Jakafi®
ruxolitinib (tablets)

For adults with intermediate- or high-risk MF[1]

Intervene with Jakafi at diagnosis

NCCN GUIDELINES® RECOMMENDED

Ruxolitinib (Jakafi) is a Category 2A* treatment option for both symptomatic lower-risk† and higher-risk MF – in patients with platelets ≥50 x 10^9/L.[2‡]

*Category 2A: Based upon lower-level evidence compared to Category 1; there is uniform NCCN consensus that the intervention is appropriate.[2]
† Lower-risk MF is defined as low or intermediate-1 risk based on DIPSS, DIPSS-Plus, and MYSEC-PM, low or intermediate risk based on MIPSS-70 (threshold of ≤3 prognostic variable points), and very low, low, or intermediate risk based on MIPSS-70+ (version 2.0; threshold of ≤3 prognostic variable points).[2]
‡ In patients who are not transplant candidates.

Indications and Usage

Jakafi is indicated 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 considerations

- Treatment with Jakafi can cause 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. In patients with cytopenias, consider dose reductions or temporarily withholding Jakafi or transfusions, as clinically indicated
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Evaluate patients prior to and while receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines

Please see related and other Important Safety Information on pages 12-13.
Please click here for Full Prescribing Information.

Experience with Jakafi since FDA approval[3§]

7+ YEARS
MORE THAN 30,000 PATIENTS TREATED

§ Estimated total patients treated with commercially available Jakafi in the United States since 2011.[3]
See Full Prescribing Information for FDA-approved indications.

When do you intervene in patients with intermediate- or high-risk MF?

Myelofibrosis (MF) is a serious disease that may require active management at diagnosis[4]

In MF, the presence of <u>any one</u> of the following risk factors* indicates that a patient is already intermediate risk[5,6]:

- Hemoglobin level <10 g/dL
- Leukocyte count >25 × 10^9/L
- Age >65 years
- Red cell transfusion dependency
- Circulating blast cells ≥1%
- Platelet count <100 × 10^9/L
- Constitutional symptoms
- Unfavorable karyotype

In a study of patients with primary MF, approximately 90% (375/428) of evaluable patients were considered to be **intermediate or high risk within 1 year of diagnosis[5]**

* As included in the Dynamic International Prognostic Scoring System Plus tool.

Risk for thrombocytopenia, anemia, and neutropenia

- 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

New or increasing splenomegaly is considered to be a marker of disease progression[7]

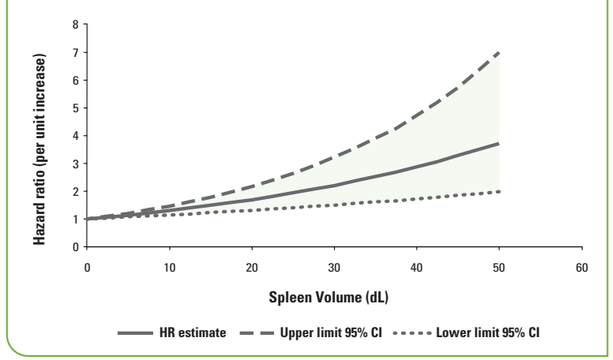
A palpable spleen of ≥5 cm below the left costal margin constitutes progressive disease,* according to the IWG-MRT and ELN response criteria[7]

In a study of 1054 patients with primary MF, approximately 90% of patients for whom data were available **had palpable splenomegaly at diagnosis[6]**

Data were available for 768 patients, 681 of whom had palpable splenomegaly.[6]

Larger baseline spleen volume was associated with incremental increases in the risk of death[8]

Relationship between spleen volume and risk of death[8]



- In a post hoc, pooled analysis of overall survival in the COMFORT studies (N=528), there was a 14% increase in the risk of death for each additional 5 dL in spleen volume at baseline over 3 years (HR, 1.14; 95% CI, 1.07-1.21)[8†]
- These increases were seen irrespective of treatment[8]

NCCN GUIDELINES RECOMMEND

Palpating the spleen at diagnosis in all patients with MPNs[2]

Imaging, including ultrasound, may be appropriate for patients with a body habitus which precludes palpation[9]

CI, confidence interval; CT, computed tomography; ELN, European LeukemiaNet; HR, hazard ratio; IWG-MRT, International Working Group-Myeloproliferative Neoplasms Research and Treatment; MF, myelofibrosis; MRI, magnetic resonance imaging; NCCN, National Comprehensive Cancer Network.

* Progressive disease assignment for splenomegaly requires confirmation by CT or MRI showing a ≥25% increase in spleen volume from baseline. Baseline values for both physical examination and imaging studies refer to pretreatment baseline and not to posttreatment measurements.[7]

† A post hoc pooled analysis of overall survival with ruxolitinib was performed using data from the two phase 3 studies: COMFORT-I, a randomized, double-blind, placebo-controlled study with 309 patients with intermediate-2–risk or high-risk MF, and COMFORT-II, a randomized, open-label study with 219 patients with intermediate-2–risk or high-risk MF. The primary endpoint in both studies was the proportion of patients achieving a ≥35% reduction in spleen volume (measured by CT or MRI) at week 24 in COMFORT-I and at week 48 in COMFORT-II.[8,10,11]

Please see related and other Important Safety Information on pages <u>12-13</u>. Please <u>click here</u> for Full Prescribing Information.

Jakafi® ruxolitinib (tablets)

For adults with intermediate- or high-risk MF[1]

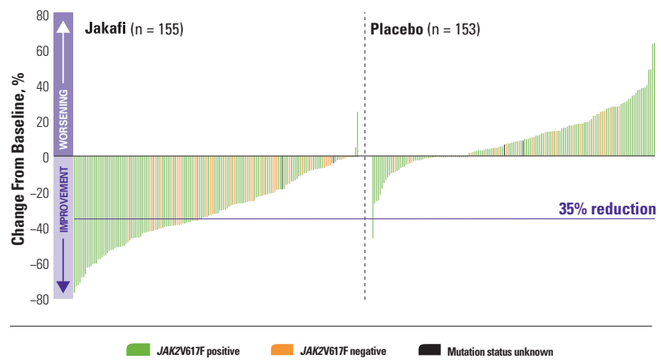
Intervene with Jakafi® (ruxolitinib) at diagnosis

COMFORT-I Primary Endpoint*

42% of patients receiving Jakafi achieved a ≥35% reduction in spleen volume at week 24 vs 0.7% of patients receiving placebo ($P < 0.0001$)[1,10]

- **4.4 years** median duration of spleen response among primary responders (n = 65)[3†]

COMFORT-I: Percent Change in Spleen Volume in Individual Patients From Baseline to Week 24 or Last Observation[1,3,10]



of patients experienced some reduction in spleen volume on Jakafi[10,12]

Most patients receiving placebo experienced an increase in spleen volume.[1,12]

Each bar represents an individual patient's response.
From *New England Journal of Medicine*, Verstovsek S, Mesa RA, Gotlib J, et al, A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis, 366(9), 799-807. Copyright © 2012 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

COMFORT-II Primary Endpoint‡

29% of patients receiving Jakafi achieved a ≥35% reduction in spleen volume at week 48 vs 0% of patients receiving best available therapy§ ($P < 0.0001$)[1,11]

* 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 MF. The primary endpoint was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline to week 24 as measured by CT or MRI.[1,10]

† Duration of spleen response was defined as the interval between the first spleen response measurement that was a ≥35% reduction from baseline and the date of the first measurement that was no longer a ≥35% reduction from baseline that was also a >25% increase from nadir.[3]

‡ 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 MF. 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.[1,11]

§ 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.[3]

Risk of infection

- 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

Significantly more patients

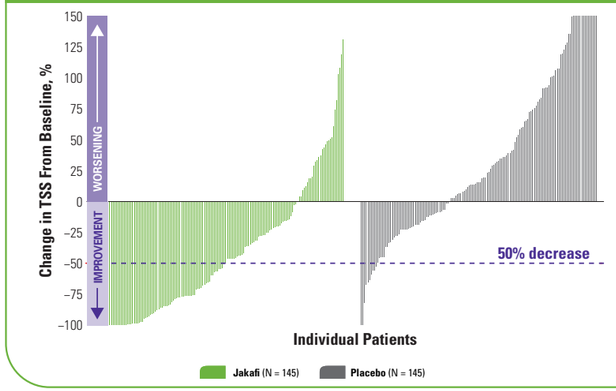
Achieved a ≥50% improvement in Total Symptom Score compared with placebo

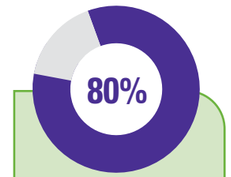
COMFORT-I Secondary Endpoint*

46% of patients receiving Jakafi achieved a ≥50% improvement in Total Symptom Score (TSS) at week 24 vs 5% of patients receiving placebo ($P < 0.0001$)[1,10]

- Median time to symptom response was <4 weeks for patients receiving Jakafi[1]

COMFORT-I: Percent Change in TSS in Individual Patients From Baseline to Week 24 or Last Observation[1,10]





of patients experienced some improvement in symptoms on Jakafi[3]

Most patients receiving placebo had worsening of symptoms.[10]

Worsening of TSS is truncated at 150%.[1]
From *New England Journal of Medicine*, Verstovsek S, Mesa RA, Gotlib J, et al, A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis, 366(9), 799-807. Copyright © 2012 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Debilitating symptoms of MF[1,10]

- Abdominal discomfort
- Early satiety
- Pain under left ribs
- Pruritus
- Night sweats
- Bone/muscle pain

* A secondary endpoint was the proportion of patients with a ≥50% reduction in TSS from baseline to week 24 as measured by the daily patient diary, the modified Myelofibrosis Symptom Assessment Form. TSS encompasses core symptoms of MF: abdominal discomfort, early satiety, pain under left ribs, pruritus, night sweats, and bone/muscle pain. Symptom scores ranged from 0 to 10, with 0 representing symptoms "absent" and 10 representing symptoms "worst imaginable." These scores were added to create the daily total score, which has a maximum of 60. At baseline, mean TSS was 18.0 in the group receiving Jakafi and 16.5 in the group receiving placebo.[1,10]

Risk of infection (continued)

- 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

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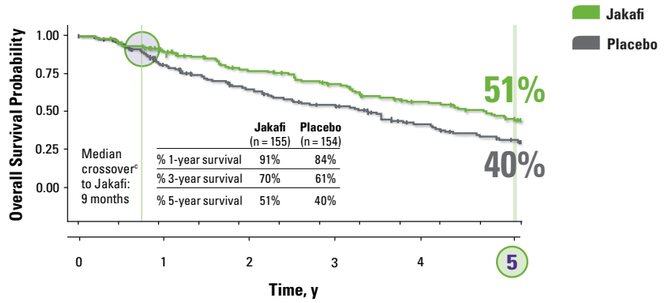
Jakafi® ruxolitinib (tablets)

Jakafi® (ruxolitinib) 5-year overall survival data

COMFORT-I 5-year analysis: Jakafi and placebo

- At 3 years, survival probability was 70% for patients originally randomized to Jakafi and 61% for those originally randomized to placebo[1]
- Overall survival was a prespecified secondary endpoint in COMFORT-I[1]

Overall Survival Kaplan-Meier Curves by Treatment Group in COMFORT-I[1,3,13,a,b]



Number of patients at risk

Jakafi	155	148	137	124	112	108	100	86	80	75	69	57
Placebo	154	144	119	105	95	85	78	72	59	51	46	38

[a] The 5-year overall survival analysis is not included in the Full Prescribing Information for Jakafi. Although the 3-year overall survival analysis is presented in the Full Prescribing Information, *P* values and hazard ratios are omitted from the overall survival Kaplan-Meier curves.[3]

[b] COMFORT-I was not designed to compare survival probabilities between Jakafi and placebo at 3 or 5 years.[3]

[c] Patients randomized to placebo were eligible to cross over to receive Jakafi because of progression-driven events or at the physician's discretion; however, these patients continued to be grouped within their original randomized assignment for analysis purposes.[3]

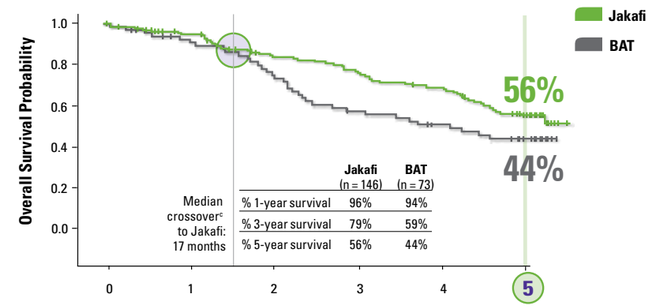
Jakafi 5-year overall survival probability was 51%[3]

All patients in the placebo group either crossed over to Jakafi at a median of 9 months or discontinued.[1]

COMFORT-II 5-year analysis: Jakafi and best available therapy

- At 3 years, survival probability was 79% for patients originally randomized to Jakafi and 59% for those originally randomized to best available therapy[1]
- Overall survival was a prespecified secondary endpoint in COMFORT-II[1]

Overall Survival Kaplan-Meier Curves by Treatment Group in COMFORT-II[1,14,a,b]



Number of patients at risk

Jakafi	146	130	109	100	88	61
BAT	73	58	48	35	30	22

BAT, best available therapy.

[a] The 5-year overall survival analysis is not included in the Full Prescribing Information for Jakafi. Although the 3-year overall survival analysis is presented in the Full Prescribing Information, *P* values and hazard ratios are omitted from the overall survival Kaplan-Meier curves.[3]

[b] COMFORT-II was not designed to compare survival probabilities between Jakafi and best available therapy at 3 or 5 years.[3]

[c] Patients randomized to best available therapy were eligible to cross over to receive Jakafi because of progression-driven events or at the physician's discretion; however, these patients continued to be grouped within their original randomized assignment for analysis purposes.[3]

Jakafi 5-year overall survival probability was 56%[14]

All patients in the best available therapy group either crossed over to Jakafi at a median of 17 months or discontinued.[1]

Risk for symptom exacerbation following interruption or discontinuation of Jakafi

- 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

Risk for symptom exacerbation following interruption or discontinuation of Jakafi (continued)

- 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

Please see related and other Important Safety Information on pages 12-13. Please click here for Full Prescribing Information.

Jakafi® ruxolitinib (tablets)

Dose optimization is key to maintaining balance of safety and efficacy

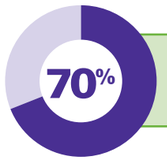
1 START: For adults with intermediate- or high-risk MF, the recommended starting doses are based on platelet counts[1]

- A complete blood count (CBC) and platelet count must be performed before initiating Jakafi® (ruxolitinib)[1]

Special populations: Please refer to the Full Prescribing Information for starting dose and other dose modifications, and when to avoid treatment in patients with renal or hepatic impairment and in those receiving concomitant strong CYP3A4 inhibitors or fluconazole.

2 MONITOR: Monitoring patients after initiation of Jakafi is essential, especially during the first 12 weeks of therapy

- A CBC and platelet count must be performed every 2 to 4 weeks until doses are stabilized, and then as clinically indicated. Doses may be titrated based on safety and efficacy[1]



of patients receiving Jakafi in COMFORT-I required a dose adjustment in the first 12 weeks of therapy[15]

Monitoring blood counts and using appropriate dose management are essential to achieve desired efficacy and manage cytopenias[1]

Risk for 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
- 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

Ensure your patients are receiving the appropriate dose of Jakafi

3 OPTIMIZE: Individualize dosing of Jakafi to optimize balance between safety and efficacy[1]

Managing anemia and thrombocytopenia

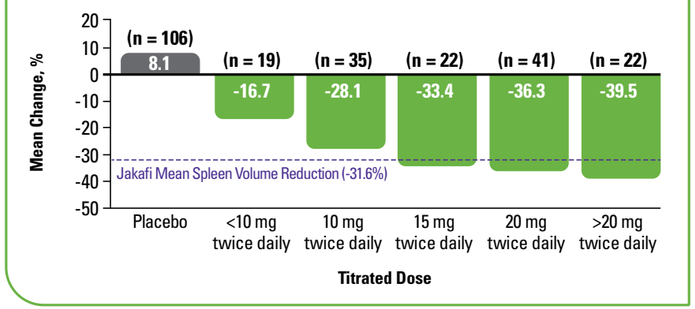
- In COMFORT-I, grades 3 and 4 thrombocytopenia or anemia occurred in 13% and 45% of patients receiving Jakafi, respectively. All grades of thrombocytopenia or anemia occurred in 70% and 96% of patients receiving Jakafi, respectively[1,10]
- Dose modifications, temporarily withholding Jakafi, and/or transfusions may be required for patients developing anemia or thrombocytopenia[1]
- Interrupt treatment for bleeding, neutropenia (ANC <0.5 × 10⁹/L), or thrombocytopenia (based on starting platelet count)[1]

<1% of patients receiving Jakafi in the COMFORT studies discontinued due to anemia or thrombocytopenia[1]

Dose may be increased in the case of an insufficient response[1]

Efficacy based on titrated dose

COMFORT-I: Mean Change in Spleen Volume by Dose at Week 24[15]



- Doses may be increased if the response is insufficient and platelet, hemoglobin, and neutrophil counts are adequate and treatment has not been reduced or interrupted in the prior 4 weeks[1]
- Doses should not be increased during the first 4 weeks of therapy and not more frequently than every 2 weeks[1]
- Discontinue Jakafi if there is no spleen size reduction or symptom improvement after 6 months of therapy[1]
- In patients with starting platelet counts ≥100 × 10⁹/L, based on limited clinical data, long-term maintenance at a 5 mg twice daily dose has not shown responses. Continued use at this dose should be limited to patients in whom the benefits outweigh the potential risks[1]

Please see related and other Important Safety Information on pages 12-13. Please click here for Full Prescribing Information complete dosing recommendations.

Jakafi® ruxolitinib (tablets)

Jakafi® (ruxolitinib) adverse reactions

COMFORT-I hematologic adverse reactions[1,10]

Hematologic Adverse Reactions	Jakafi (n = 155)		Placebo (n = 151)	
	All Grades, %	Grades 3 and 4, %	All Grades, %	Grades 3 and 4, %
Anemia	96	45	87	19
Thrombocytopenia	70	13	31	1
Neutropenia	19	7	4	2

- The most frequently observed reactions were thrombocytopenia and anemia[1]
- Perform a pre-treatment CBC, and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated[1]

COMFORT-I and COMFORT-II discontinuation rates[1,3]

Hematologic Abnormality	Discontinuation Rate,[3] %	Management[1]
Thrombocytopenia	0.7	Managed by reducing the dose or temporarily interrupting Jakafi; if clinically indicated, platelet transfusions may be administered
Anemia	0.3	Some patients may require blood transfusions and/or dose modifications of Jakafi
Neutropenia	0.3	Generally reversible; temporarily withhold Jakafi until recovery

- At week 24, the discontinuation rates for adverse reactions, regardless of causality, were 11% in patients receiving Jakafi and 11% in patients receiving placebo[1,10]
- In COMFORT-I, 70% of patients required a dose adjustment in the first 12 weeks of therapy, and 2% of patients discontinued therapy because of hematologic adverse reactions at week 24[3,15]
- <1% of patients receiving Jakafi in the COMFORT studies discontinued due to anemia or thrombocytopenia[1]

In COMFORT-I:

- 60% of patients treated with Jakafi and 38% of patients receiving placebo had red blood cell transfusions during randomized treatment[1]
- 123 of 155 patients in the group receiving Jakafi were transfusion independent at baseline, compared with 119 of 151 patients in the group receiving placebo. Of the 123 transfusion-independent patients in the group receiving Jakafi, 27% became transfusion dependent* during the 8 weeks before data cutoff, compared with 14.4% of patients in the group receiving placebo[3]

* New-onset transfusion dependency: The use of 2 or more units of red blood cell product(s) during the final 8 weeks before database lock in a patient who was not transfusion dependent at baseline.[10]

COMFORT-I nonhematologic adverse reactions[1,3]

Nonhematologic Adverse Reactions	Jakafi (n = 155)		Placebo (n = 151)	
	All Grades, %	Grades 3 and 4, %	All Grades, %	Grades 3 and 4, %
Bruising	23	<1	15	0
Dizziness	18	<1	7	0
Headache	15	0	5	0
Urinary tract infection	9	0	5	1
Weight gain	7	<1	1	<1
Flatulence	5	0	<1	0
Herpes zoster	2	0	<1	0
Additional Nonhematologic Abnormalities	**Jakafi**		**Placebo**	
	All Grades,[a] %	Grades 3 and 4, %	All Grades,[a] %	Grades 3 and 4, %
ALT	27	1	8	0
AST	18	0	7	0
Cholesterol elevation	17	0	<1	0

ALT, alanine transaminase; AST, aspartate transaminase.

[a] These lab values represent "new or worsening."

Other important safety considerations

- 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

Please see related and other Important Safety Information on pages 12-13. Please click here for Full Prescribing Information.

Jakafi® ruxolitinib (tablets)

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 $<0.5 \times 10^9$/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 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

Important Safety Information (continued)

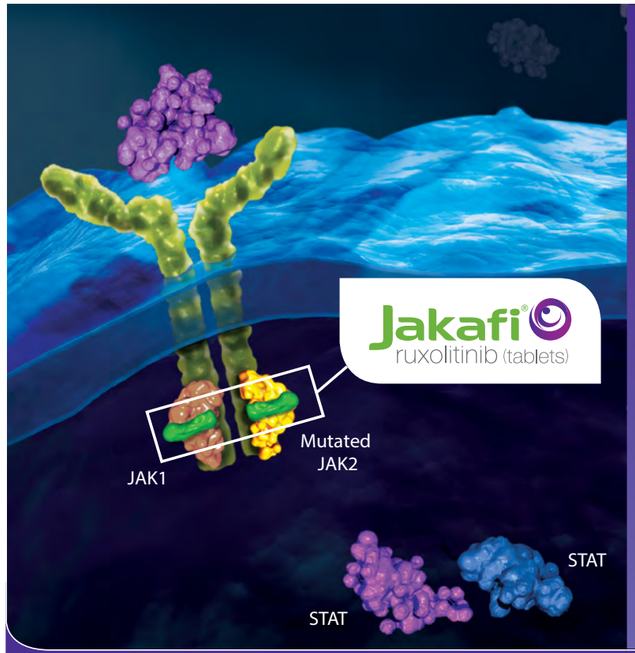
- When discontinuing Jakafi, myeloproliferative neoplasm-related symptoms may return within one week. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, DIC, or multi-organ failure. If any of these occur after discontinuation or while tapering 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.

Jakafi® ruxolitinib (tablets)

Jakafi® (ruxolitinib) is a potent and highly selective JAK1 and JAK2 inhibitor[16]

Jakafi targets a primary driver of MF[1]



JAK1

Plays major role in signaling of key proinflammatory cytokines[16]

JAK2

Mediates signals for hematopoietic growth factors[16]

Jakafi can be used for appropriate patients regardless of *JAK2* mutation status[16,17]

JAK, Janus-associated kinase; STAT, signal transducer and activator of transcription.

Other important safety considerations

- 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 see related and other Important Safety Information on pages 12-13.
Please click here for Full Prescribing Information.

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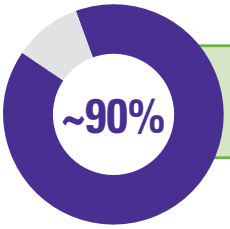
Jakafi® ruxolitinib (tablets)

For adults with intermediate- or high-risk MF[1]

Intervene with Jakafi® (ruxolitinib) at diagnosis

MF is a serious disease that may require active management at diagnosis[4]



of patients with primary MF may be appropriate for treatment with Jakafi[1,5*]

* Based on a study of patients with primary MF, approximately 90% (375/428) of evaluable patients were considered to be intermediate or high risk within 1 year of diagnosis.[5]

COMFORT-I Results:

Patients Achieving ≥35% Spleen Volume Reduction	Patients Achieving ≥50% Improvement in TSS
42%	**46%**
at 24 weeks vs 0.7% for placebo ($P < 0.0001$)[1,10]	at 24 weeks vs 5% for placebo ($P < 0.0001$)[1,10]

Overall Survival Probability

3-year	5-year
70%	**51%**
and 61% for placebo[1]	and 40% for placebo[3]

COMFORT-II Results:

Patients Achieving ≥35% Spleen Volume Reduction

29%

at 48 weeks vs 0% for BAT ($P < 0.0001$)[1,11]

Overall Survival Probability

3-year	5-year
79%	**56%**
and 59% for BAT[1]	and 44% for BAT[14]

BAT, best available therapy; TSS, Total Symptom Score.

Actively manage your patients' disease at diagnosis

Indications and Usage

Jakafi is indicated 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 considerations

- Treatment with Jakafi can cause 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. In patients with cytopenias, consider dose reductions or temporarily withholding Jakafi or transfusions, as clinically indicated
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Evaluate patients prior to and while receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines

Please see related and other Important Safety Information on pages 12-13. Please click here for Full Prescribing Information.

hcp.jakafi.com

Experience with Jakafi since FDA approval[3†]

7+ YEARS

MORE THAN **30,000** PATIENTS TREATED

† Estimated total patients treated with commercially available Jakafi in the United States since 2011.[3]
See Full Prescribing Information for FDA-approved indications.

Jakafi® ruxolitinib (tablets)