NEXTSTEPS IN DERM | GW School of Medicine & Health Sciences

Topical Ruxolitinib Therapeutic Cheat Sheet

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TRADE NAME

- Opzelura

GENERIC DOSAGE FORM[1]

- Ruxolitinib 1.5% cream

MECHANISM OF ACTION[4]

- Ruxolitnib falls under the drug class known as Janus kinase inhibitors (JAK inhibitors).
- Janus kinase (JAK) is a tyrosine kinase family of cytokine receptors (JAK1, JAK2 and JAK3).
- In conjunction with signal transducer and activator of transcription (STAT), the JAK family regulates erythropoiesis and thrombopoiesis.
- Under physiologic conditions, JAK/STAT pathway activation leads to gene transcription of cytokines and growth factors, resulting in cell growth, differentiation, and apoptosis.
- The JAK/STAT pathway therefore regulates hematopoiesis a nd modulates the immune system.
- Ruxolitinib is a selective JAK1 and JAK2 protein kinase inhibitor.
- The result of this inhibition is disruption of cytokine and growth factor signaling pathways, leading to a decrease in proinflammatory cytokines and chemokines.
- JAK1 is involved in regulating IL-2, IL6 and TNF-alpha while JAK2 is involved with many cellular functions that include proliferation and differentiation.

FDA-APPROVED USE[1]

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

LIMITATIONS OF USE/CONTRAINDICATIONS1[1]

- Use of Opzelura in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

OFF-LABEL USES[5]

- Alopecia areata
- Psoriasis
- Seborrheic dermatitis
- Lichen planus

DOSING[1]

- No more than 60-gram tube per week or one 100-gram tube per 2 weeks.
- Not for intraocular, oral, or intravaginal use.
- Atopic Dermatitis
  - Apply a thin layer twice daily to affected areas of up to 20% body surface area (BSA)
  - In the phase three clinical trials (TRuE-AD1 and TRuE-AD2), patients were treated for 8 weeks before assessing for efficacy.
    - 53.8% and 51.3% of patients respectively had at least 2 grade improvement in their IGA scores at 8 weeks.
    - Although the clinical trials had patients use Opzelura for 8 weeks, incorporating it into a patient's regimen for as needed, long term use is certainly reasonable but should be considered on a case-by-case basis.
- Nonsegmental Vitiligo
  - Apply a thin layer twice daily to affected areas of up to 10% body surface area (BSA)
  - In the clinical trials (TRuE-V1 and TRuE-V2), after treatment for 24 weeks, 30% of patients received 75% improvement of their vitiligo in both studies.
  - Patients continued to use Opzelura for another 28 weeks (a total of 52 weeks) with continued improvement in their re-pigmentation.
    - In practice, it is important to advise patients that it may take 6 months to notice significant improvement in their vitiligo and that they may need to continue it for a longer period if necessary.

SIDE EFFECTS ASSOCIATED[1]

- In atopic dermatitis, the most common adverse reactions (incidence equal or >1%) are nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increased, urticaria, folliculitis, tonsillitis, and rhinorrhea.
- In nonsegmental vitiligo, the most common adverse reactions (incidence equal or >1%) are application site acne, application site pruritus, nasopharyngitis,
  - headache, urinary traction infection, application site erythema, and pyrexia.

WARNINGS[1]

- The black box warning as below for Opzelura are based on one study of patients taking JAK inhibitors orally.
- The black box warning includes increased risk of:
  - Serious infection
  - All-cause mortality
  - Malignancies
  - Major adverse cardiovascular events (MACE)
  - Thrombosis
  - Thrombocytopenia, anemia, and neutropenia
- Since these black box warnings apply to the entire class of JAK inhibitors, they should be discussed with any patient you are considering starting on Opzelura.
- However, it is important to emphasize these were largely seen in patients taking an oral JAK inhibitor who had an inflammatory condition independently placing them at an increased risk for severe adverse events.
- It is important to be cognizant of the BSA recommendations as above (20% or less in atopic dermatitis and 10% or less in vitiligo) in effort to prevent systemic absorption.
- As such, the risk of these adverse events should be viewed as extremely low and would practically only be a consideration if a patient were applying on a very large surface area for a quite a long period of time.

DRUG INTERACTIONS[1]

- Drug interaction studies with Opzelura have not been conducted.
- Ruxolitinib is known to be a substrate for cytochrome P450 3A4 (CYP3A4). Inhibitors of CYP3A4 may increase Ruxolitinib systemic concentrations.
- However, the chance of any meaningful systemic absorption is low, so this is unlikely to have any clinical relevance.

PREGNANCY/LACTATION[1]

- Available data from pregnancies reported in clinical trials with Opzelura are not sufficient to evaluate a drug associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes.
- There are no data on the presence of Ruxolitnib in human milk, the effects on the breastfed child, or the effects on mild productions.
- In lactating rats, Ruxolitinib was present in their milk. When a drug is present in animal milk, it is likely that the drug will be presents in human milk.
- Because of the serious adverse findings in adults, advise women not to breastfeed during treatment with Opzelura and for approximately four weeks after their last dose.

MONITORING[1]

- Regularly monitor patients for infection and manage it promptly.
- Perform periodic skin examinations during treatment and following treatment as appropriate.
- Perform CBC monitoring as clinically indicated.

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