

PRIOR AUTHORIZATION POLICY

POLICY: Dermatology – Opzelura Prior Authorization Policy

- Opzelura® (ruxolitinib 1.5% cream – Incyte)

REVIEW DATE: 07/27/2022

OVERVIEW

Opzelura, a Janus kinase (JAK) inhibitor, is indicated for the following uses:¹

- **Atopic dermatitis**, for the topical short-term and non-continuous treatment of mild to moderate disease in patients ≥ 12 years of age whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.
- **Nonsegmental vitiligo**, for the topical treatment of patients ≥ 12 years of age.

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.

For atopic dermatitis, Opzelura is applied twice daily to affected areas of up to 20% body surface area (BSA). Patients should stop using Opzelura when signs and symptoms of atopic dermatitis (e.g., itch, rash, and redness) resolve. If signs and symptoms do not improve within 8 weeks, patients should be re-examined by their healthcare provider.

For vitiligo, Opzelura is applied twice daily to affected areas of up to 10% BSA.¹ Patients may require more than 24 weeks of treatment to achieve a satisfactory response. If the patient does not find the repigmentation meaningful after 24 weeks of therapy, the patient should be re-evaluated by their healthcare provider.

Clinical Efficacy

Atopic Dermatitis

Two pivotal Opzelura studies enrolled patients ≥ 12 years of age with a diagnosis of atopic dermatitis present for ≥ 2 years, affecting 3% to 20% of their BSA.^{1,2} Patients were also required to have an Investigator's Global Assessment (IGA) score of 2 or 3. While prior treatment was not a requirement for study enrollment, 90% of patients had received prior therapies for atopic dermatitis, including low-, medium-, and high-potency topical corticosteroids (49.6%, 42.4%, and 32.7% of patients, respectively), as well as topical calcineurin inhibitors (21.5% of patients). At Week 8, Opzelura cream was found to be more effective in achieving IGA treatment success, defined as an IGA score of 0 (clear) or 1 (almost clear) with a ≥ 2 -grade improvement from baseline.³ A third, non-pivotal, Phase II trial of Opzelura cream in a similar patient population included a triamcinolone acetonide 0.1% cream comparator arm.⁴ At Week 4, Opzelura 1.5% cream produced greater improvement in the Eczema Area and Severity Index score from baseline; however, the treatment difference vs. triamcinolone was not statistically significant.

Vitiligo

One Phase III Opzelura study enrolled patients ≥ 12 years of age with a diagnosis of non-segmental vitiligo and depigmented areas covering $\leq 10\%$ of their BSA.¹² While prior treatment was not a requirement for study enrollment, 61% of patients had received prior topical therapies for vitiligo, including topical corticosteroids and topical calcineurin inhibitors. Efficacy was evaluated at Week 24.

Guidelines

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Atopic Dermatitis Guidelines

Opzelura cream is not addressed in available guidelines. In general, The American Academy of Dermatology Guidelines of Care for the Management of Atopic Dermatitis (2014) and the Joint Task Force on Practice Parameters Atopic Dermatitis Practice Parameter (2012) recommend moisturizers/emollients as first-line therapy, followed by topical corticosteroids, when appropriate.^{5,6} Topical calcineurin inhibitors (i.e., tacrolimus 0.03% and 0.1% ointment [Protopic[®], generic] and pimecrolimus 1% cream [Elidel[®], generic]) should be considered when atopic dermatitis is unresponsive to topical corticosteroids or when the use of these agents is not appropriate due to safety concerns (e.g., young infants, treatment of sensitive areas such as the face, eyelids, or genitalia). The phosphodiesterase-4 inhibitor, Eucrisa[®] (crisaborole 2% ointment), is also not addressed in current US-based guidelines.

Vitiligo Guidelines

Guidelines from the British Association of Dermatologists for the management of vitiligo (2021) do not address Opzelura.¹³ A potent or very potent topical corticosteroid therapy should be offered to patients. As an alternative to topical corticosteroids, topical tacrolimus, a calcineurin inhibitor, may be considered. These therapies may also be used in combination as part of an intermittent therapy regimen. In general, a efficacy of a topical corticosteroid or topical calcineurin inhibitor may not be evident for 8 to 12 weeks.¹⁴

Safety

Opzelura carries a Boxed Warning regarding the risk of serious infections, mortality, malignancy and lymphoproliferative disorders, major adverse cardiac events, and thrombosis.¹ Other Warnings and Precautions include thrombocytopenia, anemia, neutropenia, and lipid elevations. Based on these risks, critical evaluation and monitoring of certain patients is recommended in the Opzelura prescribing information.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Opzelura cream. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Opzelura cream as well as the monitoring required for adverse events and long-term efficacy, approval requires Opzelura cream to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Opzelura cream is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Atopic Dermatitis.** Approve for 8 weeks if the patient meets all of the following (A, B, C, D, E, and F):
 - A) Patient is ≥ 12 years of age; AND
 - B) Patient has mild to moderate atopic dermatitis, according to the prescriber; AND
 - C) Patient has atopic dermatitis involvement estimated to affect $\leq 20\%$ of the body surface area; AND
 - D) Patient meets ONE of the following (i or ii):
 - i. Patient meets ALL of the following criteria (a, b, and c):
 - a) Patient has tried at least one medium-, medium-high, high-, and/or super-high-potency prescription topical corticosteroid; AND

Note: Concomitant use of a topical corticosteroid in with a topical calcineurin inhibitor would meet the requirement.

- b) This topical corticosteroid was applied daily for at least 28 consecutive days; AND
 - c) Inadequate efficacy was demonstrated with this topical corticosteroid therapy, according to the prescriber; OR
 - ii. Patient is treating atopic dermatitis affecting one of the following areas: face, eyes/eyelids, skin folds, and/or genitalia; AND
 - E) Patients meets ALL of the following (i, ii, and iii):
 - i. Patient has tried at least one topical calcineurin inhibitor; AND
Note: Examples of topical calcineurin inhibitors include tacrolimus ointment (Protopic®, generic) and pimecrolimus cream (Elidel®, generic). Concomitant use of a topical calcineurin inhibitor with a topical corticosteroid would meet the requirement.
 - ii. This topical calcineurin inhibitor was applied daily for at least 28 consecutive days; AND
 - iii. Inadequate efficacy was demonstrated with this topical calcineurin inhibitor, according to the prescriber; AND
 - F) The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist.
2. **Vitiligo.** Approve for 6 months if the patient meets all of the following (A, B, C, D, E, and F):
- A) Patient is ≥ 12 years of age; AND
 - B) Patient has nonsegmental vitiligo; AND
 - C) Patient has vitiligo involvement estimated to affect $\leq 10\%$ of the body surface area; AND
 - D) Patient meets ONE of the following (i or ii):
 - i. Patient meets ALL of the following criteria (a, b, and c):
 - a) Patient has tried at least one high-, and/or super-high-potency prescription topical corticosteroid; AND
Note: Concomitant use of a topical corticosteroid in with a topical calcineurin inhibitor would meet the requirement.
 - b) The duration of this topical corticosteroid therapy was at least 12 weeks; AND
Note: Intermittent or continuous use of a topical corticosteroid for at least 12 weeks would meet the requirement.
 - c) Inadequate efficacy was demonstrated with this topical corticosteroid therapy, according to the prescriber; OR
 - ii. Patient is treating vitiligo affecting one of the following areas: face, eyes/eyelids, skin folds, and/or genitalia; AND
 - E) Patients meets ALL of the following (i, ii, and iii):
 - i. Patient has tried at least one topical calcineurin inhibitor; AND
Note: Examples of topical calcineurin inhibitors include tacrolimus ointment (Protopic, generic) and pimecrolimus cream (Elidel, generic). Concomitant use of a topical calcineurin inhibitor with a topical corticosteroid would meet the requirement.
 - ii. This topical calcineurin inhibitor was applied daily for at least 12 weeks; AND
 - iii. Inadequate efficacy was demonstrated with this topical calcineurin inhibitor, according to the prescriber; AND
 - F) The medication is prescribed by or in consultation with a dermatologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Opzelura cream is not recommended in the following situations:

- 1. Concurrent Use with a Biologic or with other JAK inhibitors.** Use of Opzelura in combination with therapeutic biologics or other JAK inhibitors is not recommended (see Appendix for examples).¹ Use of biologics or other JAK inhibitors was prohibited during the Opzelura pivotal studies.² There are no data evaluating combination use of Opzelura with these therapies; therefore, safety and efficacy of these combinations are unknown.
- 2. Concurrent use with Other Potent Immunosuppressants** (e.g., azathioprine, cyclosporine). Use of Opzelura in combination with potent immunosuppressants is not recommended.¹ Use of systemic immunosuppressants was prohibited during the Opzelura pivotal studies.² There are no data evaluating combination of Opzelura with these therapies; therefore, safety and efficacy of these combinations are unknown.
- 3. Alopecia.** Opzelura is not indicated for the treatment of alopecia.¹ A Phase II study involving patients with alopecia areata did not find any significant improvement in hair regrowth with Opzelura 1.5% cream compared with vehicle.⁷ Additional data are needed to establish the efficacy and safety of Opzelura in patients with alopecia.
- 4. Plaque Psoriasis.** Opzelura is not indicated for the treatment of plaque psoriasis.¹ There are very limited Phase II data regarding the use of Opzelura in patients with plaque psoriasis.^{8,9} Additional data are needed to establish the efficacy and safety of Opzelura in patients with plaque psoriasis.
- 5.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Opzelura[®] cream [prescribing information]. Wilmington, DE: Incyte; April 2022.
2. Papp K, Szepletowski JC, Sun K, et al. Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: results from two phase 3, randomized, double-blind studies. *J Am Acad Dermatol.* 2021;85:863-872.
3. Data on file. Opzelura clinical presentation. Incyte Pharmaceuticals; received September 22, 2021.
4. Kim BS, Howell MD, Sun K, et al. Treatment of atopic dermatitis with ruxolitinib cream (JAK1/JAK2 inhibitor) or triamcinolone cream. *J Allergy Clin Immunol.* 2020;145(2):572-582.
5. 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.
6. Schneider L, Tilles S, Lio P, et al. Atopic dermatitis: a practice parameter update 2012. *J Allergy Clin Immunol.* 2013;131:295-299.
7. Olsen EA, Kornacki D, Sun K, et al. Ruxolitinib cream for the treatment of patients with alopecia areata: a 2-part, double-blind, randomized, vehicle-controlled phase 2 study. *J Am Acad Dermatol.* 2020;82(2):412-419.
8. US National Institutes of Health. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2021 Jun 7]. Available from: <https://clinicaltrials.gov/>. Search term: ruxolitinib cream.
9. Punwani N, Scherle P, Flores R, et al. Preliminary clinical activity of a topical JAK1/2 inhibitor in the treatment of psoriasis. *J Am Acad Dermatol.* 2012;67(4):658-664.
10. Rosmarin D, Pandya AG, Lebowitz M, et al. Ruxolitinib cream for the treatment of vitiligo: a randomized, controlled, phase 2 trial. *Lancet.* 2020;396:110-120.
11. Incyte Press Release: Incyte announces positive results from phase 3 TRuE-V program evaluating ruxolitinib cream in patients with vitiligo. Incyte Pharmaceuticals. Available from: <https://investor.incyte.com/press-releases/press-releases/2021/Incyte-Announces-Positive-Results-from-Phase-3-TRuE-V-Program-Evaluating-Ruxolitinib-Cream-in-Patients-with-Vitiligo/default.aspx>. Accessed on July 25, 2022.
12. Rosmarin D, Ezzedine K, Desai S, et al. Efficacy and safety of ruxolitinib cream for the treatment of vitiligo: week 24 pooled analysis of the True V phase 3 studies [poster 34789]. Presented at: the American Academy of Dermatology Annual Meeting; Boston, MA; March 25-29, 2022.

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13. Eleftheriadou V, Atkar R, Batchelor J, et al. British Association of Dermatologists guidelines for the management of people with vitiligo 2021. *Br J Dermatol.* 2022;186(1):18-29.
14. Mumtaz H, Anis S, Akhtar A, et al. Efficacy of tacrolimus versus clobetasol in the treatment of vitiligo. *Cureus.* 2020;12(12):e11985.

Type of Revision	Summary of Changes	Review Date
New Policy	--	10/06/2021
Early Annual Revision	<p>Vitiligo: Added new approval criteria for this indication which include an age requirement, involvement of a specialist, diagnostic confirmation, body surface area involvement limitation, and prior topical therapy.</p> <p>Conditions Not Recommended for Approval: Vitiligo removed from Conditions Not Recommended for Approval.</p>	07/27/2022

APPENDIX

Table 1. Examples of Other Therapeutic Biologics and Other JAK Inhibitors.

JAK – Janus kinase; SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous; IL – Interleukin; PDE4 – Phosphodiesterase 4; IgE – Immunoglobulin E; TSLP – Thymic stromal lymphopoietin.