BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

OPZELURA™ (ruxolitinib) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Opzelura (ruxolitinib) cream and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Dermatologist

2. Individual is 12 years of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in a **non-immune compromised** individual who is not adequately controlled with topical prescription therapies or when these therapies are not advisable (see Definitions section)

b. Topical treatment of nonsegmental vitiligo

4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. **For atopic dermatitis**:
      i. Affected area **is less than** 20% of body surface area
      ii. Intensity of pruritus is described as moderate (see Definitions section)
      iii. Appearance of lesions are described as mild or moderate (see Definitions section)
   b. **For vitiligo**:
      i. Affected area **is less than** 10% of body surface area

5. **ONE** of the following:
   a. **For atopic dermatitis:**
      i. **For eyelids, face, neck intertriginous and genital areas, or other areas at high risk for atrophy**:
         1. Failure, contraindication per FDA label, intolerance, or is not a candidate for **BOTH** of the following based on severity of disease and age of individual:
            a. **ONE** topical calcineurin inhibitor, such as pimecrolimus (generic or brand Elidel) **or** tacrolimus (generic or brand Protopic)
            b. Eucrisa (crisaborole)
      ii. **For all other body areas**:
         1. **For mild disease:** Failure, contraindication per FDA label, intolerance, or is not a candidate for **ALL** of the following based on severity of disease and age of individual:
            a. **ONE** low potency topical corticosteroids (such as desonide 0.05%, fluocinolone acetonide 0.01%, and others)
            b. **ONE** topical calcineurin inhibitor, such as pimecrolimus (generic or brand Elidel) **or** tacrolimus (generic or brand Protopic)
            c. Eucrisa (crisaborole)
         2. **For moderate disease:** Failure, contraindication per FDA label, intolerance, or is not a candidate for **ALL** of the following based on severity of disease and age of individual:
            a. **TWO** medium to high potency topical corticosteroids (such as triamcinolone acetonide 0.1%, mometasone furoate 0.1%, betamethasone dipropionate 0.05%, desoximetasone 0.05%, and others)
            b. **ONE** topical calcineurin inhibitor, such as pimecrolimus (generic or brand Elidel) **or** tacrolimus (generic or brand Protopic)
            c. Eucrisa (crisaborole)
   b. **For limited vitiligo (affects less than 10% BSA):**
      i. Failure, contraindication per FDA label, intolerance, or is not a candidate for **ONE** of the following:
         1. **ONE** mid- to high-potency topical corticosteroid
         2. For areas at high-risk for atrophy **either** pimecrolimus (generic or brand Elidel) **or** tacrolimus (generic or brand Protopic)

6. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. Will not be used in combination with therapeutic biologics, other JAK inhibitors (e.g., Jakafi, Rinvoq, Xeljanz, etc.) or potent immune suppressing agents such as azathioprine or cyclosporine

8. Individual does not have an active, serious infection, including localized infections, with bacteria, mycobacteria, fungal, or virus

9. Individual does not have active hepatitis B or hepatitis C

10. Individual is not using strong inhibitors of CYP3A4 such as ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, clarithromycin, others

Initial approval duration: 3 months

- **Criteria for continuation of coverage (renewal request):** Opzelura (ruxolitinib) cream and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Dermatologist

2. Individual's condition has responded while on therapy with response defined as **ONE** of the following:
    a. For atopic dermatitis, **TWO** of the following:
        i. No evidence of disease progression
        ii. Intensity of pruritus is described as decreased to mild or change in itch score of at least 4 over baseline
        iii. Achievement of an IGA score of 'clear (0)'
        iv. Achievement of an IGA score of 'almost clear (1)' PLUS a 2-grade improvement from baseline
    b. For vitiligo, **BOTH** of the following:
        i. No evidence of disease progression
        ii. Reduction in body surface area affected

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    a. Active serious infection
    b. Myocardial infarction or stroke
    c. Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis
    d. Thrombocytopenia, anemia, or neutropenia

6. Will not be used in combination with therapeutic biologics, other JAK inhibitors (e.g., Jakafi, Rinvoq, Xeljanz, etc.) or potent immune suppressing agents such as azathioprine or cyclosporine

7. Individual does not have an active, serious infection, including localized infections, with bacteria, mycobacteria, fungal, or virus

8. Individual does not have active hepatitis B or hepatitis C

9. Individual is not using strong inhibitors of CYP3A4 such as ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, clarithromycin, others

Renewal duration: 6 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Opzelura (ruxolitinib) cream is a Janus kinase (JAK) inhibitor 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. Opzelura (ruxolitinib) cream is also indicated for the topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older. Use of Opzelura (ruxolitinib) cream in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

Ruxolitinib inhibits JAK1 and JAK2 which mediate the signaling of several cytokines and growth factors that are important for hematopoiesis and immune function. JAK signaling involves recruitment of STATs (signal transducers and activators of transcription) to cytokine receptors, activation and subsequent localization of STATs to the nucleus leading to modulation of gene expression. The relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known.

The diagnosis of atopic dermatitis is based on clinical symptoms. There is no optimal long-term maintenance treatment and there is no known cure. In general, treatment involves elimination of exacerbating factors, restoring the skin's barrier function, hydrating the skin and use of topical anti-inflammatory agents. Patients with atopic dermatitis should avoid exacerbating factors including excessive bathing, low humidity environments, emotional stress, xerosis, and exposure to detergents. Thick creams with low water content or ointments which have zero water content protect against xerosis and should be utilized. Antihistamines are utilized as an adjunct in patients with atopic dermatitis to control pruritus and eye irritation. Sedating antihistamines such as diphenhydramine or hydroxyzine appear to be more effective than non-sedating agents.

Treatment of atopic dermatitis initially involves use of topical prescription therapies such as corticosteroids, calcineurin inhibitors (tacrolimus ointment, pimecrolimus cream) and topical phosphodiesterase 4 (PDE-4) inhibitors (crisaborole ointment). Topical corticosteroids are considered the standard of care; strength and

formulation of the preparation is selected based on severity, duration of treatment, location of exacerbation, and age of individual. Topical calcineurin and topical PDE-4 inhibitors should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas.

Vitiligo is a common, acquired, autoimmune, chronic disorder of pigmentation characterized by the development of white macules on the skin due to loss of epidermal melanocytes. Loss of skin color can affect any part of the body, including the mouth, hair, and eyes. It may be more noticeable in people with darker skin. Vitiligo is classified into two broad categories, segmental and nonsegmental. Nonsegmental vitiligo is further divided into subtypes based upon the distribution of skin lesions (i.e., generalized, acral or acrofacial, mucosal, localized, universal, and mixed pattern). Segmental vitiligo typically occurs in a dermatomal or quasi-dermatomal pattern, most frequently along the distribution of the trigeminal nerve.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Mild atopic dermatitis – Areas of dry skin, infrequent itching (with or without small areas of redness); little impact on everyday activities, sleep, and psychosocial wellbeing

Moderate atopic dermatitis – Areas of dry skin, frequent itching, redness (with or without excoriation and localized skin thickening); moderate impact on everyday activities and psychosocial wellbeing, frequently disturbed sleep

Severe atopic dermatitis – Widespread areas of dry skin, incessant itching, redness (with or without excoriation, extensive skin thickening, bleeding, oozing, cracking, and alteration of pigmentation); severe limitation of everyday activities and psychosocial functioning, nightly loss of sleep

Diagnostic criteria for atopic dermatitis: (*Diagnosis requires the presence of at least **3** major & **3** minor criteria)*

Major criteria
Pruritus
Dermatitis affecting flexural surfaces in adults and the face and extensors in infants
Chronic or relapsing dermatitis
Personal or family history of cutaneous or respiratory atopy
Minor criteria
Features of the so-called "atopic facies"
Facial pallor or erythema
Hypopigmented patches
Infraorbital darkening

Infraorbital folds or wrinkles
Cheilitis
Recurrent conjunctivitis
Anterior neck folds
Triggers of atopic dermatitis
Foods
Emotional factors
Environmental factors
Skin irritants such as wool, solvents and sweat
Complications of atopic dermatitis
Susceptibility to cutaneous viral and bacterial infections
Impaired cell-mediated immunity
Immediate skin-test reactivity
Raised serum IgE
Keratoconus
Anterior subcapsular cataracts
Others
Early age of onset
Dry skin
Ichthyosis
Hyperlinear palms
Keratosis pilaris (plugged hair follicles of proximal extremities)
Hand and foot dermatitis
Nipple eczema
White dermatographism
Perifollicular accentuation

Adapted from: Hanifin JM, Rajka G, Acta Dermatol Venereol 1980; 92(Suppl):44.

Investigator Global Assessment Scale (IGA):
Validated-Investigator-Global-Assessment-Scale_vIGA-AD_2017.pdf (eczemacouncil.org) [Accessed October 09, 2021]

The IGA score is selected using the morphologic descriptors that best describe the overall appearance of the lesions at a given time point. It is not necessary that all characteristics under Morphological Description be present.

Score	Morphological Description
0 – Clear	No inflammatory signs of atopic dermatitis (no erythema, no induration/papulation, no lichenification, no oozing/crusting). Post-inflammatory hyperpigmentation and/or hypopigmentation may be present.
1 – Almost clear	Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting.
2 – Mild	Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting.
3 – Moderate	Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present.
4 – Severe	Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread in extent. Oozing or crusting may be present.
Notes: 1. In indeterminate cases, use extent to differentiate between scores. For example: • Patient with marked erythema (deep or bright red), marked papulation and/or marked lichenification that is limited in extent (instead of widespread), would be considered “3 – Moderate”. 2. Excoriations should not be considered when assessing disease severity	

Pruritus Numerical Rating Scale (NRS):
Numerical Rating Scale - Pruritus Resources (pruritussymposium.de) [Accessed October 09, 2021]

The NRS is comprised of one item and is represented by numbers 0 (“no itch”) to 10 (“worst imaginable itch”). Patients are asked to rate the intensity of their itch using this scale. It features high reliability and concurrent validity and is a popular choice for all patients due to its simple format. Time needed for completion: 1 minute. It has been validated in several languages.

- It can be interpreted as follows:
  - NRS 0 - no pruritus
  - NRS < 3 - mild pruritus
  - NRS ≥ 3 < 7 - moderate pruritus
  - NRS ≥ 7 < 9 - severe pruritus
  - NRS ≥ 9 - very severe pruritus

On a scale from 0 (no itch) to 10 (worst imaginable itch), how would you rate your itch overall (on average) during the past 24-hour? (Select number)										
0	1	2	3	4	5	6	7	8	9	10

Therapies for stabilization and repigmentation of vitiligo

Stabilization	Repigmentation

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Oral corticosteroids Narrow Band Ultra-Violet B phototherapy Minocycline Methotrexate Vitamin supplementation	Topical corticosteroids Calcineurin inhibitors Vitamin D analogues NBUVB phototherapy Psoralen photochemotherapy Targeted phototherapy Experimental agents Afamelanotide Prostaglandin F2-alpha analogues JAK inhibitors

Management vitiligo	
Stabilization of rapidly progressive disease	• For patients with rapidly progressive, nonsegmental vitiligo (i.e., depigmented macules spreading over a few weeks or months), oral corticosteroids and/or narrowband ultraviolet B (NBUVB) first-line therapy for the stabilization (cessation of spread) of the disease
Nonsegmental vitiligo	
Involving <10% BSA	
Localized disease (limited disease)	• Mid- to high-potency topical corticosteroids **OR** • Topical calcineurin inhibitors for areas at increased risk of atrophy • Topical ruxolitinib for those who have not responded to topical corticosteroids or topical calcineurin inhibitors • Can also be considered a first-line therapy in the appropriate patient
Disseminated disease (limited but disseminated disease)	• NBUVB phototherapy for whom the use of topical therapies may be unpractical
Recalcitrant disease (limited, stable, recalcitrant disease)	• Choice of treatment depends on availability, clinical judgment, and individual preference • Options include targeted phototherapy, psoralen plus ultraviolet A (PUVA) photochemotherapy, and surgical procedures
Involving 10-40% BSA *(moderate to extensive disease)*	• NBUVB rather than PUVA as first-line therapy • Topical corticosteroids or topical calcineurin inhibitors may be used intermittently in combination with NBUVB phototherapy
Involving >40% BSA (extensive disease & desire regimentation)	• NBUVB rather than PUVA as first-line therapy • Depigmentation of residual pigmented areas with monobenzyl ether of hydroquinone (monobenzone) can be offered for individual with recalcitrant disease that does not respond to regimentation regimens and for those with extensive vitiligo who do not desire undergoing regimentation treatment

Segmental vitiligo	• Therapeutic options for stable, segmental vitiligo include topical therapies (e.g., topical corticosteroids, topical calcineurin inhibitors), targeted phototherapy, and surgical therapy

Resources:

Opzelura (ruxolitinib) cream product information, revised by Incyte Corporation 09-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 26, 2024.

Silverberg JI, Howe W. Atopic dermatitis (eczema): Pathogenesis, clinical manifestations, and diagnosis. In: UpToDate, Dellavalle RP, Levy ML, Fowler J, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated April 24, 2024. Accessed September 12, 2024.

Paller AS, Butala S, Howe W. Treatment of atopic dermatitis (eczema). In: UpToDate, Dellavalle RP, Levy ML, Fowler J, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024.Topic last updated August 30, 2024. Accessed September 12, 2024.

Lio PA, Gonzalez ME. Management of severe refractory atopic dermatitis (eczema) in children. In: UpToDate, Dellavalle RP, Levy ML, Fowler J, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Literature current through August 2024. Topic last updated June 06, 2024. Available at http://uptodate.com. Accessed September 13, 2024.

Berger TG. Evaluation and management of severe refractory atopic dermatitis (eczema) in adults. In: UpToDate, Fowler J, Levy ML, Dellavalle RP, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Literature current through August 2024. Topic last updated March 01, 2023. Available at http://uptodate.com. Accessed September 13, 2024.

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