For adults with polycythemia vera after inadequate response to or intolerance of hydroxyurea

**Individualized dosing for Jakafi**

**Indications and Usage**

Jakafi is indicated for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea.

**Important safety considerations**

- Treatment with Jakafi 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.

- 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.

Please see Important Safety Information on the last page for related and other risk information. Please [click here](#) for Full Prescribing Information for complete dosing recommendations.
Options you want for the efficacy and safety you expect

START here

- A CBC and platelet (PLT) count must be performed before initiating therapy, every 2 to 4 weeks until doses are stabilized, and then as clinically indicated.

OPTIMIZE to balance safety and efficacy

Early dose adjustments as needed help to optimize efficacy and safety

In the phase 3 RESPONSE* trial, which compared Jakafi with best available therapy (BAT) in patients with PV who had an inadequate response to or were intolerant of hydroxyurea, the composite primary endpoint was defined as hematocrit (Hct) control without phlebotomy eligibility and a >35% spleen volume reduction as measured by CT or MRI. 1

- 23% of patients receiving Jakafi achieved the composite primary endpoint at week 32 vs <1% for BAT (P < 0.0001).1

Additional dose modifications should be made with frequent monitoring of safety and efficacy. See SPECIAL POPULATIONS tab for dosing recommendations.

INCREASE DOSE

Dose modifications based on insufficient response

- Doses may be increased in 5-mg twice-daily increments to a maximum of 25 mg twice daily.
- Doses should not be increased during the first 4 weeks of therapy and not more frequently than every 2 weeks

Consider dose increases in patients who meet all of these criteria:
- Inadequate efficacy as demonstrated by one or more of the following:
  - Continued need for phlebotomy
  - White blood cell count greater than the upper limit of normal (ULN) range
  - PLT count greater than the ULN range
  - Palpable spleen that is reduced >25% from baseline

PLT count >140 × 10⁹/L
Hemoglobin <12 g/dL
ANC <1.5 × 10⁹/L

DECREASE DOSE

As shown in the chart below, dose reductions should be considered for:
- Hemoglobin <12 g/dL or
- PLT count <100 × 10⁹/L

Dosing Recommendations

If Hb 10 to <12 g/dL and PLT count 75 to <100 × 10⁹/L • Dose reductions should be considered, with the goal of avoiding dose interruptions for anemia and thrombocytopenia

If Hb 8 to <10 g/dL or PLT count 50 to <75 × 10⁹/L • Reduce dose by 5 mg twice daily • For patients on 5 mg twice daily, decrease the dose to 5 mg once daily

If Hb 6-8 g/dL or PLT count ≤50 × 10⁹/L • Interrupt Jakafi dosing

If ANC is ≥1.5 × 10⁹/L

Monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated

SPECIAL POPULATIONS

Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi.

In myelofibrosis and polycythemia vera, the most common nonhematologic adverse reactions (incidence ≥15%) were:
- Palpable spleen
- Edema
- Rash
- Diarrhea

In acute graft-versus-host disease, the most common nonhematologic adverse events were:
- Gastrointestinal symptoms
- Skin reaction
- Diarrhea

Risk for thrombocytopenia, anemia, and neutropenia

Treatment with Jakafi can cause thrombocytopenia, anemia, and neutropenia, which are each dose-related effects.

- Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi.
- Patients developing anemia should not breastfeed during treatment and for 2 weeks after the final dose as breast milk may contain Jakafi.

For patients with polycythemia vera after inadequate response to or intolerance of hydroxyurea

For patients taking Jakafi and who need help to optimize efficacy and safety

- 23% of patients receiving Jakafi achieved the composite primary endpoint at week 32 vs <1% for BAT (P < 0.0001).1

Percent of patients randomized to Jakafi who increased from the starting dose

37% (43/110) WEEK 8

Percent of patients randomized to Jakafi who decreased from the starting dose

5% (6/110) WEEK 8

Percent of patients randomized to Jakafi who discontinued treatment due to an adverse event

4% (14/110) WEEK 32

See SPECIAL POPULATIONS tab for dosing recommendations.
After recovery of hematologic parameter(s) to acceptable levels, dosing may be restarted as shown in the table below:

- Use the most severe category of patient’s hemoglobin, PLT count, or ANC abnormality to determine the corresponding maximum restarting dose.

<table>
<thead>
<tr>
<th>Hb (g/dL)</th>
<th>PLT Count (x 10⁹/L)</th>
<th>ANC (x 10⁹/L)</th>
<th>Dosing Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;8</td>
<td>&lt;50</td>
<td>&lt;1.0</td>
<td>Continue hold</td>
</tr>
<tr>
<td>8 to &lt;10</td>
<td>50 to &lt;75</td>
<td>1.0 to &lt;1.5</td>
<td>5 mg twice daily* or no more than 5 mg twice daily less than the dose that resulted in dose interruption</td>
</tr>
<tr>
<td>10 to &lt;12</td>
<td>75 to &lt;100</td>
<td>1.5 to &lt;2.0</td>
<td>10 mg twice daily* or no more than 5 mg twice daily less than the dose that resulted in dose interruption</td>
</tr>
<tr>
<td>≥12</td>
<td>≥100</td>
<td>≥2.0</td>
<td>15 mg twice daily* or no more than 5 mg twice daily less than the dose that resulted in dose interruption</td>
</tr>
</tbody>
</table>

ANC, absolute neutrophil count; Hb, hemoglobin; PLT, platelet.

* Continue treatment for at least 2 weeks. If stable, dosage may be increased by 5 mg twice daily.

Patients who required dose interruption while receiving a dose of 5 mg twice daily may restart at a dose of 5 mg twice daily or 5 mg once daily, but not higher, once:
- Hemoglobin is ≥10 g/dL
- PLT count is ≥75 x 10⁹/L, and
- ANC is ≥1.5 x 10⁹/L

Dose management after restarting treatment:
- Doses may be titrated, but the maximum total daily dose should not exceed 5 mg less than the dose that resulted in the dose interruption.
- An exception to this is dose interruption following phlebotomy-associated anemia, in which case the maximum total daily dose allowed after restarting Jakafi™ (ruxolitinib) would not be limited.

Please see Important Safety Information on the last page for related and other risk information. Please click here for Full Prescribing Information for complete dosing recommendations.

Renal or hepatic impairment:

Use a starting dose of 5 mg twice daily for patients with:
- **Hepatic Impairment**: Mild, moderate, or severe (Child-Pugh class A, B, C)
- **Renal Impairment**: Moderate (CrCl 30-59 mL/min) or severe (CrCl 15-29 mL/min)

- The recommended starting dose in patients with polycythemia vera who have end-stage renal disease and are on dialysis is 10 mg
- Additional dose modifications should be made with frequent monitoring of safety and efficacy
- Avoid use of Jakafi™ (ruxolitinib) in patients with end-stage renal disease (creatinine clearance, <15 mL/min) not requiring dialysis

Drug interactions:
- Modify the dose of Jakafi when coadministered with strong CYP3A4 inhibitors and fluconazole doses of ≥200 mg
- Avoid the use of fluconazole doses of ≥200 mg daily with Jakafi
- Additional dose modifications should be made with frequent monitoring of safety and efficacy

<table>
<thead>
<tr>
<th>For Patients Coadministered Strong CYP3A4 Inhibitors or Fluconazole Doses of ≥200 mg</th>
<th>Recommended Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting dose for patients with PV:</td>
<td>5 mg twice daily</td>
</tr>
<tr>
<td>If on stable dose for patients with PV:</td>
<td>Decrease dose by 50% (round up to the closest available tablet strength)</td>
</tr>
<tr>
<td>&gt;10 mg twice daily</td>
<td>5 mg once daily</td>
</tr>
<tr>
<td>5 mg twice daily</td>
<td>5 mg once daily</td>
</tr>
<tr>
<td>5 mg once daily</td>
<td>Avoid strong CYP3A4 inhibitor or fluconazole treatment, or interrupt treatment with Jakafi for the duration of strong CYP3A4 inhibitor or fluconazole use</td>
</tr>
</tbody>
</table>

Please see Important Safety Information on the last page for related and other risk information. Please click here for Full Prescribing Information for complete dosing recommendations.
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 × 10^9/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 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 most common nonhematologic adverse reactions (incidence ≥15%) were bruising, dizziness, headache, and diarrhea. 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 2 weeks after the final dose.

Please click here for Full Prescribing Information for Jakafi.