Jakafi® ruxolitinib (tablets)
5mg • 10mg • 15mg • 20mg • 25mg

Jakafi XR™ (ruxolitinib) extended release tablets
11mg • 22mg • 33mg • 44mg • 55mg

MF

For patients with intermediate or high-risk myelofibrosis

Individualized dosing for JAKAFI

INDICATIONS AND USAGE

JAKAFI®/JAKAFI XR™ (ruxolitinib) is for treatment of intermediate or high-risk myelofibrosis (MF), including primary MF, post–polycythemia vera MF and post–essential thrombocythemia MF in adults.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Thrombocytopenia, Anemia and Neutropenia

- JAKAFI®/JAKAFI XR™ (ruxolitinib) 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 Important Safety Information on the back cover for related and other risk information. Refer to the accompanying Full Prescribing Information for complete dosing recommendations for JAKAFI/JAKAFI XR.

HCP.Jakafi.com/MF-Dosing

Jakafi® (ruxolitinib) tablets | Jakafi XR® (ruxolitinib) extended-release tablets

In intermediate or high-risk myelofibrosis

Individualized dose adjustments for optimized efficacy and safety[1]

MF

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.

The recommended starting dose of JAKAFI for MF is based on PLT count.

PLT Count (× 10^9/L)	Recommended Starting Dose
50 to <100	5 mg twice daily
100 to 200	15 mg twice daily
>200	20 mg twice daily

JAKAFI is also available in 10 mg and 25 mg tablets

CBC, complete blood count.
Tablets shown are not actual size.

Early dose adjustments as needed help to optimize efficacy and safety

In the phase 3 COMFORT-I trial of patients with intermediate-2–risk or high-risk MF, the primary endpoint was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline to week 24.[1,2]*

- 42% of patients receiving JAKAFI achieved a ≥35% reduction in spleen volume at week 24 vs 0.7% of patients receiving placebo ($P < 0.0001$)[2]

70% of patients receiving JAKAFI in COMFORT-I required a dose adjustment in the first 12 weeks of therapy[3]

- The effectiveness and safety of JAKAFI XR has been established based on adequate and well-controlled studies of JAKAFI

See **STARTING PLT COUNT 50 TO <100 × 10^9/L** tab for recommended dose modifications in patients with a starting platelet count of 50 to <100 × 10^9/L.

See **SPECIAL POPULATIONS** tab for dosing information in patients with renal or hepatic impairment and for information on drug interactions.

OPTIMIZE to balance safety and efficacy

Starting PLT Count ≥100 × 10^9/L

INCREASE DOSE

In the case of an **insufficient response**, consider an increase in the dose if patient meets all these criteria:

- ☑ **Insufficient spleen reduction†**
- ☑ **PLT count >125 × 10^9/L at 4 weeks and never <100 × 10^9/L**
- ☑ **Absolute neutrophil count (ANC) >0.75 × 10^9/L**

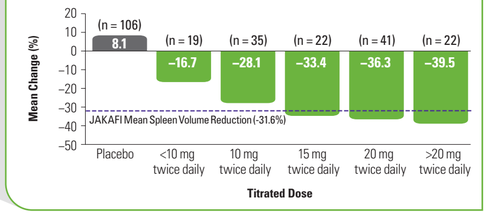
Increase dose by 5-mg twice-daily increments to a maximum of 25 mg twice daily

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

Discontinue JAKAFI if there is no spleen size reduction or symptom improvement after 6 months of therapy.

† Failure to achieve a reduction from pre-treatment baseline in either palpable spleen length of 50% or spleen volume of 35% as measured by CT or MRI.

COMFORT-I: Mean Change in Spleen Volume by Dose at Week 24[3]



Adapted with permission from *Haematologica*.

- Based on limited clinical data, long-term maintenance at 5-mg twice-daily dosing has not shown responses. Continued use at this dose should be limited to patients in whom the benefits outweigh the potential risks

MONITOR frequently

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

DECREASE DOSE

In the case of a **Hematologic Toxicity** including:

☐ **Thrombocytopenia**

Discontinuation can be avoided by reducing the dose or temporarily withholding JAKAFI

Twice-Daily Dose at Time of PLT Decline	25 mg	20 mg	15 mg	10 mg	5 mg
PLT Count (× 10^9/L)	New recommended twice daily dose				
100 to <125	20 mg	15 mg	No change		
75 to <100	10 mg			No change	
50 to <75	5 mg				No change
<50	Hold				

PLT, platelet.

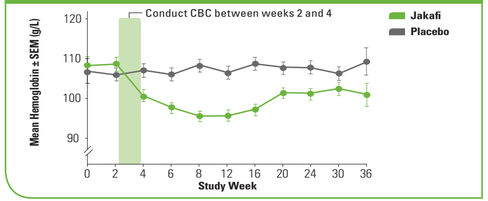
- **In patients receiving JAKAFI in the COMFORT studies, PLT counts and hemoglobin levels generally stabilized after 8 to 12 weeks[1-4]‡**

☐ **Anemia**

Dose modifications of JAKAFI and/or blood transfusions may be required for patients developing anemia

- In COMFORT-I, 60% of patients treated with JAKAFI and 38% of patients receiving placebo received red blood cell transfusions during randomized treatment[1]
- In patients receiving JAKAFI in the COMFORT studies, mean decreases in hemoglobin reached a nadir of approximately 1.5 to 2.0 g/dL below baseline after 8 to 12 weeks of therapy and then gradually recovered to a new steady state that was approximately 1.0 g/dL below baseline[1]

COMFORT-I: Mean Hemoglobin Levels Over Time[2]



CBC, complete blood count; SEM,standard error of the mean.

- **In COMFORT-I, grade 3 and 4 thrombocytopenia or anemia occurred in 13% and 45% of patients receiving JAKAFI, respectively[2]**
- **<1% of patients receiving JAKAFI in the COMFORT studies discontinued due to anemia or thrombocytopenia[1-4]**

INTERRUPT DOSE

Interrupt JAKAFI treatment for:

- Bleeding requiring intervention, regardless of current platelet count,
- Thrombocytopenia (PLT <50 × 10^9/L), **or**
- Neutropenia (ANC <0.5 × 10^9/L)

See **RESTARTING** tab for dose modifications.

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.

Please see Important Safety Information on the back cover for related and other risk information. Refer to the accompanying Full Prescribing Information for complete dosing recommendations for JAKAFI/JAKAFI XR.

* COMFORT-I (COntrolled MyeloFibrosis study with ORal JAK inhibitor Treatment-I) was a randomized, double-blind, placebo-controlled phase 3 study with 309 patients with intermediate-2–risk or high-risk myelofibrosis. The primary endpoint was the proportion of subjects achieving a ≥35% reduction in spleen volume from baseline to week 24 as measured by CT or MRI. A secondary endpoint was the proportion of subjects with a ≥50% reduction in Total Symptom Score from baseline to week 24 as measured by the daily patient diary, the modified Myelofibrosis Symptom Assessment Form.[1,2]

† COMFORT-II (COntrolled MyeloFibrosis study with ORal JAK inhibitor Treatment-II) was a randomized, open-label phase 3 study with 219 patients with intermediate-2–risk or high-risk myelofibrosis. The primary endpoint was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline at week 48 as measured by CT or MRI. Best available therapy in COMFORT-II included hydroxyurea (46.6%) and glucocorticoids (16.4%), as well as no medication, anagrelide, epoetin alfa, thalidomide, lenalidomide, mercaptopurine, thioguanine, danazol, peginterferon alfa-2a, interferon-α, melphalan, acetylsalicylic acid, cytarabine, and colchicine.[1,4,5]

Starting PLT Count 50 to <100 × 10^9/L

The recommended starting dose in MF for patients with a starting PLT count of 50 to <100 × 10^9/L is 5 mg twice daily

INCREASE DOSE

Only after the first 4 weeks of therapy and not more frequently than every 2 weeks if patient meets all these criteria:

- ☑ **Insufficient spleen reduction***
- ☑ **PLT count has remained ≥40 × 10^9/L and has not decreased by >20% in the prior 4 weeks**
- ☑ **ANC >1.0 × 10^9/L**
- ☑ **No dose reduction or interruption for an adverse event or hematological toxicity in the prior 4 weeks**

Increase dose by increments of 5 mg daily to a maximum of 10 mg twice daily

Continuation of treatment for more than 6 months should be limited to patients in whom the benefits outweigh the risks.

Discontinue JAKAFI® (ruxolitinib) if there is no spleen size reduction or symptom improvement after 6 months of therapy.

* Failure to achieve a reduction from pre-treatment baseline in either palpable spleen length of 50% or spleen volume of 35% as measured by CT or MRI.

DECREASE DOSE

Reduce the dose of JAKAFI in patients with platelet counts <35 × 10^9/L

PLT Count	Dosing Recommendations
<25 × 10^9/L	• Interrupt dosing
25 to <35 × 10^9/L **and** the platelet count decline is <20% during the prior 4 weeks	• Decrease dose by 5 mg once daily • For patients on 5 mg once daily, maintain dose at 5 mg once daily
25 to <35 × 10^9/L **and** the platelet count decline is ≥20% during the prior 4 weeks	• Decrease dose by 5 mg twice daily • For patients on 5 mg twice daily, decrease the dose to 5 mg once daily • For patients on 5 mg once daily, maintain dose at 5 mg once daily

PLT, platelet.

INTERRUPT FOR:

- Bleeding requiring intervention regardless of current platelet count,
- PLT counts <25 × 10^9/L, **or**
- ANC <0.5 × 10^9/L

RESTART

After recovery of PLT counts to >35 × 10^9/L and ANC >0.75 × 10^9/L at the higher of:

- 5 mg once daily **or**
- 5 mg twice daily below the largest dose in the week prior to the decrease in PLT count below 25 × 10^9/L or ANC below 0.5 × 10^9/L that led to dose interruption

See **SPECIAL POPULATIONS** tab for dosing information in patients with renal or hepatic impairment and for information on drug interactions.

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 for JAKAFI/JAKAFI XR.

Starting PLT Count 50 to <100 × 10^9/L

Jakafi® (ruxolitinib) tablets 5mg • 10mg • 15mg • 20mg | Jakafi XR® (ruxolitinib) extended-release tablets 11mg • 22mg • 33mg • 44mg • 66mg

In intermediate or high-risk myelofibrosis

Individualized dose adjustments for optimized efficacy and safety[1]

MF

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.

The recommended starting dose of JAKAFI for MF is based on PLT count.

PLT Count (× 10⁹/L)	Recommended Starting Dose
50 to <100	5 mg twice daily
100 to 200	15 mg twice daily
>200	20 mg twice daily

JAKAFI is also available in 10 mg and 25 mg tablets

CBC, complete blood count.
Tablets shown are not actual size.

Early dose adjustments as needed help to optimize efficacy and safety

In the phase 3 COMFORT-I trial of patients with intermediate-2–risk or high-risk MF, the primary endpoint was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline to week 24.[1,2]*

- 42% of patients receiving JAKAFI achieved a ≥35% reduction in spleen volume at week 24 vs 0.7% of patients receiving placebo ($P < 0.0001$)[2]

70% of patients receiving JAKAFI in COMFORT-I required a dose adjustment in the first 12 weeks of therapy[3]

- The effectiveness and safety of JAKAFI XR has been established based on adequate and well-controlled studies of JAKAFI

See **STARTING PLT COUNT 50 TO <100 × 10⁹/L** tab for recommended dose modifications in patients with a starting platelet count of 50 to <100 × 10⁹/L.

See **SPECIAL POPULATIONS** tab for dosing information in patients with renal or hepatic impairment and for information on drug interactions.

OPTIMIZE to balance safety and efficacy

Starting PLT Count ≥100 × 10⁹/L

INCREASE DOSE

In the case of an **insufficient response**, consider an increase in the dose if patient meets all these criteria:

- ☑ **Insufficient spleen reduction†**
- ☑ **PLT count >125 × 10⁹/L at 4 weeks and never <100 × 10⁹/L**
- ☑ **Absolute neutrophil count (ANC) >0.75 × 10⁹/L**

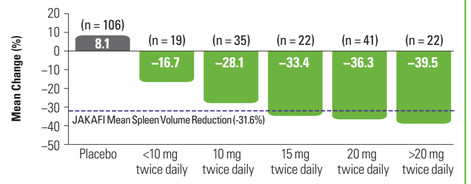
Increase dose by 5-mg twice-daily increments to a maximum of 25 mg twice daily

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

Discontinue JAKAFI if there is no spleen size reduction or symptom improvement after 6 months of therapy.

† Failure to achieve a reduction from pre-treatment baseline in either palpable spleen length of 50% or spleen volume of 35% as measured by CT or MRI.

COMFORT-I: Mean Change in Spleen Volume by Dose at Week 24[3]



Adapted with permission from Hematologica.

- Based on limited clinical data, long-term maintenance at 5-mg twice-daily dosing has not shown responses. Continued use at this dose should be limited to patients in whom the benefits outweigh the potential risks

MONITOR frequently

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

DECREASE DOSE

In the case of a **Hematologic Toxicity** including:

☐ **Thrombocytopenia**

Discontinuation can be avoided by reducing the dose or temporarily withholding JAKAFI

Twice-Daily Dose at Time of PLT Decline	25 mg	20 mg	15 mg	10 mg	5 mg
PLT Count (× 10⁹/L)	New recommended twice daily dose				
100 to <125	20 mg	15 mg	No change		
75 to <100	10 mg			No change	
50 to <75	5 mg				No change
<50	Hold				

PLT, platelet.

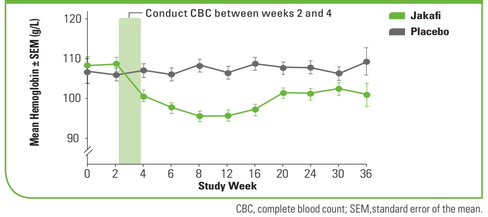
- **In patients receiving JAKAFI in the COMFORT studies, PLT counts and hemoglobin levels generally stabilized after 8 to 12 weeks[1-4*‡]**

☐ **Anemia**

Dose modifications of JAKAFI and/or blood transfusions may be required for patients developing anemia

- In COMFORT-I, 60% of patients treated with JAKAFI and 38% of patients receiving placebo received red blood cell transfusions during randomized treatment[1]
- In patients receiving JAKAFI in the COMFORT studies, mean decreases in hemoglobin reached a nadir of approximately 1.5 to 2.0 g/dL below baseline after 8 to 12 weeks of therapy and then gradually recovered to a new steady state that was approximately 1.0 g/dL below baseline[1]

COMFORT-I: Mean Hemoglobin Levels Over Time[2]



CBC, complete blood count; SEM,standard error of the mean.

- **In COMFORT-I, grade 3 and 4 thrombocytopenia or anemia occurred in 13% and 45% of patients receiving JAKAFI, respectively[2]**
- **<1% of patients receiving JAKAFI in the COMFORT studies discontinued due to anemia or thrombocytopenia[1-4]**

INTERRUPT DOSE

Interrupt JAKAFI treatment for:

- Bleeding requiring intervention, regardless of current platelet count,
- Thrombocytopenia (PLT <50 × 10⁹/L), **or**
- Neutropenia (ANC <0.5 × 10⁹/L)

See **RESTARTING** tab for dose modifications.

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.

Please see Important Safety Information on the back cover for related and other risk information. Refer to the accompanying Full Prescribing Information for complete dosing recommendations for JAKAFI/JAKAFI XR.

* COMFORT-I (COntrolled MyeloFibrosis study with ORal JAK inhibitor Treatment-I) was a randomized, double-blind, placebo-controlled phase 3 study with 309 patients with intermediate-2–risk or high-risk myelofibrosis. The primary endpoint was the proportion of subjects achieving a ≥35% reduction in spleen volume from baseline to week 24 as measured by CT or MRI. A secondary endpoint was the proportion of subjects with a ≥50% reduction in Total Symptom Score from baseline to week 24 as measured by the daily patient diary, the modified Myelofibrosis Symptom Assessment Form.[1,2]

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Restarting dose in case of hematologic toxicity in patients with starting PLT count ≥100 × 10⁹/L

Treatment interruption and restarting dosing

- After recovery of PLT counts >50 × 10⁹/L and ANC >0.75 × 10⁹/L, dosing may be restarted
- The maximum allowable dose that may be used in restarting JAKAFI® (ruxolitinib) after a previous interruption is as shown below

Maximum restarting doses for JAKAFI after safety interruption for thrombocytopenia

Current PLT Count (× 10⁹/L)	Maximum Dose When Restarting Treatment With JAKAFI[a]
≥125	20 mg twice daily
100 to <125	15 mg twice daily
75 to <100	10 mg twice daily for at least 2 weeks; if stable, may increase to 15 mg twice daily
50 to <75	5 mg twice daily for at least 2 weeks; if stable, may increase to 10 mg twice daily
<50	Continue hold

[a] Maximum doses are displayed. When restarting, begin with a dose at least 5 mg twice daily below the dose at interruption.
PLT, platelet.

- Following treatment interruption for ANC <0.5 × 10⁹/L, after ANC recovers to ≥0.75 × 10⁹/L, restart dosing at the higher of 5 mg once daily or 5 mg twice daily below the largest dose in the week prior to the treatment interruption

Restarting dose in case of bleeding

- Once the bleeding event has resolved, consider resuming treatment at the prior dose if the underlying cause of bleeding has been controlled. If the bleeding event has resolved but the underlying cause persists, consider resuming treatment with JAKAFI at a lower dose

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 for JAKAFI/JAKAFI XR.

Jakafi® (ruxolitinib) tablets | Jakafi XR® (ruxolitinib) extended-release tablets

In intermediate or high-risk myelofibrosis

Individualized dose adjustments for optimized efficacy and safety[1]

MF

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.

The recommended starting dose of JAKAFI for MF is based on PLT count.

PLT Count (× 10⁹/L)	Recommended Starting Dose
50 to <100	5 mg twice daily
100 to 200	15 mg twice daily
>200	20 mg twice daily

JAKAFI is also available in 10 mg and 25 mg tablets

CBC, complete blood count.
Tablets shown are not actual size.

Early dose adjustments as needed help to optimize efficacy and safety

In the phase 3 COMFORT-I trial of patients with intermediate-2–risk or high-risk MF, the primary endpoint was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline to week 24.[1,2]*

- 42% of patients receiving JAKAFI achieved a ≥35% reduction in spleen volume at week 24 vs 0.7% of patients receiving placebo ($P < 0.0001$)[2]



of patients receiving JAKAFI in COMFORT-I required a dose adjustment in the first 12 weeks of therapy[3]

- The effectiveness and safety of JAKAFI XR has been established based on adequate and well-controlled studies of JAKAFI

See **STARTING PLT COUNT 50 TO <100 × 10⁹/L** tab for recommended dose modifications in patients with a starting platelet count of 50 to <100 × 10⁹/L.

See **SPECIAL POPULATIONS** tab for dosing information in patients with renal or hepatic impairment and for information on drug interactions.

OPTIMIZE to balance safety and efficacy

Starting PLT Count ≥100 × 10⁹/L

INCREASE DOSE

In the case of an **insufficient response**, consider an increase in the dose if patient meets all these criteria:

- ☑ **Insufficient spleen reduction**†
- ☑ **PLT count >125 × 10⁹/L at 4 weeks and never <100 × 10⁹/L**
- ☑ **Absolute neutrophil count (ANC) >0.75 × 10⁹/L**

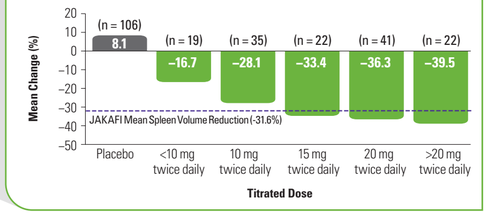
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Doses should not be increased during the first 4 weeks of therapy and not more frequently than every 2 weeks.

Discontinue JAKAFI if there is no spleen size reduction or symptom improvement after 6 months of therapy.

† Failure to achieve a reduction from pre-treatment baseline in either palpable spleen length of 50% or spleen volume of 35% as measured by CT or MRI.

COMFORT-I: Mean Change in Spleen Volume by Dose at Week 24[3]



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- Based on limited clinical data, long-term maintenance at 5-mg twice-daily dosing has not shown responses. Continued use at this dose should be limited to patients in whom the benefits outweigh the potential risks

MONITOR frequently

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

DECREASE DOSE

In the case of a **Hematologic Toxicity** including:

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Discontinuation can be avoided by reducing the dose or temporarily withholding JAKAFI

Twice-Daily Dose at Time of PLT Decline	25 mg	20 mg	15 mg	10 mg	5 mg
PLT Count (× 10⁹/L)	New recommended twice daily dose				
100 to <125	20 mg	15 mg	No change		
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<50	Hold				

PLT, platelet.

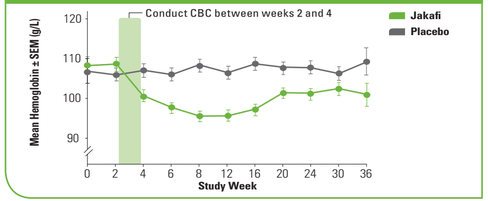
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COMFORT-I: Mean Hemoglobin Levels Over Time[2]



CBC, complete blood count; SEM,standard error of the mean.

- **In COMFORT-I, grade 3 and 4 thrombocytopenia or anemia occurred in 13% and 45% of patients receiving JAKAFI, respectively[2]**
- **<1% of patients receiving JAKAFI in the COMFORT studies discontinued due to anemia or thrombocytopenia[1-4]**

INTERRUPT DOSE

Interrupt JAKAFI treatment for:

- Bleeding requiring intervention, regardless of current platelet count,
- Thrombocytopenia (PLT <50 × 10⁹/L), **or**
- Neutropenia (ANC <0.5 × 10⁹/L)

See **RESTARTING** tab for dose modifications.

Risk of Infection (continued)

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.

Please see Important Safety Information on the back cover for related and other risk information. Refer to the accompanying Full Prescribing Information for complete dosing recommendations for JAKAFI/JAKAFI XR.

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† COMFORT-II (COntrolled MyeloFibrosis study with ORal JAK inhibitor Treatment-II) was a randomized, open-label phase 3 study with 219 patients with intermediate-2–risk or high-risk myelofibrosis. The primary endpoint was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline at week 48 as measured by CT or MRI. Best available therapy in COMFORT-II included hydroxyurea (46.6%) and glucocorticoids (16.4%), as well as no medication, anagrelide, epoetin alfa, thalidomide, lenalidomide, mercaptopurine, thioguanine, danazol, peginterferon alfa-2a, interferon-α, melphalan, acetylsalicylic acid, cytarabine, and colchicine.[1,4,5]

Special Populations

Renal or hepatic impairment

Impairment Status	PLT Count (× 10⁹/L)	Recommended Starting Dose
Renal impairment: Moderate (CrCl 30-59 mL/min) or severe (CrCl 15-29 mL/min) **OR** **Hepatic impairment:** Mild, moderate, or severe (Child-Pugh class A, B, C)	>150	No modification needed
	100 to 150	10 mg twice daily
	50 to <100	5 mg daily
	<50	Avoid use
End-stage renal disease on dialysis	100 to 200	15 mg once daily after dialysis session
	>200	20 mg once daily after dialysis session
End-stage renal disease (CrCl <15 mL/min) not requiring dialysis	Avoid use	

CrCl, creatinine clearance; PLT, platelet.

- Additional dose modifications should be made with frequent monitoring of safety and efficacy

Drug interactions

- Modify the dose of JAKAFI® (ruxolitinib) 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 careful monitoring of safety and efficacy

For Patients Coadministered Strong CYP3A4 Inhibitors or Fluconazole Doses of ≤200 mg	Recommended Dose Modification
Starting dose for patients with MF with a PLT count:	
≥100 × 10⁹/L	10 mg twice daily
50 to <100 × 10⁹/L	5 mg once daily
If on stable dose for patients with MF:	
≥10 mg twice daily	Decrease dose by 50% (round up to the closest available tablet strength)
5 mg twice daily	5 mg once daily
5 mg once daily	Avoid strong CYP3A4 inhibitor or fluconazole treatment, or interrupt treatment with JAKAFI for the duration of strong CYP3A4 inhibitor or fluconazole use

MF, myelofibrosis; PLT, platelet.

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 for JAKAFI/JAKAFI XR.

IMPORTANT SAFETY INFORMATION

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.

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.

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 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 myelofibrosis, 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 click here for Full Prescribing Information for JAKAFI/JAKAFI XR.

References: 1. JAKAFI/JAKAFI XR Prescribing Information. Wilmington, DE: Incyte Corporation. **2.** Verstovsek S, Mesa RA, Gotlib J, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. *N Engl J Med.* 2012;366(9):799-807. **3.** Verstovsek S, Mesa RA, Gotlib J, et al. Efficacy, safety and survival with ruxolitinib in patients with myelofibrosis: results of a median 2-year follow-up of COMFORT-I. *Haematologica.* 2013;98(12):1865-1871. **4.** Harrison C, Kiladjian J-J, Al-Ali HK, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. *N Engl J Med.* 2012;366(9):787-798. **5.** Data on file. Incyte Corporation. Wilmington, DE.

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Jakafi® ruxolitinib (tablets) 5mg • 10mg • 15mg • 20mg • 25mg

Jakafi XR® (ruxolitinib) extended release tablets 11mg • 22mg • 33mg • 44mg • 55mg