

**Category**

Best Pharmaceutical Product

**Drug / Device Name**

Opzelura® (ruxolitinib) cream

**Compound/ Tech Name**

ruxolitinib cream

**Trade Name**

Opzelura

**Date of Approval**

2021-09-09

**Indications**

Opzelura is indicated for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adult and pediatric patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or for whom those therapies are not advisable, as well as for the topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older.

**Therapeutic Categories**

Topical JAK1/JAK2 inhibitor

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**Background information and need for drug/device**

Opzelura® (ruxolitinib) cream 1.5% is a cream formulation of Incyte's selective JAK1/JAK2 inhibitor, ruxolitinib. In 2021, Opzelura became the first and only FDA-approved topical JAK inhibitor for the treatment of mild-moderate atopic dermatitis (AD), the most common type of eczema. Then, importantly, in July 2022, Opzelura became the first and only FDA-approved treatment for repigmentation of nonsegmental vitiligo.

Vitiligo is a chronic autoimmune condition characterized by skin depigmentation that results from the loss of pigment-producing cells called melanocytes. The condition occurs with similar frequency in all ethnic groups across ages, although initial symptoms usually appear before age 30.

In the United States, more than 1.5 million people are diagnosed with vitiligo and the overall prevalence is estimated to be 2-3 million, with the majority of patients (approximately 85%) suffering from nonsegmental vitiligo(3). However, until Opzelura, there were no FDA-approved therapies for repigmentation.

There are many misconceptions about vitiligo, and those living with the condition can experience stigma or discrimination from those who do not fully understand their changing appearance and the causes of it (for example, thinking vitiligo is contagious or caused by the sun).

Vitiligo can have a profound impact on people's lives . Some patients anecdotally explain that losing pigment from vitiligo can feel like losing their identity and call the condition "life-altering ." Given the visual nature of vitiligo and lack of societal awareness of the condition, many assume it is "just a cosmetic condition," which can leave people living with it feeling misunderstood and hesitant to open up about their experiences and needs.

In the absence of FDA-approved therapies for repigmentation, some patients say they accepted vitiligo as "something they have to live with." Now, Opzelura offers members of the vitiligo community who choose to pursue treatment with a much-needed pharmacological option.

**\*\*See attachment for referenced content**

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### **History of the development of the drug/device**

Ruxolitinib, the active ingredient of Opzelura, is a potent and selective JAK1/JAK2 inhibitor developed by Incyte through years of pioneering research into the therapeutic potential of the JAK-STAT pathway . During its clinical development, ruxolitinib was found to possess several properties that would facilitate its formulation as a topical treatment to address the role of JAK-STAT signaling in immune-mediated dermatological diseases. Following physicochemical evaluation, the monophosphate salt form of ruxolitinib solubilized into an oil-in-water emulsion cream and was selected for further development; formulation studies on cadaver skin supported a 1.5% w/w concentration.

A preclinical study in minipigs compared the pharmacokinetics of topical administration of 1.5% ruxolitinib cream to that of 15mg ruxolitinib administered orally . Twice-daily administration of ruxolitinib cream produced a 507-fold higher dermal concentration at steady state, whereas a 31-fold lower area under the plasma concentration time curve was observed compared to oral dosing. The ability of ruxolitinib cream to achieve pharmacologically active concentrations on the skin with low systemic absorption supported advancement into clinical studies.

Following the preclinical stage, the first approval of Opzelura came in 2021 for mild-to-moderate AD based on two 8-week Phase 3 studies, wherein over half of treated patients achieved clear or almost clear skin and clinically meaningful itch relief, with some seeing itch reduction within days. With this approval, Opzelura became the first and only topical JAK inhibitor for AD7.

Less than a year later, Opzelura became the first pharmacological therapy FDA-approved for repigmentation of nonsegmental vitiligo in patients 12 years of age and older<sup>1</sup>. In clinical studies, one-third of patients using Opzelura saw at least 75% improvement to vitiligo areas on the face at Week 24, and 20-26% reached at least 50% improvement to vitiligo areas throughout the entire body. Prior to Opzelura, no other FDA-approved pharmacologic options existed for this patient population.

**\*\* See referenced content in the attached**

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**Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition**

As the first and only FDA-approved topical JAK inhibitor, Opzelura is innovative in many ways.

For those with AD, chronic, recurrent itch is frequently reported among patients as the most burdensome symptom. Phase 3 clinical studies of Opzelura assessed clinically meaningful itch improvement as a key secondary endpoint, which was reported by >50% of patients<sup>1</sup>. Additionally, a follow-up Phase 2 study that evaluated onset of itch reduction with Opzelura showed patients experienced rapid and substantial improvement in itch beginning as early as 15 minutes after application and further improving through 28 days of treatment. The study met its primary endpoint with patients experiencing a mean 3.4-point reduction in worst itch on a 0-10 scale by Day 2.

For those with vitiligo, the approval of Opzelura represented a significant milestone for an underserved patient population with high unmet medical need and significant disease burden. In 2021, the FDA held a Patient-Focused Drug Development meeting with vitiligo patients and caregivers focused on the impact of vitiligo as a serious chronic disease.

Vitiligo repigmentation is a gradual process wherein melanocytes must regenerate from reservoirs located in hair follicles and slowly migrate outwards to the epidermis. To this end, clinical studies of Opzelura assessed the degree of repigmentation after 6 months and 12 months of treatment showing continued improvement. Data from two follow-up extension cohorts showed that a second year of treatment increased response among patients who had not yet achieved 90% improvement to vitiligo on the face; the durability of repigmentation was maintained without treatment among patients who had achieved 90% improvement.

In addition to addressing key features of vitiligo that are of significance to patients, multiple clinical studies of ruxolitinib cream in various other immune-mediated dermatologic conditions are also ongoing to realize its full potential beyond the current uses.

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**Please provide appropriate references (ie Pubmed links)**

See full list of references in the attached.

Opzelura® (ruxolitinib) cream Full Prescribing Information. U.S. Food and Drug Administration. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=24da5509-6631-4795-9d42-273faecd08e7>

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