

Ruxolitinib Extended Release (Jakafi XR) for the Management of Myelofibrosis, Polycythemia Vera, and Graft-Versus-Host Disease

Description: This document provides guidance on the safe use, monitoring, and adverse event management associated with ruxolitinib extended release in its approved indications.

Background: Ruxolitinib extended release (Jakafi XR) is an oral Janus Associated Kinase (JAK)1/JAK2 inhibitor formulated for once-daily administration for the treatment of myelofibrosis (MF), polycythemia vera (PV), and graft-versus-host disease (GVHD). A bioequivalence study in healthy adults showed that the XR formulation provides overall ruxolitinib exposure comparable to the immediate-release (IR) formulation.¹

FDA-Approved Indications²:

- Intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera (PV) MF, and post-essential thrombocythemia MF in adults
- PV in adults who have had an inadequate response to or are intolerant of hydroxyurea
- Steroid-refractory acute GVHD in adult and pediatric patients 12 years and older
- Chronic graft-versus-host disease after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older

Common Adverse Reactions²:

- MF / PV (≥15%):
 - Hematologic (>20%):
 - Thrombocytopenia
 - Anemia
 - Non-hematologic (≥15%):
 - Bruising
 - Dizziness
 - Headache
 - Diarrhea

Acute GVHD (> 50%)	Chronic GVHD
Hematologic: • Anemia • Thrombocytopenia • Neutropenia	Hematologic (>35%) • Anemia • Thrombocytopenia
Non-hematologic • Infections (pathogen not specified) • Edema	Non-hematologic (≥20%) • Infections (pathogen not specified) • Viral infections

IMPORTANT NOTICE: NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, does not provide individual medical advice, and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual's sole responsibility to seek guidance from a qualified healthcare professional. *Updated October 2026 PQI-289*

Treatment-Emergent Adverse Events (TEAEs) in Healthy Participants in a Bioequivalence Study of Ruxolitinib IR and XR¹:

Event, n (%)	Ruxolitinib IR (n=168)	Ruxolitinib XR (n=169)
TEAEs	34 (20.2)	20 (11.8)
Most common TEAEs		
Headache	8 (4.8)	10 (5.9)
Nasal Congestion	2 (1.2)	5 (3)
Platelet count increased	2 (1.2)	4 (2.4)
Oropharyngeal pain	2 (1.2)	3 (1.8)
Treatment-related TEAEs	10 (6)	12 (7.1)

PQI Process:

- Dosing and Dosing Modifications²:
 - Ruxolitinib IR/XR is dosed based on indication and/or platelet count.
 - Doses should be individualized based on safety and efficacy.
 - Starting doses may need to be modified in patients with renal or hepatic impairment.
 - Advise patients not to breastfeed during treatment and for 2 weeks after final dose.
 - The following table outlines dosing equivalency between the IR and XR formulations:

Ruxolitinib IR (BID)	Ruxolitinib XR (QD)
5 mg	11 mg
10 mg	22 mg
15 mg	33 mg
20 mg	44 mg
25 mg	55 mg

- Monitoring²:
 - Prior to initiation of treatment:
 - Perform a complete blood count (CBC) with differential; for patients with aGVHD or cGVHD, also assess bilirubin.
 - Inquire about past infections, including tuberculosis, herpes simplex, herpes zoster, and hepatitis B.
 - Serious infections should be resolved before starting therapy.
 - During treatment:
 - Perform a CBC every 2 to 4 weeks until doses are stabilized, and then as clinically indicated.
 - For patients with aGVHD or cGVHD, monitor CBC, including platelet count and ANC, and bilirubin every 2 to 4 weeks until doses are stabilized, then as clinically indicated.
 - Assess lipid parameters approximately 8 to 12 weeks following initiation of therapy.
 - Monitor for development of Major Adverse Cardiovascular Events (MACE).

- Assess patients for signs and symptoms of infection and initiate appropriate treatment promptly.
 - Perform periodic skin examinations due to the risk of non-melanoma skin cancer.
 - Evaluate and treat symptoms of thrombosis promptly.
 - Monitor for development of secondary malignancies, particularly in patients who are current or past smokers.
- Symptom exacerbation following interruption or discontinuation with MF:
 - Consider gradual tapering rather than abrupt discontinuation when appropriate; if symptoms occur after discontinuation or during tapering, evaluate and treat as appropriate and consider resuming treatment.
- Drug-Drug Interactions²:
 - Fluconazole
 - Avoid concomitant fluconazole doses greater than 200 mg daily.
 - For fluconazole doses $\leq$ 200 mg, modify the ruxolitinib dose according to the indication:
 - aGVHD: ruxolitinib IR 5 mg once daily; do not use ruxolitinib XR.
 - cGVHD: ruxolitinib IR 5 mg twice daily or ruxolitinib XR 11 mg once daily.
 - For other indications, reduce the ruxolitinib IR/XR dosage as recommended in the prescribing information.
 - Strong CYP3A4 Inhibitors
 - Reduce the ruxolitinib IR/XR dosage as recommended, except in patients with aGVHD or cGVHD.
 - For patients with aGVHD or cGVHD, monitor blood counts more frequently for toxicity and modify the ruxolitinib IR/XR dosage for adverse reactions if they occur.
 - Strong CYP3A4 Inducers
 - May decrease ruxolitinib exposure and reduce efficacy. Monitor patients frequently and adjust ruxolitinib IR/XR doses based on safety and efficacy.

Patient-Centered Activities²:

- Counsel patients to avoid grapefruit/grapefruit juice, as grapefruit may inhibit CYP3A4 and increase ruxolitinib exposure (not specifically mentioned in the PI).
- If a dose is missed, the patient should not take an additional dose, but should take the next usual prescribed dose.
- Counsel patients to swallow ruxolitinib XR whole. Do not split, chew, or crush.
- Counsel patients on risk of thrombocytopenia, anemia, and neutropenia; advise patients that routine CBC monitoring is required. Advise patients to report any unusual bleeding or bruising.
- Inform patients of the signs and symptoms of infection and advise them to report these promptly.
- Advise patients to continue taking their medication as prescribed and not to interrupt, discontinue, or change their dose without consulting their healthcare provider, as disease symptoms may return after treatment is stopped.
- Inform patients that there is an increased risk of non-melanoma skin cancer and advise them to report any new or changing skin lesions or a history of skin cancer.
- Inform patients of the potential for increased blood cholesterol levels and that periodic monitoring may be required.

- Advise patients, particularly current or former smokers or those with cardiovascular risk factors, to seek medical attention immediately for signs or symptoms of cardiovascular events, deep vein thrombosis (DVT), or pulmonary embolism (PE).
- Advise patients, particularly current or former smokers or those with a history of malignancy, that JAK inhibitors have been associated with an increased risk of certain cancers.
- Advise patients to inform their healthcare provider or pharmacist of all prescription medications, over-the-counter medications, herbal products, and dietary supplements they are taking.
- Inform women not to breastfeed during treatment and for 2 weeks after the final dose.
- Refer to [Patient Education Sheet \(PES\)](#) for further details.

References:

1. Xiaohua Gong, Zhiyin Xun, Jay Getsy, Ryan McGee, John Mondick, Naresh Punwani; Bioequivalence of ruxolitinib once-daily extended-release vs twice-daily immediate-release tablets in healthy adults. *Blood* 2025; 146 (Supplement 1): 5045.
2. Jakafi (ruxolitinib) / Jakafi XR (ruxolitinib) extended-release tablets [prescribing information]. Wilmington, DE: Incyte Corporation; July 2026.