NEW DRUG APPROVAL

Brand Name	Opzelura™
Generic Name	ruxolitinib
Drug Manufacturer	Incyte Corporation

New Drug Approval

FDA Approval Date: September 21, 2021
Review Designation: Priority
Type of Review: Type 10 - New Indication Submitted as Distinct NDA; New Drug Application (NDA): 215309
Dispensing Restrictions: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Atopic dermatitis is a chronic, pruritic, inflammatory skin disease that occurs most frequently in children but also affects adults. Atopic dermatitis is often associated with an elevated serum level of immunoglobulin E (IgE) and a personal or family history of atopy, which describes a group of disorders that includes eczema, asthma, and allergic rhinitis. Although sensitization to environmental or food allergens is clearly associated with the atopic dermatitis phenotype, it does not seem to be a causative factor but may be a contributory factor in a subgroup of patients with severe disease.

Atopic dermatitis affects approximately 5 to over 20 percent of children worldwide, with large variations among countries and ethnic groups. Countries in Africa, Oceania, and the Asia-Pacific region have higher rates of atopic dermatitis than countries in the Indian subcontinent and Northern/Eastern Europe. In the United States, the overall prevalence is approximately 16 percent, with the highest rates reported in African American children (19 percent).

Data on the prevalence of atopic dermatitis in adults are limited. Population-based studies from Scandinavian countries report prevalence rates of 10 to 14 percent among adults. In a United States, cross-sectional study including nearly 1300 adults, the prevalence of atopic dermatitis was 7.3 percent (95% CI 5.9-8.8).

Efficacy

Two double-blind, randomized, vehicle-controlled trials of identical design (Trial 1 and Trial 2, NCT03745638 and NCT03745651, respectively) enrolled a total of 1249 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. Females constituted 62% of subjects, 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. At baseline, subjects had a mean affected BSA of 9.8% and 39% had affected areas on the face, 25% of subjects had an IGA score of 2 and 75% had a score of 3. 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. Efficacy was also assessed using a ≥ 4-point improvement in Itch NRS.

Table: Efficacy Results at Week 8 in Subjects with Atopic Dermatitis (Trials 1 and 2).

	Trial 1			Trial 2		
	OPZELURA (N = 253)	Vehicle (N = 126)	Treatment Difference and 95% Confidence Interval	OPZELURA (N = 228)	Vehicle (N = 118)	Treatment Difference and 95% Confidence Interval
IGA-TS*	53.8% (136/253)	15.1% (19/126)	38.9% (30.3%, 47.4%)	51.3% (117/228)	7.6% (9/118)	44.1% (36.2%, 52.0%)
Itch NRS (≥ 4 point reduction) (n/N)†	52.2% (84/161)	15.4% (12/78)	36.7% (25.5%, 48.0%)	50.7% (74/146)	16.3% (13/80)	35.8% (24.4%, 47.2%)

* Defined as an IGA score of 0 or 1 with a ≥ 2-grade improvement from baseline

† N = subjects with a baseline Itch NRS score ≥ 4.

Safety

ADVERSE EVENTS

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

WARNINGS & PRECAUTIONS

- Serious Infections: Serious bacterial, mycobacterial, fungal and viral infections have occurred. Regularly monitor patients for infection and manage it promptly.
- Non-melanoma Skin Cancers. Basal cell and squamous cell carcinoma have occurred. Perform periodic skin examinations during treatment and following treatment as appropriate.
- Thrombosis. Thromboembolic events have occurred.
- Thrombocytopenia, Anemia and Neutropenia: Thrombocytopenia, anemia and neutropenia have occurred. Perform CBC monitoring as clinically indicated.

CONTRAINDICATIONS

None

Clinical Pharmacology

MECHANISMS OF ACTION

Ruxolitinib, a Janus kinase (JAK) inhibitor, inhibits JAK1 and JAK2 which mediate the signaling of a number of 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.

Dose & Administration

ADULTS

- Apply a thin layer twice daily to affected areas of up to 20% body surface area. Do not use more than 60 grams per week.
- For topical use only (Not for ophthalmic, oral, or intravaginal use).

PEDIATRICS

- The safety and effectiveness of Opzelura™ for the topical treatment of atopic dermatitis have been established in pediatric patients aged 12 to 17 years of age with mild-to-moderate atopic dermatitis.
- The safety and effectiveness of Opzelura™ in pediatric patients younger than 12 years of age have not been established.

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Cream: 1.5% ruxolitinib.