Original Effective Date: 02/01/2022
Current Effective Date: 07/17/2025
Last P&T Approval/Version: 04/30/2025
Next Review Due By: 04/2026
Policy Number: C22277-A

Opzelura (ruxolitinib)

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, Nonsegmental 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. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. ATOPIC DERMATITIS:
   1. Documented diagnosis of mild to moderate atopic dermatitis (eczema)
      AND

2. Documentation treatment area is ≤ 20%
   AND
3. Documentation of inadequate response, serious side effects, or contraindication to TWO of the following: topical corticosteroids or preferred/formulary topical calcineurin inhibitor (tacrolimus, pimecrolimus)
   AND
4. Documentation of prescriber baseline assessment of disease activity (e.g., affected BSA, severity of eczematous lesions, pruritus, etc.)
   AND
5. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or serious side effects to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).

B. NONSEGMENTAL VITILIGO:

1. Documented diagnosis of nonsegmental vitiligo
   AND
2. Documentation treatment area is ≤10% BSA
   AND
3. Documentation that the member experienced an inadequate treatment response, serious side effects, or contraindication (e.g., areas involving the face, neck or intertriginous areas) to at least TWO preferred/formulary medium or higher potency topical steroids (see Appendix)
   AND
4. Documentation that member experienced an inadequate treatment response, serious side effects or contraindication to ONE preferred/formulary topical calcineurin inhibitor (tacrolimus, pimecrolimus)
   AND
5. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., depigmentation, vitiligo scoring tools, quality of life, etc.)

CONTINUATION OF THERAPY:

A. ATOPIC DERMATITIS, NONSEGMENTAL VITILIGO:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. 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, repigmentation, vitiligo scoring tool improvement, quality of life improvement)

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

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

AGE RESTRICTIONS:

12 years of age and older

QUANTITY:
Maximum of 60 grams/week, 100 grams/2 weeks

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 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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

Topical Steroids by Potency

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.

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 pruritus 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.

Vitiligo is an acquired depigmenting disorder that does not have prevalence in one gender or another and which affects all age groups. Vitiligo is characterized by the progressive loss of melanocytes, leaving white patches on the skin. It is usually diagnosed by clinical examination alone supported by Wood's lamp examination. Vitiligo technically comprises two different forms – segmental and non- segmental. Both forms can be classified by their disease activity – rapidly progressing or stable. Assessment is made through visualization of lesions and BSA impacted. There are standardized assessments that can be used (Vitiligo Signs of Activity Score (VSAS), Vitiligo Disease Activity Score (VDAS) and Vitiligo Disease Improvement Score (VDIS)). Quality of life should also be considered.

Therapeutic options for vitiligo include topical therapy, phototherapy, and surgical interventions depending on the type, extent, and activity. For topical treatment, potent to very potent corticosteroids and the topical calcineurin inhibitors tacrolimus and pimecrolimus can be recommended. The topical JAK inhibitor ruxolitinib is approved for treatment of non-segmental vitiligo and can also be used. Where recommended, Most studies used potent to very potent corticosteroids once daily, applied topically for 3– 6 months. Alternating dosing schedules (2 weeks on/2 weeks off) may enable longer treatment periods. Topical calcineurin inhibitors are first-line treatment in adults and children with limited involvement, especially for lesions in the face, neck and body folds with thin skin (e.g. inguinal, axillary regions). The treatment should be prescribed initially for 6 months. When effective, prolonged treatment (e.g. up to 12 months or more) can be proposed.

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.

Exclusions/Discontinuation:

Do not use for atopic dermatitis in immunocompromised patients per FDA label.
Do not use concurrently with other therapeutic biologics, other JAK inhibitors, or potent immunosuppressants such as azathioprine or cyclosporine.
If signs and symptoms of atopic dermatitis do not improve within 8 weeks, patients should be re-examined by their healthcare provider.
Satisfactory patient response for vitiligo 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.

OTHER SPECIAL CONSIDERATIONS:

DOSAGE AND ADMINISTRATION

Instruct patients to apply a thin layer of Opzelura twice daily to affected areas. Do not use more than 60 grams per week. Opzelura is for topical use only. Opzelura is not for ophthalmic, oral, or intravaginal use.

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

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Opzelura CREA 1.5% 60-gram tube

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Quantity Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q2 2025
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Background References	Q4 2024
REVISION- Notable revisions: Diagnosis Required Medical Information References	Q2 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy FDA-Approved Uses References	Q2 2023
REVISION- Notable revisions: Required Medical Information FDA Approved Uses	Q4 2022
Q2 2022 Established tracking in new format	Historical changes on file