The standard of care, now once daily[1]

Jakafi XR™ (ruxolitinib) extended release tablets

11mg • 22mg • 33mg • 44mg • 55mg

DOSING GUIDE

For PV in adults who have had an inadequate response to or are intolerant of HU[1]

AVAILABLE DOSAGES[1]

JAKAFI® (ruxolitinib) dosages	JAKAFI XR™ (ruxolitinib) dosages
5 mg twice daily	11 mg once daily
10 mg twice daily	22 mg once daily
15 mg twice daily	33 mg once daily
20 mg twice daily	44 mg once daily
25 mg twice daily	55 mg once daily

Dose modifications should be considered based on monitoring complete blood count (CBC), including platelet counts, absolute neutrophil count (ANC), and hemoglobin; treatment interruption and restarting dosing; or other adverse reactions, as described in the Full Prescribing Information for JAKAFI and JAKAFI XR.[1]

HU=hydroxyurea; PV=polycythemia vera.

Evaluate all current JAKAFI patients and new patient starts for once-daily JAKAFI XR

INDICATIONS AND USAGE

JAKAFI®/JAKAFI XR™ (ruxolitinib) is for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Thrombocytopenia, Anemia and Neutropenia

- JAKAFI/JAKAFI XR can cause dose-related effects of thrombocytopenia, anemia and neutropenia. 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/JAKAFI XR. Platelet transfusions may be necessary.
- Patients developing anemia may require blood transfusions and/or dose modifications of JAKAFI/JAKAFI XR.
- Severe neutropenia (ANC $<0.5 \times 10^9$/L) was generally reversible by withholding JAKAFI/JAKAFI XR until recovery.

Please see related and other Important Safety Information throughout. Please see Full Prescribing Information for JAKAFI and JAKAFI XR.

Once-daily dosing with JAKAFI XR™ (ruxolitinib)[1]

Dose optimization is key to maintaining the balance between safety and efficacy[1]

1 START[1]

- For patients with PV who have had an inadequate response to or are intolerant of HU, the recommended starting dose of JAKAFI XR is 22 mg once daily
- A CBC count must be performed before initiating JAKAFI XR
- Before initiating JAKAFI XR, inquire about past infections, including tuberculosis, herpes simplex, herpes zoster, and hepatitis B

Taking JAKAFI XR

- JAKAFI XR is dosed orally and can be administered with or without food
- Patients must swallow JAKAFI XR tablets whole. Do not split, chew, or crush tablets

JAKAFI XR is also available in tablets of:

Tablet images shown are for demonstration purposes only and do not represent actual medications.

2 MONITOR[1]

- A CBC must be performed before initiating JAKAFI XR, every 2 to 4 weeks until doses are stabilized, and then as clinically indicated
- Assess lipid parameters approximately 8 to 12 weeks following initiation of JAKAFI XR
- If a dose is missed, patients should not take an additional dose but should take the next usual prescribed dose

3 OPTIMIZE[1]

Individualize dosing of JAKAFI XR to optimize the balance between safety and efficacy

- Dosing may be reduced or temporarily interrupted based on Hb, platelet, or neutrophil counts
- Additionally, dosing may be increased to achieve desired clinical response
- Interrupt treatment for bleeding

The effectiveness and safety of JAKAFI XR have been established based on adequate and well-controlled studies of JAKAFI® (ruxolitinib). JAKAFI XR received approval based on comprehensive data demonstrating bioequivalence to JAKAFI.

IMPORTANT SAFETY INFORMATION (continued)

Risk of Infection

Tuberculosis

- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting JAKAFI/JAKAFI XR until active serious infections have resolved. Observe patients receiving JAKAFI/JAKAFI XR for signs and symptoms of infection and manage promptly.
- Tuberculosis (TB) infection with JAKAFI/JAKAFI XR has been reported. Observe patients taking JAKAFI/JAKAFI XR for signs and symptoms of active TB and manage promptly. Prior to initiating, 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 in patients with evidence of active or latent TB. Continuation during treatment of active TB should be based on the overall risk-benefit determination.

Decrease dose for anemia or thrombocytopenia[1]

Dosing Recommendations	
If Hb is 10 g/dL to <12 g/dL and platelet count is 75 to <100 × 10^9/L	Dose reductions should be considered, with the goal of avoiding dose interruptions for anemia and thrombocytopenia
If Hb is 8 g/dL to <10 g/dL or platelet count is 50 to <75 × 10^9/L	• Reduce JAKAFI XR dose by 11 mg once daily • For patients on 11 mg once daily, interrupt dosing
If Hb is <8 g/dL or platelet count is <50 × 10^9/L	Interrupt JAKAFI XR dosing

Increase dose for insufficient response[1]

If the response is insufficient and platelet, Hb, and neutrophil counts are adequate, JAKAFI XR doses may be increased in increments of 11 mg once daily to a maximum of 55 mg once daily

- Doses should not be increased during the first 4 weeks of therapy and should not be increased more frequently than every 2 weeks

Consider dose increases in patients who meet all of these criteria:

- Inadequate efficacy as demonstrated by 1 or more of the following:
  - Continued need for phlebotomy
  - WBC count greater than the ULN range
  - Platelet count greater than the ULN range
  - Palpable spleen that is reduced <25% from baseline
- Platelet count ≥140 × 10^9/L
- Hb ≥12 g/dL
- ANC ≥1.5 × 10^9/L

Hb=hemoglobin; ULN=upper limit of normal; WBC=white blood cell.

IMPORTANT SAFETY INFORMATION (continued)

Risk of Infection (continued)

Progressive Multifocal Leukoencephalopathy

- Progressive multifocal leukoencephalopathy (PML) has occurred with JAKAFI/JAKAFI XR treatment. If PML is suspected, stop JAKAFI/JAKAFI XR and evaluate.

Herpes Zoster and Herpes Simplex

- Herpes zoster infection, reactivation and/or dissemination has been reported in patients receiving JAKAFI/JAKAFI XR. Advise patients about early signs and symptoms of herpes zoster and seek treatment. Monitor patients for the development of herpes simplex infections. If a patient develops evidence of dissemination of herpes simplex, consider interrupting treatment.

Hepatitis B

- 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.

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Interrupting/restarting dosing[1]

Interrupt JAKAFI XR™ (ruxolitinib) treatment for:

- Anemia (Hb <8 g/dL)
- Thrombocytopenia (platelet count <50 × 10^9/L), **or**
- Neutropenia (ANC <1 × 10^9/L)

After recovery of hematologic parameter(s) to acceptable levels, dosing may be restarted. Use the **most severe category** of patients' Hb, platelet count, **or** ANC abnormality to determine the corresponding maximum restarting dose:

Hemoglobin, Platelet Count, or ANC	JAKAFI XR Maximum Restarting Dose
Hb is <8 g/dL or platelet count is <50 × 10^9/L or ANC is <1 × 10^9/L	Continue hold
Hb is 8 g/dL to <10 g/dL or platelet count is 50 to <75 × 10^9/L or ANC is 1 to <1.5 × 10^9/L	11 mg once daily[a] or no more than 11 mg once daily less than the dose that resulted in dose interruption
Hb is 10 g/dL to <12 g/dL or platelet count is 75 to <100 × 10^9/L or ANC is 1.5 to <2 × 10^9/L	22 mg once daily[a] or no more than 11 mg once daily less than the dose that resulted in dose interruption
Hb is ≥12 g/dL or platelet count is ≥100 × 10^9/L or ANC is ≥2 × 10^9/L	33 mg once daily[a] or no more than 11 mg once daily less than the dose that resulted in dose interruption

[a]Continue JAKAFI XR treatment for at least 2 weeks; if stable, may increase dose by 11 mg once daily.

Patients who required dose interruption while receiving a dose of JAKAFI XR 11 mg once daily may restart JAKAFI XR at a dose of 11 mg once daily, but not higher, when they have:

- Hb ≥10 g/dL
- Platelet count ≥75 × 10^9/L
- ANC ≥1.5 × 10^9/L

Dose management after restarting treatment in PV:

- After restarting JAKAFI XR following treatment interruption, doses may be titrated, but the maximum total daily dose should not exceed 11 mg once daily 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 maximal total daily dose allowed after restarting JAKAFI XR would not be limited

Special populations:

- Avoid fluconazole doses >200 mg daily with JAKAFI XR
- Avoid use of JAKAFI XR in patients with end-stage renal disease (CLcr <15 mL/min) not requiring dialysis

IMPORTANT SAFETY INFORMATION (continued)

Symptom Exacerbation Following Interruption or Discontinuation of Treatment

- When discontinuing JAK-Inhibitors, including JAKAFI/JAKAFI XR, myeloproliferative neoplasm-related signs and symptoms may flare. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, disseminated intravascular coagulation (DIC), or multi-organ failure. If any of these occur after discontinuation or while tapering JAKAFI/JAKAFI XR, evaluate and treat any intercurrent illness and consider restarting or increasing the dose. Instruct patients not to interrupt or discontinue JAKAFI/JAKAFI XR without consulting their physician. When discontinuing or interrupting JAKAFI/JAKAFI XR for reasons other than life-threatening toxicities, consider gradual tapering rather than abrupt discontinuation.

Non-Melanoma Skin Cancer (NMSC)

- NMSC including basal cell, squamous cell, and Merkel cell carcinoma have occurred. Perform periodic skin examinations.

Dose modifications for special populations[1]

Modify the dose of JAKAFI XR accordingly in patients with moderate or severe renal impairment, patients with hepatic impairment, and patients on dialysis.

Renal Impairment Status/ Hepatic Impairment Status	Platelet Count	Recommended Starting Dosage
Renal impairment: Moderate (CLcr of 30–59 mL/min) or severe (CLcr of 15–29 mL/min) **or** **Hepatic impairment:** Mild, moderate, or severe (Child-Pugh class A, B, C)	Any	JAKAFI XR 11 mg once daily

Patients with ESRD on dialysis

- Do not use JAKAFI XR for patients with PV who have ESRD (CLcr <15 mL/min) and are on dialysis with any platelet count
- Avoid use of JAKAFI XR in patients with ESRD (CLcr <15 mL/min) not requiring dialysis

Concomitant use with strong CYP3A4 inhibitors with fluconazole

- Modify the dose of JAKAFI XR when coadministered with strong CYP3A4 inhibitors and fluconazole doses of ≤200 mg
- Avoid the use of fluconazole doses >200 mg daily with JAKAFI XR
- Additional dose modifications should be made with frequent monitoring of safety and efficacy

For Patients Coadministered Strong CYP3A4 Inhibitors or Fluconazole Doses ≤200 mg	Recommended Dose Modification
Starting dose for patients with PV	JAKAFI XR 11 mg once daily
If on stable dose for patients with PV	
JAKAFI XR ≥22 mg once daily	Reduce JAKAFI XR dose by 50% (round up to the closest available tablet strength)
JAKAFI XR 11 mg once daily	Avoid strong CYP3A4 inhibitor or fluconazole treatment or interrupt treatment with JAKAFI XR for the duration of strong CYP3A4 or fluconazole use

CLcr=creatinine clearance; ESRD=end-stage renal disease.

IMPORTANT SAFETY INFORMATION (continued)

Lipid Elevations

- Treatment with JAKAFI/JAKAFI XR has been associated with increases in total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Assess lipid parameters 8-12 weeks after initiation.

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Established by its legacy, now with the choice of once-daily administration[1]

IncyteCARES offers dedicated support for JAKAFI XR access

Scan the QR code or call IncyteCARES Monday through Friday, 8 AM–8 PM ET at **1-855-452-5234** for benefit verification assistance.

IMPORTANT SAFETY INFORMATION (continued)

Major Adverse Cardiovascular Events (MACE)

- Another JAK-inhibitor has increased the risk of major adverse cardiovascular events (MACE), including cardiovascular death, myocardial infarction, and stroke (compared to those treated with TNF blockers), in patients with rheumatoid arthritis, a condition for which JAKAFI®/JAKAFI XR™ (ruxolitinib) is not indicated. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur.

Thrombosis

- Another JAK-inhibitor has increased the risk of thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis (compared to those treated with TNF blockers), in patients with rheumatoid arthritis, a condition for which JAKAFI/JAKAFI XR is not indicated. In patients with myelofibrosis (MF) and polycythemia vera (PV), the rates of thromboembolic events were similar in JAKAFI/JAKAFI XR and control treated patients. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately.

Secondary Malignancies

- Another JAK-inhibitor has increased the risk of lymphoma and other malignancies, excluding NMSC (compared to those treated with TNF blockers), in patients with rheumatoid arthritis, a condition for which JAKAFI/JAKAFI XR is not indicated. Patients who are current or past smokers are at additional increased risk.

Adverse Reactions

- In polycythemia vera, the most common hematologic adverse reactions (incidence >20%) were thrombocytopenia and anemia. The most common nonhematologic adverse reactions (incidence ≥15%) were bruising, dizziness, headache and diarrhea.

Drug Interactions

- Avoid concomitant use with fluconazole doses greater than 200 mg. Dose modifications may be required when administering fluconazole doses of 200 mg or less, or with strong CYP3A4 inhibitors, or in patients with renal or hepatic impairment. Patients should be closely monitored and the dose titrated based on safety and efficacy.

Pregnancy

- Use during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking JAKAFI/JAKAFI XR should not breastfeed during treatment and for 2 weeks after the final dose.

Please see related and other Important Safety Information throughout. Please see Full Prescribing Information for JAKAFI and JAKAFI XR.

Reference: 1. JAKAFI/JAKAFI XR Prescribing Information. Wilmington, DE: Incyte Corporation.