ITCH-SCRATCH-INFLAMMATION
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NEW for uncontrolled, mild to moderate atopic dermatitis (AD) in non-immunocompromised patients aged ≥12 years[1]

THE ONE-OF-A-KIND TOPICAL JAK INHIBITOR

JAK=Janus kinase.

Opzelura™ (ruxolitinib) cream 1.5%

INDICATION

OPZELURA is 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.

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.

IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

Patients treated with oral Janus kinase inhibitors for inflammatory conditions are at risk for developing serious infections that may lead to hospitalization or death. Reported infections include:

- **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. Carefully consider the benefits and risks of treatment prior to initiating OPZELURA in patients with chronic or recurrent infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with OPZELURA.

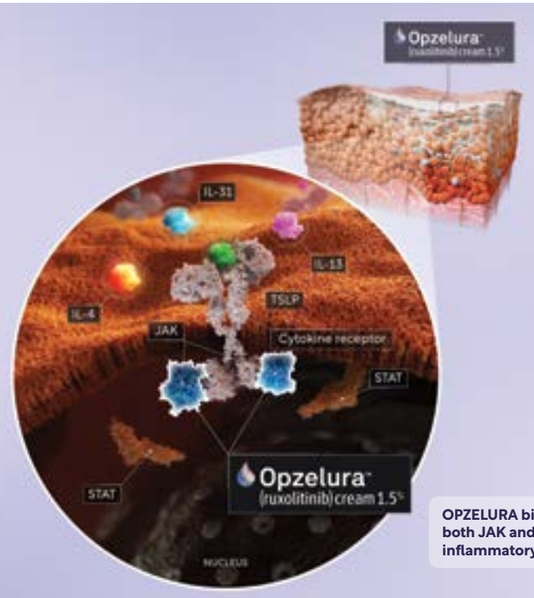
Please see Important Safety Information throughout and Full Prescribing Information and Medication Guide.

Incyte Dermatology

DISCOVER THE POTENTIAL OF THE JAK-STAT PATHWAY IN ATOPIC DERMATITIS (AD)

TARGET A SOURCE OF **ITCH AND INFLAMMATION**[1-3]

OPZELURA is designed to target the signaling of several key JAK-mediated cytokines believed to contribute to itch and inflammation, including[1,2,4,5]: **IL-4, IL-13, IL-31, TSLP**



OPZELURA binds to the JAK enzyme, inhibiting both JAK and STAT activation. As a result, inflammatory mediators are interrupted.[1,3]

The relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known.[1]

Based on preclinical data. Illustrative simulation.

JAKs are intracellular signaling enzymes that act downstream of many inflammatory cytokines involved in AD pathogenesis.[2]

See the full MOA story

IMPORTANT SAFETY INFORMATION (continued)

SERIOUS INFECTIONS (continued)

No cases of active tuberculosis (TB) were reported in clinical trials with OPZELURA. Cases of active TB were reported in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider evaluating patients for latent and active TB infection prior to administration of OPZELURA. During OPZELURA use, monitor patients for the development of signs and symptoms of TB.

Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical trials with Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA. If a patient develops herpes zoster, consider interrupting OPZELURA treatment until the episode resolves.

Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking oral ruxolitinib. OPZELURA initiation is not recommended in patients with active hepatitis B or hepatitis C.

POWERFUL ITCH AND INFLAMMATION RELIEF

>50%

A Clear Difference

of patients achieved clear or almost clear skin (IGA 0/1) with ≥2-point improvement from baseline at week 8*
(53.8% vs 15.1% and 51.3% vs 7.6% vehicle†; $P<0.0001$)[1,6]

>50%

Meaningful Itch Relief

of patients achieved a clinically meaningful improvement in itch (itch NRS4‡) at week 8
(52.2% vs 15.4% and 50.7% vs 16.3% vehicle†; $P<0.0001$)[1,6]

Onset of Itch Reduction

Itch NRS4 response seen as early as day 3
(18.4% vs 4.2% and 13.2% vs 0% vehicle†)[7]

>60%

Significant EASI Improvement

of patients achieved a ≥75% improvement in lesion extent and severity (EASI-75§) at week 8
(vs 24.6% and 14.4% vehicle†; $P<0.0001$).[6]
Mild defined as EASI score 1.1–7.0.[8]
In TRuE-AD1 and TRuE-AD2, respectively, 46% and 50% of patients on OPZELURA vs 56% and 44% of patients on vehicle had a baseline EASI score of 1.1–7.0.[7]

All images are patient portrayals.

OPZELURA was studied in 1249 adult and adolescent patients ≥12 years of age in 2 identically designed double-blind, randomized, vehicle-controlled trials (TRuE-AD1 and TRuE-AD2). In both studies, patients had an affected BSA of 3%-20% and an IGA score of 2 or 3 on a severity scale of 0-4. Patients were randomized to monotherapy with OPZELURA or vehicle BID for 8 weeks.[1,6]
*Measured by IGA-TS, defined as the achievement of clear (IGA 0) or almost clear (IGA 1) skin with at least a 2-point improvement from baseline.[1]
†In TRuE-AD1 and TRuE-AD2, respectively.[1,6]
‡Itch NRS4 is defined as the achievement of at least a 4-point improvement in daily itch on a 0- to 10-point scale, considered a clinically meaningful response; patients in the analysis had an NRS score ≥4 at baseline.[1,6]
§EASI-75 is defined as the achievement of at least 75% improvement in EASI score from baseline.[6]

BID=twice daily; BSA=body surface area; EASI=Eczema Area and Severity Index; IGA=Investigator's Global Assessment; IGA-TS=Investigator's Global Assessment Treatment Success; IL=interleukin; JAK-STAT=Janus kinase-signal transducer and activator of transcription; NRS=numeric rating scale; STAT=signal transducer and activator of transcription; TSLP=thymic stromal lymphopoietin.

IMPORTANT SAFETY INFORMATION (continued)

MORTALITY

Higher rate of all-cause mortality, including sudden cardiovascular death, has been observed in patients treated with oral Janus kinase inhibitors for inflammatory conditions.

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. Patients who are current or past smokers are at additional increased risk. Non-melanoma skin cancers, including basal cell and squamous cell carcinoma, have occurred in patients treated with OPZELURA. Perform periodic skin examinations during OPZELURA treatment and following treatment as appropriate.

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SEE THE **OPZELURA DIFFERENCE**

TREATMENT SUCCESS (IGA-TS*) ACHIEVED AT WEEK 8[7]

SIGNIFICANT SKIN CLEARANCE WITHIN WEEKS[1,7]

PATIENT 1

Actual clinical trial participant. Individual results may vary.

PATIENT 2

Actual clinical trial participant. Individual results may vary.

IMPORTANT SAFETY INFORMATION (continued)

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)

Higher rate of MACE (including cardiovascular death, myocardial infarction, and stroke) has been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if these symptoms occur.

THROMBOSIS

Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis has been observed in patients treated with oral Janus kinase inhibitors for inflammatory conditions. Many of these adverse reactions were serious and some resulted in death. Patients with symptoms of thrombosis should be promptly evaluated.

Thromboembolic events were observed in clinical trials with OPZELURA. There was no clear relationship between platelet count elevations and thrombotic events. OPZELURA should be used with caution in patients who may be at increased risk of thrombosis.

NONGREASY, NONSTEROIDAL CREAM FORMULATION

RETHINK AD RELIEF WITH **OPZELURA**

Patient portrayal.

- The most common adverse reactions (≥1%) were nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increased, urticaria, folliculitis, tonsillitis, and rhinorrhea[1]
- Adverse reactions occurring in <1% for OPZELURA vs 0% for vehicle were neutropenia, allergic conjunctivitis, pyrexia, seasonal allergy, herpes zoster, otitis externa, staphylococcal infection, and acneiform dermatitis[1]
- Low rate of application site reactions such as burning (0.8% with OPZELURA vs 4.4% with vehicle) and pruritus (0% with OPZELURA vs 2.4% with vehicle)[6]
- Discontinuation due to TEAEs with OPZELURA vs vehicle: 0.8% with OPZELURA vs 3.2% with vehicle in TRuE-AD1 and TRuE-AD2[6]

- **Can be applied as a thin layer** twice daily to affected skin on up to 20% BSA (no more than 60 g per week)[1]
- **Directly applied on AD lesions,** including in sensitive skin areas[1]

For topical use only. Not for ophthalmic, oral, or intravaginal use. Stop using when signs and symptoms (eg, itch, rash, and redness) of AD resolve. If signs and symptoms do not improve within 8 weeks, patients should be reexamined by their healthcare provider.[1]

*IGA-TS is defined as the achievement of clear (IGA 0) or almost clear (IGA 1) skin with at least a 2-point improvement from baseline.[1]
TEAE=treatment-emergent adverse event.

IMPORTANT SAFETY INFORMATION (continued)

Thrombocytopenia, Anemia and Neutropenia

Thrombocytopenia, anemia and neutropenia were reported in the clinical trials with OPZELURA. Consider the benefits and risks for individual patients who have a known history of these events prior to initiating therapy with OPZELURA. Perform CBC monitoring as clinically indicated. If signs and/or symptoms of clinically significant thrombocytopenia, anemia, and neutropenia occur, patients should discontinue OPZELURA.

Lipid Elevations

Treatment with oral ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

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THE ONE-OF-A-KIND
TOPICAL JAK INHIBITOR

- **Targets key cytokine signals** believed to contribute to itch and inflammation[1,6]
  Relevance to therapeutic effectiveness is not currently known.
- **Clear or almost clear skin** (IGA 0/1)* in >50% of patients at week 8
  (53.8% vs 15.1% and 51.3% vs 7.6% vehicle†; *P*<0.0001)[1,6]
- **Meaningful itch relief** (Itch NRS4) in >50% of patients at week 8
  (52.2% vs 15.4% and 50.7% vs 16.3% vehicle†; *P*<0.0001)[1,6‡]
  – **Itch NRS4 response seen as early as day 3**
  (18.4% vs 4.2% and 13.2% vs 0% vehicle†)[7]
- **Safety and tolerability results:** The most common adverse reactions (≥1%) were nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increased, urticaria, folliculitis, tonsillitis, and rhinorrhea. See Important Safety Information throughout[1]
- **Nonsteroidal, injection-free**, can be used in sensitive skin areas[1§]

§For topical use only. Not for ophthalmic, oral, or intravaginal use. Stop using when signs and symptoms (eg, itch, rash, and redness) of AD resolve. If signs and symptoms do not improve within 8 weeks, patients should be reexamined by their healthcare provider.[1]

WITH COPAY SAVINGS CARD, ELIGIBLE‖ PATIENTS MAY PAY AS LITTLE AS $10 PER TUBE

Visit **OpzeluraHCP.com** to learn more

OPZELURA was studied in 1249 adult and adolescent patients ≥12 years of age in 2 identically designed double-blind, randomized, vehicle-controlled trials (TRuE-AD1 and TRuE-AD2). In both studies, patients had an affected BSA of 3%-20% and an IGA score of 2 or 3 on a severity scale of 0-4. Patients were randomized to monotherapy with OPZELURA or vehicle BID for 8 weeks.[1,6]
*With a ≥2-grade improvement from baseline.[1]
†In TRuE-AD1 and TRuE-AD2, respectively.[1,6]
‡≥4-point improvement in NRS among patients with a score of ≥4 at baseline.[1]
‖Eligibility required. Individual savings limited to $2,076.50/tube, $10,000 per year. For use only with commercial insurance. The card may not be used if you are enrolled in a government-funded prescription insurance program or if you pay cash for your prescription. Must be used for an FDA-approved indication. Must be used for an FDA-approved indication. **Additional Terms and Conditions apply.**

References: 1. Opzelura. Prescribing Information. Incyte Corporation; 2021. **2.** 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. **3.** Smith P, Yao W, Shepard S, et al. Developing a JAK inhibitor for targeted local delivery: ruxolitinib cream. *Pharmaceutics.* 2021;13(7):1044. doi:10.3390/pharmaceutics13071044. **4.** Cevikbas F, Wang X, Akiyama T, et al. A sensory neuron-expressed IL-31 receptor mediates T helper cell-dependent itch: involvement of TRPV1 and TRPA1. *J Allergy Clin Immunol.* 2014;133(2):448-460. **5.** Wilson SR, Thé L, Batia LM, et al. The epithelial cell-derived atopic dermatitis cytokine TSLP activates neurons to induce itch. *Cell.* 2013;155(2):285-295. **6.** 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.* Published online May 3, 2021. doi:10.1016/j.jaad.2021.04.085. **7.** Data on file. Incyte Corporation. 2021. **8.** Leshem YA, Hajar T, Hanifin JM, Simpson EL. What the Eczema Area and Severity Index score tells us about the severity of atopic dermatitis: an interpretability study. *Br J Dermatol.* 2015;172(5):1353-1357.

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions
The most common adverse reactions (≥1%) are nasopharyngitis (3%), diarrhea (1%), bronchitis (1%), ear infection (1%), eosinophil count increased (1%), urticaria (1%), folliculitis (1%), tonsillitis (1%), and rhinorrhea (1%).

Pregnancy
There will be a pregnancy registry that monitors pregnancy outcomes in pregnant persons exposed to OPZELURA during pregnancy. Pregnant persons exposed to OPZELURA and healthcare providers should report OPZELURA exposure by calling 855-4MEDINFO or 855-463-3463.

Lactation
Advise women not to breastfeed during treatment with OPZELURA and for four weeks after the last dose (approximately 5 elimination half-lives).

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Incyte Dermatology