



Opzelura (ruxolitinib) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date
4/1/2023

Date of Origin

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Opzelura™ (ruxolitinib) Cream	<p>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</p> <p>Topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older</p> <p>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</p>		1

See package insert for FDA prescribing information: <https://dailymed.nlm.nih.gov/dailymed/index.cfm>

CLINICAL RATIONALE

Atopic Dermatitis	<p>Atopic dermatitis (AD), also known as atopic eczema, is a chronic, pruritic inflammatory dermatosis affecting up to 25% of children and 1-5% of adults. AD follows a relapsing course and is associated with elevated serum immunoglobulin (IgE) levels and a personal or family history of type I allergies, allergic rhinitis, and/or asthma. Onset is most common between 3 and 6 months of age, with approximately 60% of patients developing the eruption in the first year of life and 90% by age 5. While the majority of affected individuals have resolution of disease by adulthood, 10 to 30% do not, and a smaller percentage first develop symptoms as adults. AD has a complex pathogenesis involving genetic, immunologic, and environmental factors, which lead to a dysfunctional skin barrier and dysregulation of the immune system. Clinical findings include erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and lichenification. These clinical findings vary by patient age and chronicity of lesions. Pruritus is a hallmark of the condition that is responsible for much of the disease burden borne by patients and their families. Typical patterns include facial, neck and extensor involvement in infants and children; flexure involvement in any age group, with sparing of groin and axillary regions.(2)</p> <p>Goals of treatment are to reduce symptoms (pruritus and dermatitis), prevent exacerbations, and minimize therapeutics risks.(3) Despite its relapsing and remitting nature, the majority of patients with AD can achieve clinical improvement and disease control with nonpharmacological interventions (e.g., emollient use), conventional topical therapies (including corticosteroids and calcineurin inhibitors) and environmental and occupational modifications, when necessary.(3-5) The American Academy of Dermatology (AAD) guidelines suggest application of moisturizers should</p>
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be an integral part of the treatment of patients with AD as there is strong evidence that their use reduces disease severity and need for pharmacologic intervention. They are an important component of maintenance treatment and prevention of flares.(4) The AAD recommends topical corticosteroids (TCS) for patients who fail to respond to good skin care and regular use of emollients alone. Proactive, intermittent use of topical corticosteroids as maintenance therapy (1-2 times weekly) on areas that commonly flare is recommended to help prevent relapses and is more effective than use of emollients alone. Monitoring by physical exam for cutaneous side effects during long-term, potent steroid use is suggested. Proactive, once to twice weekly application of mid-potency TCS for up to 40 weeks has not demonstrated adverse events (e.g., purpura, telangiectasia, striae, focal hypertrichosis, acneiform/rosacea-like eruptions, skin atrophy) in clinical trials.(4) It is recommended that patients with acute flares use super high or high potency topical corticosteroids for one to two weeks, and then replace these with lower potency preparations until the lesions resolve.(6) AAD notes that mid- to higher potency topical corticosteroids are appropriate for short courses to gain rapid control of symptoms, but long-term management should use the least-potent corticosteroid that is effective.(4)

Topical calcineurin inhibitors (TCIs) (e.g., pimecrolimus, tacrolimus) are recommended by the AAD as second-line therapy and are effective for acute and chronic treatment. They are particularly useful in selected clinical situations such as recalcitrance to steroids; for sensitive areas (face, anogenital, skin folds); for steroid-induced atrophy; and when there is long-term uninterrupted topical steroid use. TCIs are recommended for use on actively affected areas as a steroid-sparing agent. Proactive, intermittent use of TCIs as maintenance therapy (2-3 times per week) on areas that commonly flare is recommended to help prevent relapses while reducing need for topical corticosteroids and is more effective than use of emollients alone.(4) Prescribing information for Elidel® (pimecrolimus) cream and Protopic® (tacrolimus) ointment indicate evaluation after 6 weeks if symptoms of AD do not improve for adults and pediatrics.(7,8)

Phototherapy is recommended as a treatment for both acute and chronic AD in children and adults, after failure of the mentioned above. Systemic immunomodulator agents are indicated and recommended for the subset of adult and pediatric patients in whom optimized topical regimens using emollients, topical anti-inflammatory therapies, adjunctive methods, and/or phototherapy do not adequately control the signs and symptoms of disease. Photo therapy and systemic immunomodulating agents may also be used in patients whose medical, physical, and/or psychological states are greatly affected by their skin disease. Oral cyclosporine, azathioprine, methotrexate, and mycophenolate mofetil are the most commonly used systemic immunomodulators and most efficacious for treating AD. The AAD recommends that systemic corticosteroids should be avoided if possible and should exclusively be reserved for acute, severe exacerbations and as a short-term bridge to other systemic, steroid sparing therapies.(5)

The American Academy of Family Physicians recommend the following for the treatment of AD:(9)

- Maintenance treatment should consist of twice daily application of an emollient and once daily bathing using a soap-free cleanser
- Mild flare:
 - Continue maintenance treatment with twice daily topical steroid (low to medium potency)

	<ul style="list-style-type: none"> ○ If there is clinical improvement, continue maintenance therapy ○ If no clinical improvement or inadequate improvement, start treatment options for moderate AD ● Moderate flare: <ul style="list-style-type: none"> ○ Continue maintenance treatment with twice daily topical steroid (medium to high potency) AND twice daily topical calcineurin inhibitor ○ Additional therapies to add on include Eucrisa, twice weekly bleach baths, wet wrap therapy ○ If there is clinical improvement, switch to mild treatment options ○ If no clinical improvement or inadequate improvement, start treatment options for severe AD ● Severe flare: <ul style="list-style-type: none"> ○ Continue maintenance treatment with twice daily topical steroid (high potency) AND twice daily topical calcineurin inhibitor ○ Additional therapies to add on include twice weekly bleach baths, wet wrap therapy ○ Referral to a specialist
Vitiligo	<p>Vitiligo is an acquired skin pigmentation disorder characterized by well defined, depigmented areas of the skin. The depigmentation is due to a loss of epidermal melanocytes. Vitiligo can present in a localized or generalized distribution, with the lesions coalescing into larger depigmented areas. The underlying cause of vitiligo is yet unknown.(10) Vitiligo is commonly classified into two different forms, segmental and non-segmental. Non-segmental vitiligo (NSV) tends to evolve over time in both distribution and extension patterns. NSV is an umbrella term for a number of different subtypes of vitiligo. These include acrofacial, generalized, mucosal (multifocal), and universal. NSV is characterized by depigmented lesions that vary in size and often involve both sides of the body. Involvement of the scalp and other hair-bearing areas may manifest with patches of gray or white hairs, while body hair is generally spared. Segmental vitiligo (SV) tends to have an earlier age of onset, that rapidly progresses but has a limited course. Depigmentation spreads within a segment within 6-24 months and then stops. Hair follicles are more frequently involved early in the disease course with SV, with up to 50% of patients exhibiting poliosis, a localized cluster of white hair shafts, in affected areas.(11)</p> <p>The diagnosis of vitiligo is based off of clinical presentation and with a Woods lamp, which is a handheld ultraviolet device. The Woods lamp is also used to track progression of lesions over time. There are a number of other indications that can mimic vitiligo and it is important to rule those out with a close examination of the skin. Vitiligo does not cause scaling or textural changes in the skin.(10) The British Association of Dermatology guidelines recommend first line therapy with potent or very potent topical corticosteroids once daily avoiding the periocular area. Topical calcineurin inhibitors may be considered in patients with facial vitiligo or used in an intermittent regimen in combination with potent corticosteroids for patients with lesions in areas of thinner skin. Topical therapies should be evaluated every 3 to 6 months to check for improvement. Phototherapy is also recommended as a second-line option in patients that have had an inadequate response to topical therapies.(12)</p>
Efficacy (1)	<p><i>Atopic Dermatitis</i></p> <p>Two double-blind, randomized, vehicle-controlled trials of identical design (TRuE-AD1 and TRuE-AD2, NCT03745638 and NCT03745651, respectively) enrolled a total of 1249 adult and pediatric subjects aged 12 and 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.</p>

	<p>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 greater than or equal to 2 grade improvement from baseline. Efficacy was also assessed using a \geq 4-point improvement in Itch NRS. Opzelura was 38.9% and 44.1% more effective than placebo for IGA-TS and 36.7% and 35.8% more effective than placebo for Itch NRS in trials 1 and trial 2 respectively.</p> <p><i>Nonsegmental Vitiligo</i></p> <p>Two double-blind, randomized, vehicle-controlled trials of identical design (TRuE-V1 and TRuE-V2, NCT04052425 and NCT04057573, respectively) enrolled a total of 674 adult and pediatric subjects aged 12 years and older. Subjects had depigmented areas affecting greater than or equal to 0.5% facial body surface area (F-BSA), greater than or equal to 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.</p> <p>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 and the proportion of participants achieving at least 90% improvement in F-VASI (F-VASI90). Opzelura was 22.5% and 16.9% more effective than placebo for F-VASI75 and 13.3% and 13.5% more effective than placebo for F-VASI90 in trials 1 and trial 2 respectively.</p>
Safety(1)	<p>Opzelura carries the following boxed warnings:</p> <ul style="list-style-type: none"> • 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 <ul style="list-style-type: none"> ○ Reported infections include: <ul style="list-style-type: none"> ▪ Active tuberculosis, which may present with pulmonary or extrapulmonary disease ▪ Invasive fungal infections, including candidiasis and pneumocystosis ▪ Bacterial, viral, and other infections due to opportunistic pathogens ○ Avoid use of Opzelura in patients with an active, serious infection, including localized infections. If a serious infection develops, interrupt Opzelura until the infection is controlled. The risks and benefits of treatment with Opzelura should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Opzelura. • 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

	<ul style="list-style-type: none"> Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis, some fatal, have occurred in patients treated with Janus kinase inhibitors for inflammatory conditions compared to placebo. Many of these adverse reactions were serious and some resulted in death. Patients with symptoms of thrombosis should be promptly evaluated <p>Opzelura does not have any FDA labeled contraindications for use.</p>
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REFERENCES

Number	Reference
1	Opzelura prescribing information. Incyte Corp. July 2022.
2	Eichenfield LF, Tom WL, Chamlin SL, Feldman SR, Hanifin JM, Simpson EL, et al. Guidelines of Care for the Management of Atopic Dermatitis: Section 1. Diagnosis and Assessment of Atopic Dermatitis. <i>J Am Acad Dermatol</i> . 2014 Feb;70(2):338-51.
3	Sidbury R, Tom WL, Bergman JN, Cooper KD, Silverman RA, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches. <i>J Am Acad Dermatol</i> . 2014 Dec;71(6):1218-33.
4	Eichenfield L, Tom W, Berger T, et al. Guidelines of care for the management of atopic dermatitis. Section 2. Management and treatment of atopic dermatitis with topical therapies. <i>J Am Acad Dermatol</i> 2014;71(1):116-32.
5	Sidbury, Robert, MD., et al. Guidelines of Care for the Management of Atopic Dermatitis. Section 3. Management and Treatment with Phototherapy and Systemic Agents. <i>J Am Acad Dermatol</i> 2014; 71 (2): 327-349.
6	Schneider L, Tilles S, Lio P, et al. Atopic dermatitis: a practice parameter update 2012. <i>J Allergy Clin Immunol</i> 2013; 131:295.
7	Elidel prescribing information. Valeant Pharmaceuticals. September 2020.
8	Protopic prescribing information. Astellas Pharma US Inc. February 2019.
9	Frazier W, Bhardwaj N. Atopic Dermatitis: Diagnosis and Treatment. <i>Am Fam Physician</i> . 2020 May 15;101(10):590-598. PMID: 32412211.
10	Alikhan A, Felsten LM, Daly M, Petronic-Rosic V. Vitiligo: a comprehensive overview Part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up. <i>J Am Acad Dermatol</i> 2011; 65:473.
11	Ezzedine K, Lim HW, Suzuki T, et al. Revised classification/nomenclature of vitiligo and related issues: the Vitiligo Global Issues Consensus Conference. <i>Pigment Cell Melanoma Res</i> 2012; 25:E1.
12	Eleftheriadou, V., Atkar, R., Batchelor, J., McDonald, B., Novakovic, L., Patel, J., Ravenscroft, J., Rush, E., Shah, D., Shah, R., Shaw, L., Thompson, A., Hashme, M., Exton, L., Mohd Mustapa, M., Manounah, L. and (2022), British Association of Dermatologists guidelines for the management of people with vitiligo 2021*. <i>Br J Dermatol</i> , 186: 18-29. https://doi.org/10.1111/bjd.20596 .

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
Opzelura	ruxolitinib phosphate cream	1.5 %	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Opzelura	Ruxolitinib Phosphate Cream	1.5 %	60	GRAMS	30	Days				

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Opzelura	ruxolitinib phosphate cream	1.5 %	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Opzelura	Ruxolitinib Phosphate Cream	1.5 %	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	<p>Evaluation</p> <p>Target Agent(s) will be approved when ALL of the following are met:</p> <ol style="list-style-type: none"> 1. If the request is for use in vitiligo AND vitiligo is NOT restricted from coverage under the patient's benefit AND 2. ONE of the following: <ol style="list-style-type: none"> A. The patient has a diagnosis of mild to moderate atopic dermatitis AND ALL of the following: <ol style="list-style-type: none"> 1. The patient's affected body surface area (BSA) is less than or equal to 20% AND 2. The patient is NOT immunocompromised AND 3. ONE of the following: <ol style="list-style-type: none"> A. The patient has tried and had an inadequate response to at least a low-potency topical corticosteroid used for a minimum of 4 weeks OR B. The patient has an intolerance or hypersensitivity to therapy with a topical corticosteroid OR C. The patient has an FDA labeled contraindication to ALL topical corticosteroids AND 4. ONE of the following:

Module	Clinical Criteria for Approval
	<ul style="list-style-type: none"> A. The patient has tried and had an inadequate response to a topical calcineurin inhibitor used for a minimum of 6 weeks OR B. The patient has an intolerance or hypersensitivity to therapy with a topical calcineurin inhibitor OR C. The patient has an FDA labeled contraindication to ALL topical calcineurin inhibitors AND <p>5. The patient will be using standard maintenance therapy (e.g., topical emollients, good skin care practices) in combination with the requested agent OR</p> <ul style="list-style-type: none"> B. The patient has a diagnosis of nonsegmental vitiligo AND BOTH of the following: <ul style="list-style-type: none"> 1. The patient's affected body surface area (BSA) is less than or equal to 10% AND 2. ONE of the following: <ul style="list-style-type: none"> A. The patient has tried and had an inadequate response to at least a potent topical corticosteroid used for a minimum of 2 weeks OR B. The patient has an intolerance or hypersensitivity to therapy with a topical corticosteroid OR C. The patient has an FDA labeled contraindication to ALL topical corticosteroids OR D. The prescriber has provided information indicating why the patient cannot use at least a potent topical corticosteroid for the treatment of vitiligo OR C. The patient has another FDA approved indication for the requested agent AND 3. ONE of the following: <ul style="list-style-type: none"> A. The patient's age is within FDA labeling for the requested indication for the requested agent OR B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication AND 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., dermatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis AND 5. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): <ul style="list-style-type: none"> A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) OR B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: <ul style="list-style-type: none"> 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent AND 2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) AND 6. The patient does NOT have any FDA labeled contraindications to the requested agent <p>Length of Approval: 3 months for atopic dermatitis and 6 months for nonsegmental vitiligo</p> <p>NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below.</p>

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	<p>Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met:</p> <ul style="list-style-type: none"> 1. The requested quantity (dose) does NOT exceed the program quantity limit OR 2. ALL of the following: <ul style="list-style-type: none"> A. The requested quantity (dose) is greater than the program quantity limit AND B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication AND C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit OR 3. ALL of the following: <ul style="list-style-type: none"> A. The requested quantity (dose) is greater than the program quantity limit AND B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication AND

Module	Clinical Criteria for Approval
	<p data-bbox="354 184 1398 239">c. The prescriber has provided information in support of therapy with a higher dose for the requested indication</p> <p data-bbox="228 279 1354 308">Length of Approval: 3 months for atopic dermatitis and 6 months for nonsegmental vitiligo</p>

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
Agents NOT to be used Concomitantly
Adbry (tralokinumab-ldrm)
Actemra (tocilizumab)
Arcalyst (rilonacept)
Avsola (infliximab-axxq)
Benlysta (belimumab)
Cibinqo (abrocitinib)
Cimzia (certolizumab)
Cinqair (reslizumab)
Cosentyx (secukinumab)
Dupixent (dupilumab)
Enbrel (etanercept)
Entyvio (vedolizumab)
Fasenra (benralizumab)
Humira (adalimumab)
Ilaris (canakinumab)
Ilumya (tildrakizumab-asmn)
Inflectra (infliximab-dyyb)
Infliximab
Kevzara (sarilumab)
Kineret (anakinra)
Nucala (mepolizumab)

Contraindicated as Concomitant Therapy

Olumiant (baricitinib)
Opzelura (ruxolitinib)
Orencia (abatacept)
Otezla (apremilast)
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)
Rinvoq (upadacitinib)
Rituxan (rituximab)
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Siliq (brodalumab)
Simponi (golimumab)
Simponi ARIA (golimumab)
Skyrizi (risankizumab-rzaa)
Sotyktu (deucravacitinib)
Stelara (ustekinumab)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tysabri (natalizumab)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib extended release)
Xolair (omalizumab)
Zeposia (ozanimod)