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](HCP.Jakafi.com/PV-Dosing) for Full Prescribing Information for complete dosing recommendations.
For adults with polycythemia vera who have inadequate response to or intolerance of hydroxyurea, phlebotomy eligibility and a ≥35% spleen volume reduction as measured by CT or MRI.1,2

In the phase 3 RESPONSE* trial, which compared Jakafi with best available treatment (BAT) in patients with PV who had an inadequate response to or were intolerant of hydroxyurea, required phlebotomy for observation (15%).1,2

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 dose titration rule is for hematologically-associated anemia, in which case the maximum total daily dose allowed after restarting Jakafi (ruxolitinib) would not be limited.
### Options you want for the efficacy and safety you expect

#### 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 polycythemia vera who had an inadequate response to or were intolerant of BAT, 23% of patients receiving Jakafi achieved the Hct control end point. Monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated.

### Dosing Recommendations

**For Patients Coadministered Strong CYP3A4 Inhibitors or Fluconazole:**

- If on stable dose for patients with PV:
  - 5 mg once daily
  - 5 mg once daily
- If on an adequate starting dose of ruxolitinib, discontinue ruxolitinib, and start a new dose of Jakafi

- If on a stable dose of Jakafi and switch to or start strong CYP3A4 inhibitors or fluconazole, discontinue Jakafi and start a new dose of ruxolitinib

**For Patients Not Coadministered Strong CYP3A4 Inhibitors or Fluconazole:**

- If on stable dose of ruxolitinib:
  - 5 mg twice daily
  - 5 mg once daily
- If on an adequate starting dose of ruxolitinib, discontinue ruxolitinib, and start a new dose of Jakafi

**Special Populations**

- **Renal or hepatic impairment:**
  - Use a starting dose of 5 mg twice daily for patients with end-stage renal disease and 8 mg twice daily for patients with mild (CrCl 30-59 mL/min) or moderate (CrCl 15-29 mL/min) renal impairment
  - Use a starting dose of 10 mg twice daily for patients with mild (CrCl 30-59 mL/min) or moderate (CrCl 15-29 mL/min) renal impairment

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

#### Risk of thrombocytopenia, anemia, and neutropenia

- 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.
- Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary.
- In 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.

#### 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 1 week.
- Consider dose increases in patients who meet all of these criteria:
  - Inadequate efficacy as demonstrated by one or more of the following:
    - Hemoglobin <12 g/dL
    - PLT count <100 × 10^9/L
    - White blood cell count greater than the upper limit of normal (ULN) range
  - Continuation need for phlebotomy
  - Hemoglobin ≥12 g/dL
  - PLT count ≥75 × 10^9/L
  - White blood cell count within the ULN range

- Consider dose decreases in patients who meet all of these criteria:
  - PLT count ≥140 × 10^9/L
  - Hemoglobin <5.5 g/dL

- Hemoglobin ≥12 g/dL and PLT count ≥75 × 10^9/L
- For patients on 5 mg twice daily, decrease the dose to 5 mg once daily

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

#### Special Populations

- **Hepatic Impairment:**
  - 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 in patients with end-stage renal disease (creatinine clearance <15 mL/min) not requiring dialysis.

### Please see Important Safety Information on the back cover for related and other risk information

Please click here for Full Prescribing Information for complete dosing recommendations.

See prescribing information on the back cover 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 × 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 click here for Full Prescribing Information for Jakafi.

References: