) not controlled by topical prescription medications, more individuals assigned to ruxolitinib cream (0.75% or 1.5%) achieved clear or almost clear skin and reduced pruritis with no increase in adverse effects compared with vehicle [1]. Based on these findings, topical ruxolitinib has been approved by the US Food and Drug Administration for the short-term treatment of mild to moderate AD in immunocompetent individuals with the characteristics of the study participants. Although topical ruxolitinib appears promising, more data are needed regarding its systemic absorption and long-term safety before its use becomes routine.

The FDA approval was based on data from the TRuE-AD (Topical Ruxolitinib Evaluation in Atopic Dermatitis) clinical trial program, consisting of two randomized, double-blind, vehicle-controlled Phase 3 studies (TRuE-AD1 and TRuE-AD 2) evaluating the safety and efficacy of Opzelura in more than 1,200 adolescents and adults with mild to moderate AD. Results from the studies showed patients experienced significantly clearer skin and itch reduction when treated with Opzelura cream 1.5% twice daily (BID), compared to vehicle (non-medicated cream):

- Significantly more patients treated with Opzelura achieved Investigator's Global Assessment (IGA) Treatment Success (IGA-TS, primary endpoint) at Week 8 (defined as an IGA score of 0 [clear] or 1 [almost clear] with at least a 2-point improvement from baseline): 53.8% in TRuE-AD1 and 51.3% in TRuE-AD2, compared to vehicle (15.1% in TRuE-AD1, 7.6% in TRuE-AD2; P<0.0001).
- Significantly more patients treated with Opzelura experienced a clinically meaningful reduction in itch from baseline at Week 8, as measured by a ≥4-point reduction in the itch Numerical Rating Scale (itch NRS4): 52.2% in TRuE-AD1 and 50.7% in TRuE-AD2, compared to vehicle (15.4% in TRuE-AD1, 16.3% in TRuE-AD2; P<0.0001), among patients with an NRS score of at least 4 at baseline.

In clinical trials, the most common (≥1%) treatment-emergent adverse reactions in patients treated with Opzelura were nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increased, urticaria, folliculitis, tonsillitis and rhinorrhea2. See Important Safety Information below, including Boxed Warnings for serious infections, mortality, malignancy, major adverse cardiovascular events and thrombosis, seen with JAK inhibitors for inflammatory conditions..

Opzelura (ruxolitinib) cream 1.5% was FDA-approved for the topical treatment of nonsegmental vitiligo (NSV) in adult and pediatric patients 12 years of age and older. Opzelura is a topical Janus kinase (JAK) 1 and JAK 2 inhibitor. This approval makes Opzelura the first FDA-approved treatment for NSV, and the drug works by promoting repigmentation.

In NSV, Opzelura is for continuous topical use twice daily to affected areas of up to 10% body surface area (BSA). According to the drug's prescribing information, satisfactory patient response may require treatment with Opzelura for more than 24 weeks: "If the patient does not find the repigmentation meaningful by 24 weeks, the patient should be re-evaluated by the healthcare provider." In AD, Opzelura is not approved for chronic use; it is applied continuously twice daily for up to 8 weeks, and then it is applied as needed.

Approval for the NSV indication was based on data from two duplicate Phase 3 clinical trials [TRuE-V1 (NCT04052425) and TRuE-V2 (NCT04057573)] evaluating Opzelura in 674 patients 12 years of age and older with NSV. Trial participants were required to have depigmentation affecting ≥0.5% facial BSA, ≥3% nonfacial BSA, and a total BSA (facial and nonfacial) not exceeding 10%. At Week 24, about 30% of patients treated with Opzelura twice a day achieved at least a 75% improvement from baseline in the facial Vitiligo Area Scoring Index (F-VASI75), the primary endpoint, compared with about 8% and 13% of those in the vehicle groups of the two trials. At Week 52, about 50% of patients treated with Opzelura achieved F-VASI75 and about 20% of patients achieved a 75% reduction in the total body Vitiligo Area Scoring Index (T-VASI75).

**CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:**
All other uses of Opzelura (ruxolitinib) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Opzelura (ruxolitinib) include: no FDA labeled contraindications at this time.

**OTHER SPECIAL CONSIDERATIONS:**
DOSAGE AND ADMINISTRATION
ATOPIC DERMATITIS
Instruct patients to apply a thin layer of OPZELURA twice daily to affected areas of up to 20% body surface area. Do not use more than 60 grams per week. OPZELURA is for topical use only. OPZELURA is not for ophthalmic, oral, or intravaginal use. Stop using when signs and symptoms (e.g., itch, rash, and redness) of atopic dermatitis resolve. If signs and symptoms do not improve within 8 weeks, patients should be reexamined by their healthcare provider

VITILIGO:
Instruct patients to apply a think layer of OPZELURA twice daily to affected areas of up to 10% of total body surface area. Do not use more than 60 grams per week. It may require 24 weeks of treatment for a satisfactory response; if after 24 weeks of therapy, meaningful repigmentation has not been observed, reexamination by health care provider is recommended.

BLACK BOX WARNING: WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE), AND THROMBOSIS

- Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving Janus kinase inhibitors for inflammatory conditions.
- Higher rate of all-cause mortality, including sudden cardiovascular death have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions.
- Lymphoma and other malignancies have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions.
- Higher rate of MACE (including cardiovascular death, myocardial infarction, and stroke)

has been observed in patients treated with Janus kinase inhibitors for inflammatory conditions.

- Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis, some fatal, have occurred in patients treated with Janus kinase inhibitors for inflammatory conditions.

## CODING/BILLING INFORMATION

*Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement*

| HCPCS CODE | DESCRIPTION |
|---|---|
| NA | |

**AVAILABLE DOSAGE FORMS**:
Opzelura Cream 1.5% 60-gram tube

## REFERENCES


1. Opzelura (ruxolitinib) [prescribing information]. Wilmington, DE: Incyte Corporation; July 2022.
2. Papp K, Szepietowski JC, Kircik L, et al. Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: results from 2 phase 3, randomized, double-blind studies. J Am Acad Dermatol. 2021;85(4):863-872. doi:10.1016/j.jaad.2021.04.085
3. Weidinger S, Novak N. Atopic dermatitis. Lancet. 2016 Mar 12;387(10023):1109-1122. doi: 10.1016/S0140-6736(15)00149-X. Epub 2015 Sep 13. PMID: 26377142.
4. Gong X, Chen X, Kuligowski ME, Liu X, Liu X, Cimino E, McGee R, Yeleswaram S. Pharmacokinetics of Ruxolitinib in Patients with Atopic Dermatitis Treated With Ruxolitinib Cream: Data from Phase II and III Studies. Am J Clin Dermatol. 2021 Jul;22(4):555-566. doi: 10.1007/s40257-021-00610-x. Epub 2021 May 12.
5. Scuron MD, Fay BL, Connell AJ, Peel MT, Smith PA. Ruxolitinib Cream Has Dual Efficacy on Pruritus and Inflammation in Experimental Dermatitis. Front Immunol. 2021 Feb 15;11:620098. doi: 10.3389/fimmu.2020.620098. eCollection 2020.
6. Rosmarin D, Passeron T, Pandya AG, Grimes P, Harris JE, Desai SR, Lebwohl M, Ruer-Mulard M, Seneschal J, Wolkerstorfer A, Kornacki D, Sun K, Butler K, Ezzedine K; TRuE-V Study Group. Two Phase 3, Randomized, Controlled Trials of Ruxolitinib Cream for Vitiligo. N Engl J Med. 2022 Oct 20;387(16):1445-1455. doi: 10.1056/NEJMoa2118828.