### Indication and Usage

Jakafi® (ruxolitinib) is an oral tablet that allows for individualized dosing.

- Jakafi is indicated for treatment of steroid-refractory acute graft-versus-host disease (GVHD) in adult and pediatric patients 12 years and older.
- Recommended starting dose: 5 mg orally BID.
- Evaluate blood parameters before and during treatment with Jakafi.
- Consider increasing dose to 10 mg BID after ≥3 days of treatment if ANC and platelet counts are not decreased by 50% or more relative to the first day of dosing.

### Dose Modifications

#### Clinically Significant Thrombocytopenia

- After supportive measures, reduce by 1 dose level; resume at prior dose level upon platelet recovery.

#### Jakafi-related ANC < 1 × 10^9/L

- Hold for up to 14 days; resume at 1 dose level lower upon recovery.

#### Elevated Total Bilirubin (No Liver GVHD)

- 3.0−5.0 × ULN: continue at 1 dose level lower until recovery.
- >5.0−10.0 × ULN: hold for up to 14 days until ≤1.5 × ULN; resume at current dose upon recovery.
- >10.0 × ULN: hold for up to 14 days until ≤1.5 × ULN; resume at 1 dose level lower upon recovery.

#### Elevated Total Bilirubin (Liver GVHD)

- >3.0 × ULN: continue at 1 dose level lower until recovery.

#### Hepatic Impairment

- Mild, Moderate, or Severe (NCI criteria): no dose modification needed.
- Stage 3 or 4 liver GVHD: monitor blood counts more frequently for toxicity; consider 5 mg QD.

#### Renal Impairment

- Moderate (CLcr 30 to 59 mL/min) or severe impairment (CLcr ≤ 15 mL/min): start at 5 mg QD.
- ESRD (CLcr ≤ 15 mL/min) on dialysis: start at 5 mg once after dialysis session.
- ESRD (CLcr <15 mL/min) not requiring dialysis: avoid use.

#### Use with Strong CYP3A4 Inhibitors or Fluconazole

- With fluconazole: no adjustment.
- With ketoconazole: 5 mg QD.
- With itraconazole: monitor blood counts more frequently for toxicity and adjust Jakafi dose if necessary.
- With other CYP3A4 inhibitors: no adjustment.

#### Use with Strong CYP3A4 Inducers

- No dose adjustment is recommended.
- Monitor patients frequently and adjust dose based on safety and efficacy.

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1 aGVHD, acute graft-versus-host disease; ANC, absolute neutrophil count; BID, twice daily; CLcr, creatinine clearance; CYP3A4, cytochrome P450 3A4 isozyme; ESRD, end-stage renal disease; QD, once daily; ULN, upper limit of normal.

Please see Important Safety Information for Jakafi on back.
**Indication and Usage**

Jakafi is indicated for treatment of steroid-refractory acute graft-versus-host disease (GVHD) in adult and pediatric patients 12 years and older.

**Important Safety Information**

- Treatment with Jakafi® (ruxolitinib) can cause thrombocytopenia, anemia and neutropenia, which are each dose-related effects. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated.
- Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary.
- Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi.
- Severe neutropenia (ANC <0.5 × 10⁹/L) was generally reversible by withholding Jakafi until recovery.
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines.
- Tuberculosis (TB) infection has been reported. Observe patients taking Jakafi for signs and symptoms of active TB and manage promptly. Prior to initiating Jakafi, evaluate patients for TB risk factors and test those at higher risk for latent infection. Consult a physician with expertise in the treatment of TB before starting Jakafi in patients with evidence of active or latent TB. Continuation of Jakafi during treatment of active TB should be based on the overall risk-benefit determination.
- Progressive multifocal leukoencephalopathy (PML) has occurred with Jakafi treatment. If PML is suspected, stop Jakafi and evaluate.
- Advise patients about early signs and symptoms of herpes zoster and to seek early treatment.
- Increases in hepatitis B viral load with or without associated elevations in alanine aminotransferase and aspartate aminotransferase have been reported in patients with chronic hepatitis B virus (HBV) infections. Monitor and treat patients with chronic HBV infection according to clinical guidelines.
- When discontinuing Jakafi, myeloproliferative neoplasm-related symptoms may return within one week. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, DIC, or multi-organ failure. If any of these occur after discontinuation or while tapering Jakafi, evaluate and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi without consulting their physician. When discontinuing or interrupting Jakafi for reasons other than thrombocytopenia or neutropenia, consider gradual tapering rather than abrupt discontinuation.
- Non-melanoma skin cancers including basal cell, squamous cell, and Merkel cell carcinoma have occurred. Perform periodic skin examinations.
- Treatment with Jakafi has been associated with increases in total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Assess lipid parameters 8-12 weeks after initiating Jakafi. Monitor and treat according to clinical guidelines for the management of hyperlipidemia.
- In myelofibrosis and polycythemia vera, the three most common nonhematologic adverse reactions (incidence >10%) were bruising, dizziness and headache. In acute graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >50%) were infections and edema.
- Dose modifications may be required when administering Jakafi with strong CYP3A4 inhibitors or fluconazole or in patients with renal or hepatic impairment. Patients should be closely monitored and the dose titrated based on safety and efficacy.
- Use of Jakafi during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking Jakafi should not breastfeed during treatment and for two weeks after the final dose.

Please see [Full Prescribing Information](https://hcp.Jakafi.com/gvhd) for Jakafi.