

ruxolitinib (Opzelura™)

Policy # 00774

Original Effective Date: 03/14/2022

Current Effective Date: 09/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Atopic Dermatitis

Based on review of available data, the Company may consider ruxolitinib (Opzelura™)[†] for the treatment of atopic dermatitis to be **eligible for coverage**.^{**}

Patient Selection Criteria

Coverage eligibility for ruxolitinib (Opzelura) will be considered when the following criteria are met:

Initial:

- Patient has a diagnosis of mild to moderate atopic dermatitis; AND
- Requested drug will be for short-term and non-continuous use; AND
- Patient is NOT immunocompromised; AND
- Patient is 12 years of age or older; AND
- Patient has 3% to 20% of their body surface area (BSA), excluding the scalp, impacted by atopic dermatitis; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility, based on clinical trials, and will be denied as not medically necessary** if not met).*
- Patient has had atopic dermatitis for at least 6 months; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has tried and failed (e.g., intolerance or inadequate response) a prescription GENERIC medium to very high potency topical corticosteroid product for at least TWO CONSECUTIVE weeks unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient. Examples of medium to very high potency generic topical steroid products include betamethasone valerate, desoximetasone, fluocinolone acetonide, fluticasone propionate, hydrocortisone butyrate, mometasone furoate, prednicarbate, triamcinolone acetonide, trianex, triderm,

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amcinonide, augmented betamethasone dipropionate, apexicon E, betamethasone dipropionate, diflorasone diacetate, fluocinonide, fluocinonide E, clobetasol emollient, clobetasol propionate, clodan, diflorasone diacetate, and halobetasol propionate; AND

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC topical tacrolimus or GENERIC topical pimecrolimus for at least SIX CONSECUTIVE weeks unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Requested medication will NOT be used in combination with therapeutic biologics (such as dupilumab [Dupixent]®)‡, other Janus kinase (JAK) inhibitors (such as tofacitinib [Xeljanz/XR]®, upadacitinib [Rinvoq]®)‡, or potent immunosuppressants (such as azathioprine or cyclosporine).

Continuation:

- Patient received an initial authorization; AND
- Requested drug will be for short-term and non-continuous use; AND
- Requested medication will NOT be used in combination with therapeutic biologics (such as dupilumab [Dupixent]), other Janus kinase (JAK) inhibitors (such as tofacitinib [Xeljanz/XR], upadacitinib [Rinvoq]), or potent immunosuppressants (such as azathioprine or cyclosporine); AND
- Patient has had a clinically meaningful beneficial response to Opzelura therapy as compared to their baseline status (before Opzelura therapy) as evidenced by TWO or more of the following:
 - Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
 - Reduction in the frequency or intensity of pruritus
 - Reduction in the frequency of disease exacerbations/flare
 - Reduction in the BSA with atopic dermatitis involvement (a 20% reduction in percent BSA involved over baseline)
 - Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.).

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

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Nonsegmental Vitiligo

Based on review of available data, the Company may consider ruxolitinib (Opzelura) for the treatment of nonsegmental vitiligo to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for ruxolitinib (Opzelura) will be considered when the following criteria are met:

Initial:

- Patient has a diagnosis of nonsegmental vitiligo; AND
- Patient is 12 years of age or older; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) a GENERIC medium to very high potency topical corticosteroid (e.g., betamethasone valerate, desoximetasone, fluocinolone acetonide, fluticasone propionate, hydrocortisone butyrate, mometasone furoate, prednicarbate, triamcinolone acetonide, trianex, triderm, amcinonide, augmented betamethasone dipropionate, apexicon E, betamethasone dipropionate, diflorasone diacetate, fluocinonide, fluocinonide E, clobetasol emollient, clobetasol propionate, clodan, cormax, diflorasone diacetate, and halobetasol propionate) for a clinically sufficient duration unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC tacrolimus ointment for a clinically sufficient duration unless there is clinical evidence or patient history that suggests the use of this product will be ineffective or cause an adverse reaction to the patient; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Requested medication will NOT be used in combination with therapeutic biologics (such as dupilumab [Dupixent], other Janus kinase (JAK) inhibitors (such as tofacitinib [Xeljanz/XR], upadacitinib [Rinvoq]), or potent immunosuppressants (such as azathioprine or cyclosporine).

Continuation:

- Patient received an initial authorization; AND
- Requested medication will NOT be used in combination with therapeutic biologics (such as dupilumab [Dupixent], other Janus kinase (JAK) inhibitors (such as tofacitinib [Xeljanz/XR], upadacitinib [Rinvoq]), or potent immunosuppressants (such as azathioprine or cyclosporine); AND

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- Patient has had a clinically meaningful beneficial response to Opzelura therapy as compared to their baseline status (before Opzelura therapy).

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of ruxolitinib (Opzelura) when any of the following are NOT met for the requested condition to be **not medically necessary**.**

Atopic Dermatitis

- For initial requests: Patient has 3% to 20% of their body surface area (BSA), excluding the scalp, impacted by atopic dermatitis
- For initial requests: Patient has had atopic dermatitis for at least 6 months
- For initial requests: Patient has tried and failed a prescription GENERIC medium to very high potency topical corticosteroid product for at least TWO CONSECUTIVE weeks
- For initial requests: Patient has tried and failed GENERIC topical tacrolimus or GENERIC topical pimecrolimus for at least SIX CONSECUTIVE weeks
- For continuation requests: Patient has had a clinically meaningful beneficial response to Opzelura therapy as compared to their baseline status (before Opzelura therapy) as evidenced by TWO or more of the following:
 - Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
 - Reduction in the frequency or intensity of pruritus
 - Reduction in the frequency of disease exacerbations/flare
 - Reduction in the BSA with atopic dermatitis involvement (a 20% reduction in percent BSA involved over baseline)
 - Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.).

Nonsegmental Vitiligo

- For initial requests: Patient has tried and failed a GENERIC medium to very high potency topical corticosteroid for a clinically sufficient duration
- For initial requests: Patient has tried and failed GENERIC tacrolimus ointment for a clinically sufficient duration
- For continuation requests: Patient has had a clinically meaningful beneficial response to Opzelura therapy as compared to their baseline status (before Opzelura therapy).

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of ruxolitinib (Opzelura) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational**.*

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider a quantity override for ruxolitinib (Opzelura) to be **eligible for coverage**.**

Patient Selection Criteria

A quantity override for ruxolitinib (Opzelura), up to 240 grams per 28 days, will be considered when the following criterion is met:

- Patient requires more than 120 grams of the requested drug every 28 days

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of ruxolitinib (Opzelura) in quantities greater than 120 grams per 28 days when there is no documentation that the patient requires more than 120 grams per 28 days be **not medically necessary****

Background/Overview

Opzelura 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. It is also indicated for the topical treatment of nonsegmental vitiligo in adults and pediatric patients 12 years of age and older. The package insert notes that Opzelura use in combination with therapeutic biologics, such as Dupixent, other JAK inhibitors (such as Xeljanz or Rinvoq), or potent immunosuppressants such as azathioprine or cyclosporine is not recommended. Opzelura is applied as a thin layer twice daily to affected areas for both indications. No more than 60 grams per week should be used.

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Atopic Dermatitis

Atopic dermatitis is a chronic inflammatory skin condition associated with dry skin, pruritus, and inflammation. There are various treatment options for atopic dermatitis, including first line agents such as topical corticosteroids (many of which are in generic form) and topical immunomodulatory agents such as generic tacrolimus and generic pimecrolimus. For those that are refractory to topical therapies, systemic immunomodulatory agents are an option for therapy. Opzelura offers another topical option for the treatment of atopic dermatitis. Its place in therapy is currently undefined. Opzelura has not yet been integrated into the American Academy of Dermatology guidelines at the time of this publication.

Nonsegmental Vitiligo

Vitiligo is a chronic autoimmune disease that targets melanocytes, causing skin depigmentation that leaves the skin looking white or pink in appearance. It can affect any part of the body yet is asymptomatic in most patients. There are two different types of vitiligo: segmental and nonsegmental, which is the most common type of vitiligo. Segmental vitiligo may begin during childhood or early adulthood. It typically occurs in a dermatomal or quasi-dermatomal pattern, most frequently along the distribution of the trigeminal nerve. The affected areas typically stabilize within a year and rarely spread beyond that dermatome. Segmental vitiligo can be classified as monosegmental, bisegmental, or plurisegmental. Nonsegmental vitiligo consists of several different subtypes. These include generalized, acrofacial or acral, mucosal, universal, and vitiligo minor. Generalized vitiligo is characterized by a random distribution of depigmented macules or patches that are often bilateral and symmetrical and occur commonly on the face, trunk, and extremities. Acrofacial or acral vitiligo is vitiligo that is mainly confined to the face and distal extremities. Mucosal vitiligo involves the oral and genital mucosa. Universal vitiligo is typically a form of progression of generalized vitiligo and is characterized by complete or nearly complete depigmentation of the skin. Vitiligo minor, which is more commonly seen in individuals of a darker complexion, is characterized by an incomplete loss of pigmentation, and is also called hypochromic vitiligo. Treatment for this condition mainly consists of off-label use of topical or oral corticosteroids, topical calcineurin inhibitors, and phototherapy. Opzelura is the first approved drug for the treatment of vitiligo.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Opzelura 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 is also indicated for the topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Atopic Dermatitis

Two double-blind, randomized, vehicle-controlled trials of identical design (Trial 1 and Trial 2, respectively) enrolled a total of 1,249 subjects aged 12 and older. A total of 20% of subjects were 12 to 17 years of age and 9% were 65 years or older. Subjects had affected body surface area (BSA) of 3 to 20%, and an Investigator's Global Assessment (IGA) score of 2 (mild) to 3 (moderate) on a severity scale of 0 to 4. The baseline Itch Numerical Rating Scale (Itch NRS), defined as the 7-day average of the worst level of itch intensity in the last 24 hours, was 5 on a scale of 0 to 10.

In both trials, subjects were randomized 2:2:1 to treatment with Opzelura, ruxolitinib cream 0.75%, or vehicle cream twice daily (BID) for 8 weeks. The primary efficacy endpoint was the proportion of subjects at week 8 achieving IGA treatment success (IGA-TS) defined as a score of 0 (clear) or 1 (almost clear) with ≥ 2 grade improvement from baseline. In Trial 1, 53.8% of Opzelura patients achieved the primary endpoint vs. 15.1% in the vehicle group. In Trial 2, 51.3% of Opzelura patients achieved the primary endpoint vs. 7.6% in the vehicle group.

Nonsegmental Vitiligo

Two double-blind, randomized, vehicle-controlled trials of identical design (Trial 1 and Trial 2, respectively) enrolled a total of 674 adult and pediatric subjects aged 12 years and older. Subjects had depigmented areas affecting $\geq 0.5\%$ facial body surface area (F-BSA), $\geq 3\%$ non-facial BSA, and total body vitiligo area (facial and non-facial, including hands, feet, upper and lower extremities, and trunk body areas) of up to 10% BSA. At baseline, subjects had a mean affected F-BSA of 1% and a mean affected total BSA of 7.4%. Phototherapy was not permitted during the trial. In both trials, subjects were randomized 2:1 to treatment with Opzelura or vehicle cream twice daily (BID) for 24 weeks followed by an additional 28 weeks of treatment with Opzelura BID for all subjects. Lesions on the face were assessed with the facial Vitiligo Area Scoring Index (F-VASI) and lesions on the total body (including the face) were assessed with the total body Vitiligo Area Scoring Index (T-VASI). The primary efficacy endpoint was the proportion of subjects achieving at least 75% improvement in F-VASI (F-VASI75) at week 24. In Trial 1, 29.9% of Opzelura patients achieved the primary endpoint vs. 7.5% in the vehicle group. In Trial 2, 15.5% of Opzelura patients achieved the primary endpoint vs. 2.2% in the vehicle group.

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References

1. Opzelura [package insert]. Incyte Corporation. Wilmington, Delaware. Updated July 2022.
2. Sidbury R, et al. Guidelines of care for the management of atopic dermatitis Section 3. Management and treatment with phototherapy and systemic agents. J Am Acad Dermatol. 2014;71(2): 327-349.
3. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis. Section 2: management and treatment of atopic dermatitis with topical therapies. J Am Acad Dermatol. 2014;71(1):116-132.
4. FDA Approves Incyte's Opzelura for Certain Patients with Vitiligo. IPD Analytics. PDF file. Accessed August 2022.
5. Vitiligo: Pathogenesis, clinical features, and diagnosis. UpToDate. Accessed October 2022.

Policy History

Original Effective Date: 03/14/2022

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02/03/2022 Medical Policy Committee review

02/09/2022 Medical Policy Implementation Committee approval. New policy.

10/06/2022 Medical Policy Committee review

10/11/2022 Medical Policy Implementation Committee approval. Updated with newest FDA indication for the treatment of nonsegmental vitiligo.

08/03/2023 Medical Policy Committee review

08/09/2023 Medical Policy Implementation Committee approval. Updated policy criteria for atopic dermatitis to require patients to try and fail one generic topical corticosteroid product and one generic topical calcineurin inhibitor product instead of trying and failing two of each.

08/01/2024 Medical Policy Committee review

08/14/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

08/07/2025 Medical Policy Committee review

08/13/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 08/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.