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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.

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 preferred/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. Documentation of prescriber baseline assessment of disease activity (e.g., affected BSA, severity of eczematous lesions, pruritis, etc.)
AND
5. Prescriber attests member is not immunocompromised
AND
6. Prescriber attests that Opzelura (ruxolitinib) will not be used concurrently with other therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine

B. NONSEGMENTAL VITILIGO:

REVIEWER NOTE: PLEASE FIRST REFER TO STATE AND LINE OF BUSINESS EXPLANATION OF BENEFITS TO DETERMINE IF HAIR LOSS/COSMETIC INDICATIONS ARE A COVERED BENEFIT.

Opzelura (ruxolitinib) is excluded from coverage for nonsegmental vitiligo per Social Security 1927(d)(2)(A)

A State may exclude or otherwise restrict coverage of a covered outpatient drug if the drug is contained in the list:

- Agents when used for anorexia, weight loss, or weight gain.
- Agents when used to promote fertility.
- **Agents when used for cosmetic purposes or hair growth.**
- Agents when used for the symptomatic relief of cough and colds.
- Agents when used to promote smoking cessation.
- Prescription vitamins and mineral products, except prenatal vitamins and fluoride preparations.
- Nonprescription drugs, except, in the case of pregnant women when recommended in accordance with the Guideline referred to in section 1905(bb)(2)(A), agents approved by the Food and Drug Administration under the over-the-counter monograph process for purposes of promoting, and when used to promote, tobacco cessation.
- Covered outpatient drugs which the manufacturer seeks to require as a condition of sale that associated tests or monitoring services be purchased exclusively from the manufacturer or its designee.
- Barbiturates.
- Benzodiazepines.
- Agents when used for the treatment of sexual or erectile dysfunction, unless such agents are used to treat a condition, other than sexual or erectile dysfunction, for which the agents have been approved by the Food and Drug Administration.

CONTINUATION OF THERAPY:

A. ATOPIC DERMATITIS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history
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)

DURATION OF APPROVAL:
Initial authorization: 3 months, Continuation of Therapy: 3 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, 240 grams/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 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:

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 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.

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

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.

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; January 2023
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. Sidbury R, Alikhan A, Bercovitch L, Cohen DE, Darr JM, Drucker AM, Eichenfield LF, Frazer-Green L, Paller AS, Schwarzenberger K, Silverberg JI, Singh AM, Wu PA, Davis DMR, Guidelines of care for the management of atopic dermatitis in adults with topical therapies, Journal of the American Academy of Dermatology (2023), doi: https://doi.org/10.1016/j.jaad.2022.12.029.

SUMMARY OF REVIEW/REVISIONS	DATE
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