HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use JAKAFI safely and effectively. See full prescribing information for JAKAFI.

JAKAFI®(ruxolitinib) tablets, for oral use
Initial U.S. Approval: 2011

RECENT MAJOR CHANGES

Dosage and Administration (2.1 – 2.6) 06/2013
Warnings and Precautions (5.2) 06/2013

INDICATIONS AND USAGE

Jakafi is a kinase inhibitor indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis. (1)

DOSAGE AND ADMINISTRATION

- The starting dose of Jakafi is 20 mg given orally twice daily for patients with a platelet count greater than 200 X 10^9/L, and 15 mg twice daily for patients with a platelet count between 100 X 10^9/L and 200 X 10^9/L (2.1)
- The starting dose of Jakafi is 5 mg twice daily for patients with a platelet count between 50 X 10^9/L and less than 100 X 10^9/L. (2.1)
- Monitor complete blood counts every 2 to 4 weeks until doses are stabilized, and then as clinically indicated. Modify or interrupt dosing for thrombocytopenia. (2.1) (2.2)
- Increase dose based on response and as recommended to a maximum of 25 mg twice daily for patients with starting platelet counts 100 X 10^9/L or greater and to a maximum of 10 mg twice daily for patients with starting platelet count between 50 X 10^9/L and less than 100 X 10^9/L. Discontinue after 6 months if no spleen reduction or symptom improvement (2.3) (2.5)

DOSAGE FORMS AND STRENGTHS

Tablets: 5 mg, 10 mg, 15 mg, 20 mg and 25 mg. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Thrombocytopenia, Anemia and Neutropenia: Manage by dose reduction, or interruption, or transfusion. (5.1)
- Risk of Infection: Assess patients for signs and symptoms of infection and initiate appropriate treatment promptly. Serious infections should have resolved before starting therapy with Jakafi. (5.2)

ADVERSE REACTIONS

The most common hematologic adverse reactions (incidence > 20%) are thrombocytopenia and anemia. The most common non-hematologic adverse reactions (incidence >10%) are bruising, dizziness and headache. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Incyte Corporation at 1-855-463-3463 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

DRUG INTERACTIONS

- Strong CYP3A4 Inhibitors: Reduce Jakafi starting dose to 10 mg twice daily for patients with a platelet count greater than or equal to 100 X 10^9/L and concurrent use of strong CYP3A4 inhibitors. Avoid in patients with platelet counts less than 100 X 10^9/L. (2.4) (7.1)

USE IN SPECIFIC POPULATIONS

- Renal Impairment: Reduce Jakafi starting dose to 10 mg twice daily for patients with moderate (CrCl 30-59 mL/min) or severe renal impairment (CrCl 15-29 mL/min) and a platelet count between 100 X 10^9/L and 150 X 10^9/L. Avoid in patients with end stage renal disease (CrCl less than 15 mL/min) not requiring dialysis and in patients with moderate or severe renal impairment and a platelet count less than 100 X 10^9/L. (2.5) (8.6)
- Hepatic Impairment: Reduce Jakafi starting dose to 10 mg twice daily for patients with any degree of hepatic impairment and a platelet count between 100 X 10^9/L and 150 X 10^9/L. Avoid in patients with hepatic impairment with platelet counts less than 100 X 10^9/L. (2.5) (8.7)
- Nursing Mothers: Discontinue nursing or discontinue the drug taking into account the importance of the drug to the mother. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 5/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

Jakafi is indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis.

2. DOSAGE AND ADMINISTRATION

2.1 Recommended Starting Dose

The recommended starting dose of Jakafi is based on platelet count (*Table 1*). A complete blood count (CBC) and platelet count must be performed before initiating therapy, every 2 to 4 weeks until doses are stabilized, and then as clinically indicated [*see Warnings and Precautions (5.1)*]. Doses may be titrated based on safety and efficacy.

Table 1: Proposed Jakafi Starting Doses

Platelet Count	Starting Dose
Greater than 200 X 10^9/L	20 mg orally twice daily
100 X 10^9/L to 200 X 10^9/L	15 mg orally twice daily
50 X 10^9/L to less than 100 X 10^9/L	5 mg orally twice daily

2.2 Dose Modification Guidelines for Hematologic Toxicity for Patients Starting Treatment with a Platelet Count of 100 X 10^9/L or Greater

Treatment Interruption and Restarting Dosing

Interrupt treatment for platelet counts less than 50 X 10^9/L or absolute neutrophil count (ANC) less than 0.5 X 10^9/L.

After recovery of platelet counts above 50 X 10^9/L and ANC above 0.75 X 10^9/L, dosing may be restarted. Table 2 illustrates the maximum allowable dose that may be used in restarting Jakafi after a previous interruption.

Table 2: Maximum Restarting Doses for Jakafi After Safety Interruption for Thrombocytopenia for Patients Starting Treatment with a Platelet Count of 100 X 10^9/L or Greater

Current Platelet Count	Maximum Dose When Restarting Jakafi Treatment*
Greater than or equal to 125 X 10^9/L	20 mg twice daily
100 to less than 125 X 10^9/L	15 mg twice daily
75 to less than 100 X 10^9/L	10 mg twice daily for at least 2 weeks; if stable, may increase to 15 mg twice daily
50 to less than 75 X 10^9/L	5 mg twice daily for at least 2 weeks; if stable, may increase to 10 mg twice daily
Less than 50 X 10^9/L	Continue hold

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

Following treatment interruption for ANC below 0.5 X 10^9/L, after ANC recovers to 0.75 X 10^9/L or greater, 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.

Dose Reductions

Dose reductions should be considered if the platelet counts decrease as outlined in Table 3 with the goal of avoiding dose interruptions for thrombocytopenia.

Table 3: Dosing Recommendations for Thrombocytopenia for Patients Starting Treatment with a Platelet Count of 100 X 10^9/L or Greater

	Dose at Time of Platelet Decline				
Platelet Count	25 mg twice daily	20 mg twice daily	15 mg twice daily	10 mg twice daily	5 mg twice daily
	New Dose	New Dose	New Dose	New Dose	New Dose
100 to less than 125 X 10^9/L	20 mg twice daily	15 mg twice daily	No Change	No Change	No Change
75 to less than 100 X 10^9/L	10 mg twice daily	10 mg twice daily	10 mg twice daily	No Change	No Change
50 to less than 75 X 10^9/L	5 mg twice daily	5 mg twice daily	5 mg twice daily	5 mg twice daily	No Change
Less than 50 X 10^9/L	Hold	Hold	Hold	Hold	Hold

2.3 Dose Modification Based on Insufficient Response for Patients Starting Treatment with a Platelet Count of 100 X 10^9/L or Greater

If the response is insufficient and platelet and neutrophil counts are adequate, 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 every 2 weeks.

Consider dose increases in patients who meet all of the following conditions:

a. Failure to achieve a reduction from pretreatment baseline in either palpable spleen length of 50% or a 35% reduction in spleen volume as measured by CT or MRI;
b. Platelet count greater than 125 X 10^9/L at 4 weeks and platelet count never below 100 X 10^9/L;
c. ANC Levels greater than 0.75 X 10^9/L.

Based on limited clinical data, long-term maintenance at a 5 mg twice daily dose has not shown responses and continued use at this dose should be limited to patients in whom the benefits outweigh the potential risks. Discontinue Jakafi if there is no spleen size reduction or symptom improvement after 6 months of therapy.

2.4 Dose Modifications for Hematologic Toxicity for Patients Starting Treatment with Platelet Counts of 50 X 10^9/L to Less Than 100 X 10^9/L

This section applies only to patients with platelet counts of 50 X 10^9/L to less than 100 X 10^9/L prior to any treatment with ruxolitinib. See Section 2.2 for dose modifications for hematological toxicity in patients whose platelet counts were 100 X 10^9/L or more prior to starting treatment with ruxolitinib.

Treatment Interruption and Restarting Dosing

Interrupt treatment for platelet counts less than 25 X 10^9/L or ANC less than 0.5 X 10^9/L.

After recovery of platelet counts above 35 X 10^9/L and ANC above 0.75 X 10^9/L, dosing may be restarted. 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 decrease in platelet count below 25 X 10^9/L or ANC below 0.5 X 10^9/L that led to dose interruption.

Dose Reductions

Reduce the dose of ruxolitinib for platelet counts less than 35 X 10^9/L as described in Table 4.

Table 4: Dosing Modifications for Thrombocytopenia for Patients with Starting Platelet Count of 50 X 10^9/L to Less Than 100 X 10^9/L

Platelet Count	Dosing Recommendations
Less than 25 X 10^9/L	·Interrupt dosing.
25 X 10^9/L to less than 35 X 10^9/L AND the platelet count decline is less than 20% during the prior four weeks	·Decrease dose by 5 mg once daily. ·For patients on 5 mg once daily, maintain dose at 5 mg once daily.
25 X 10^9/L to less than 35 X 10^9/L AND the platelet count decline is 20% or greater during the prior four 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.

2.5 Dose Modifications Based on Insufficient Response for Patients with Starting Platelet Count of 50 X 10^9/L to Less Than 100 X 10^9/L

Do not increase doses during the first 4 weeks of therapy, and do not increase the dose more frequently than every 2 weeks.

If the response is insufficient as defined in Section 2.3, doses may be increased by increments of 5 mg daily to a maximum of 10 mg twice daily if:

a) the platelet count has remained at least 40 x 10^9/L, and
b) the platelet count has not fallen by more than 20% in the prior 4 weeks, and
c) the ANC is more than 1 x 10^9/L, and
d) the dose has not been reduced or interrupted for an adverse event or hematological toxicity in the prior 4 weeks.

Continuation of treatment for more than 6 months should be limited to patients in whom the benefits outweigh the potential risks. Discontinue Jakafi if there is no spleen size reduction or symptom improvement after 6 months of therapy.

2.6 Dose Modification for Bleeding

Interrupt treatment for bleeding requiring intervention regardless of current platelet count. 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.

2.7 Dose Adjustment with Concomitant Strong CYP3A4 Inhibitors

On the basis of pharmacokinetic studies in healthy volunteers, when administering Jakafi with strong CYP3A4 inhibitors (such as but not limited to boceprevir, clarithromycin, conivaptan, grapefruit juice, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, mibefradil, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole), the recommended starting dose is 10 mg twice daily for patients with a platelet count greater than or equal to 100 X 10^9/L. Additional dose modifications should be made with careful monitoring of safety and efficacy.

Concurrent administration of Jakafi with strong CYP3A4 inhibitors should be avoided in patients with platelet counts less than 100 X 10^9/L [*see Drug Interactions (7.1)*].

2.8 Organ Impairment

Renal Impairment

On the basis of pharmacokinetic studies in volunteers with renal impairment, the recommended starting dose is 10 mg twice daily for patients with a platelet count between 100 X 10^9/L and 150 X 10^9/L and moderate (CrCl 30-59 mL/min) or severe renal impairment (CrCl 15-29 mL/min). Additional dose modifications should be made with careful monitoring of safety and efficacy.

The recommended starting dose for patients with end stage renal disease on dialysis is 15 mg for patients with a platelet count between 100 X 10^9/L and 200 X 10^9/L or 20 mg for patients with a platelet count of greater than 200 X 10^9/L. Subsequent doses should be administered on dialysis days following each dialysis session. Additional dose modifications should be made with careful monitoring of safety and efficacy.

Jakafi should be avoided in patients with end stage renal disease (CrCl less than 15 mL/min) not requiring dialysis and in patients with moderate or severe renal impairment with platelet counts less than 100 X 10^9/L [*see Use in Specific Populations (8.6)*].

Hepatic Impairment

On the basis of pharmacokinetic studies in volunteers with hepatic impairment, the recommended starting dose is 10 mg twice daily for patients with a platelet count between 100 X 10^9/L and 150 X 10^9/L. Additional dose modifications should be made with careful monitoring of safety and efficacy.

Jakafi should be avoided in patients with hepatic impairment with platelet counts less than 100 X 10^9/L [*see Use in Specific Populations (8.7)*].

2.9 Method of Administration

Jakafi is dosed orally and can be administered with or without food.

If a dose is missed, the patient should not take an additional dose, but should take the next usual prescribed dose.

When discontinuing Jakafi therapy for reasons other than thrombocytopenia, gradual tapering of the dose of Jakafi may be considered, for example by 5 mg twice daily each week.

For patients unable to ingest tablets, Jakafi can be administered through a nasogastric tube (8 French or greater) as follows:

- Suspend one tablet in approximately 40 mL of water with stirring for approximately 10 minutes.
- Within 6 hours after the tablet has dispersed, the suspension can be administered through a nasogastric tube using an appropriate syringe.

The tube should be rinsed with approximately 75 mL of water. The effect of tube feeding preparations on Jakafi exposure during administration through a nasogastric tube has not been evaluated.

3. DOSAGE FORMS AND STRENGTHS

5 mg tablets - round and white with "INCY" on one side and "5" on the other.

10 mg tablets - round and white with "INCY" on one side and "10" on the other.

15 mg tablets - oval and white with "INCY" on one side and "15" on the other.

20 mg tablets - capsule-shaped and white with "INCY" on one side and "20" on the other.

25 mg tablets - oval and white with "INCY" on one side and "25" on the other.

4. CONTRAINDICATIONS

None.

5. WARNINGS AND PRECAUTIONS

5.1 Thrombocytopenia, Anemia and Neutropenia

Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia. [*see Dosage and Administration (2.1)*].

Thrombocytopenia was generally reversible and was usually managed by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary [*see Dosage and Administration (2.2), and Adverse Reactions (6.1)*].

Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi.

Severe neutropenia (ANC less than 0.5 X 10^9/L) was generally reversible. Withhold Jakafi until recovery [*see Adverse Reactions (6.1)*].

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. [*see Dosage and Administration (2.2), and Adverse Reactions (6.1)*].

5.2 Risk of Infection

Serious bacterial, mycobacterial, fungal and viral infections may occur. Active serious infections should have resolved before starting therapy with Jakafi. Observe patients receiving Jakafi for signs and symptoms of infection and initiate appropriate treatment promptly.

PML

Progressive multifocal leukoencephalopathy (PML) has been reported with ruxolitinib treatment for myelofibrosis. If PML is suspected, stop Jakafi and evaluate.

Herpes Zoster

Advise patients about early signs and symptoms of herpes zoster and to seek treatment as early as possible if suspected [*see Adverse Reactions (6.1)*].

6. ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Myelosuppression [*see Warnings and Precautions (5.1)*]
- Risk of Infection [*see Warnings and Precautions (5.2)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of Jakafi was assessed in 617 patients in six clinical studies with a median duration of follow-up of 10.9 months, including 301 patients with myelofibrosis in two Phase 3 studies.

In these two Phase 3 studies, patients had a median duration of exposure to Jakafi of 9.5 months (range 0.5 to 17 months), with 88.7% of patients treated for more than 6 months and 24.6% treated for more than 12 months. One hundred and eleven (111) patients started treatment at 15 mg twice daily and 190 patients started at 20 mg twice daily.

In a double-blind, randomized, placebo-controlled study of Jakafi, 155 patients were treated with Jakafi. The most frequent adverse drug reactions were thrombocytopenia and anemia [*see Table 5*]. Thrombocytopenia, anemia and neutropenia are dose related effects. The three most frequent non-hematologic adverse reactions were bruising, dizziness and headache [*see Table 4*].

Discontinuation for adverse events, regardless of causality, was observed in 11.0% of patients treated with Jakafi and 10.6% of patients treated with placebo.

Following interruption or discontinuation of Jakafi, symptoms of myelofibrosis generally return to pretreatment levels over a period of approximately 1 week. There have been isolated cases of patients discontinuing Jakafi during acute intercurrent illnesses after which the patient's clinical course continued to worsen; however, it has not been established whether discontinuation of

therapy contributed to the clinical course in these patients. When discontinuing therapy for reasons other than thrombocytopenia, gradual tapering of the dose of Jakafi may be considered [*see Dosage and Administration (2.6)*].

Table 4 presents the most common adverse reactions occurring in patients who received Jakafi in the double-blind, placebo-controlled study during randomized treatment.

Table 5: Adverse Reactions Occurring in Patients on Jakafi in the Double-blind, Placebo-controlled Study During Randomized Treatment

	Jakafi (N=155)			Placebo (N=151)		
Adverse Reactions	**All Grades[a] (%)**	**Grade 3 (%)**	**Grade 4 (%)**	**All Grades (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Bruising[b]	23.2	0.6	0	14.6	0	0
Dizziness[c]	18.1	0.6	0	7.3	0	0
Headache	14.8	0	0	5.3	0	0
Urinary Tract Infections[d]	9.0	0	0	5.3	0.7	0.7
Weight Gain[e]	7.1	0.6	0	1.3	0.7	0
Flatulence	5.2	0	0	0.7	0	0
Herpes Zoster[f]	1.9	0	0	0.7	0	0

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0
[b] includes contusion, ecchymosis, hematoma, injection site hematoma, periorbital hematoma, vessel puncture site hematoma, increased tendency to bruise, petechiae, purpura
[c] includes dizziness, postural dizziness, vertigo, balance disorder, Meniere's Disease, labyrinthitis
[d] includes urinary tract infection, cystitis, urosepsis, urinary tract infection bacterial, kidney infection, pyuria, bacteria urine, bacteria urine identified, nitrite urine present
[e] includes weight increased, abnormal weight gain
[f] includes herpes zoster and post-herpetic neuralgia

Description of Selected Adverse Drug Reactions

Anemia

In the two Phase 3 clinical studies, median time to onset of first CTCAE Grade 2 or higher anemia was approximately 6 weeks. One patient (0.3%) discontinued treatment because of anemia. In patients receiving Jakafi, 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 reach a new steady state that was approximately 1.0 g/dL below baseline. This pattern was observed in patients regardless of whether they had received transfusions during therapy.

In the randomized, placebo-controlled study, 60% of patients treated with Jakafi and 38% of patients receiving placebo received red blood cell transfusions during randomized treatment. Among transfused patients, the median number of units transfused per month was 1.2 in patients treated with Jakafi and 1.7 in placebo treated patients.

Thrombocytopenia

In the two Phase 3 clinical studies, in patients who developed Grade 3 or 4 thrombocytopenia, the median time to onset was approximately 8 weeks. Thrombocytopenia was generally reversible with dose reduction or dose interruption. The median time to recovery of platelet counts above 50 X 10^9/L was 14 days. Platelet transfusions were administered to 4.7% of patients receiving Jakafi and to 4.0% of patients receiving control regimens. Discontinuation of treatment because of thrombocytopenia occurred in 0.7% of patients receiving Jakafi and 0.9% of patients receiving control regimens. Patients with a platelet count of 100 X 10^9/L to 200 X 10^9/L before starting Jakafi had a higher frequency of Grade 3 or 4 thrombocytopenia compared to patients with a platelet count greater than 200 X 10^9/L (16.5% versus 7.2%).

Neutropenia

In the two Phase 3 clinical studies, 1.0% of patients reduced or stopped Jakafi because of neutropenia.

Table 5 provides the frequency and severity of clinical hematology abnormalities reported for patients receiving treatment with Jakafi or placebo in the placebo-controlled study.

Table 6: Worst Hematology Laboratory Abnormalities in the Placebo-controlled Study[a]

	Jakafi (N=155)			Placebo (N=151)		
Laboratory Parameter	**All Grades[b] (%)**	**Grade 3 (%)**	**Grade 4 (%)**	**All Grades (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Thrombocytopenia	69.7	9.0	3.9	30.5	1.3	0
Anemia	96.1	34.2	11.0	86.8	15.9	3.3
Neutropenia	18.7	5.2	1.9	4.0	0.7	1.3

[a] Presented values are worst Grade values regardless of baseline
[b] National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0

Additional Data from the Placebo-controlled Study

25.2% of patients treated with Jakafi and 7.3% of patients treated with placebo developed newly occurring or worsening Grade 1 abnormalities in alanine transaminase (ALT). The incidence of greater than or equal to Grade 2 elevations was 1.9% for Jakafi with 1.3% Grade 3 and no Grade 4 ALT elevations.

17.4% of patients treated with Jakafi and 6.0% of patients treated with placebo developed newly occurring or worsening Grade 1 abnormalities in aspartate transaminase (AST). The incidence of Grade 2 AST elevations was 0.6% for Jakafi with no Grade 3 or 4 AST elevations.

16.8% of patients treated with Jakafi and 0.7% of patients treated with placebo developed newly occurring or worsening Grade 1 elevations in cholesterol. The incidence of Grade 2 cholesterol elevations was 0.6% for Jakafi with no Grade 3 or 4 cholesterol elevations.

7. DRUG INTERACTIONS

7.1 Drugs That Inhibit or Induce Cytochrome P450 Enzymes

Ruxolitinib is predominantly metabolized by CYP3A4.

Strong CYP3A4 inhibitors: The C_{max} and AUC of ruxolitinib increased 33% and 91%, respectively, with Jakafi administration (10 mg single dose) following ketoconazole 200 mg twice daily for four days, compared to receiving Jakafi alone in healthy subjects. The half-life was also prolonged from 3.7 to 6.0 hours with concurrent use of ketoconazole. The change in the pharmacodynamic marker, pSTAT3 inhibition, was consistent with the corresponding ruxolitinib AUC following concurrent administration with ketoconazole.

When administering Jakafi with strong CYP3A4 inhibitors a dose reduction is recommended [*see Dosage and Administration (2.4)*]. Patients should be closely monitored and the dose titrated based on safety and efficacy.

Mild or moderate CYP3A4 inhibitors: There was an 8% and 27% increase in the C_{max} and AUC of ruxolitinib, respectively, with Jakafi administration (10 mg single dose) following erythromycin, a moderate CYP3A4 inhibitor, at 500 mg twice daily for 4 days, compared to receiving Jakafi alone in healthy subjects. The change in the pharmacodynamic marker, pSTAT3 inhibition was consistent with the corresponding exposure information.

No dose adjustment is recommended when Jakafi is coadministered with mild or moderate CYP3A4 inhibitors (eg, erythromycin).

CYP3A4 inducers: The C_{max} and AUC of ruxolitinib decreased 32% and 61%, respectively, with Jakafi administration (50 mg single dose) following rifampin 600 mg once daily for 10 days, compared to receiving Jakafi alone in healthy subjects. In addition, the relative exposure to ruxolitinib's active metabolites increased approximately 100%. This increase may partially explain the reported disproportionate 10% reduction in the pharmacodynamic marker pSTAT3 inhibition.

No dose adjustment is recommended when Jakafi is coadministered with a CYP3A4 inducer. Patients should be closely monitored and the dose titrated based on safety and efficacy.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies of Jakafi in pregnant women. In embryofetal toxicity studies, treatment with ruxolitinib resulted in an increase in late resorptions and reduced fetal weights at maternally toxic doses. Jakafi should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Ruxolitinib was administered orally to pregnant rats or rabbits during the period of organogenesis, at doses of 15, 30 or 60 mg/kg/day in rats and 10, 30 or 60 mg/kg/day in rabbits. There was no evidence of teratogenicity. However, decreases of approximately 9% in fetal

weights were noted in rats at the highest and maternally toxic dose of 60 mg/kg/day. This dose results in an exposure (AUC) that is approximately 2 times the clinical exposure at the maximum recommended dose of 25 mg twice daily. In rabbits, lower fetal weights of approximately 8% and increased late resorptions were noted at the highest and maternally toxic dose of 60 mg/kg/day. This dose is approximately 7% the clinical exposure at the maximum recommended dose.

In a pre- and post-natal development study in rats, pregnant animals were dosed with ruxolitinib from implantation through lactation at doses up to 30 mg/kg/day. There were no drug-related adverse findings in pups for fertility indices or for maternal or embryofetal survival, growth and development parameters at the highest dose evaluated (34% the clinical exposure at the maximum recommended dose of 25 mg twice daily).

8.3 Nursing Mothers

It is not known whether ruxolitinib is excreted in human milk. Ruxolitinib and/or its metabolites were excreted in the milk of lactating rats with a concentration that was 13-fold the maternal plasma. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Jakafi, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

The safety and effectiveness of Jakafi in pediatric patients have not been established.

8.5 Geriatric Use

Of the total number of myelofibrosis patients in clinical studies with Jakafi, 51.9% were 65 years of age and older. No overall differences in safety or effectiveness of Jakafi were observed between these patients and younger patients.

8.6 Renal Impairment

The safety and pharmacokinetics of single dose Jakafi (25 mg) were evaluated in a study in healthy subjects [CrCl 72-164 mL/min (N=8)] and in subjects with mild [CrCl 53-83 mL/min (N=8)], moderate [CrCl 38-57 mL/min (N=8)], or severe renal impairment [CrCl 15-51 mL/min (N=8)]. Eight (8) additional subjects with end stage renal disease requiring hemodialysis were also enrolled.

The pharmacokinetics of ruxolitinib was similar in subjects with various degrees of renal impairment and in those with normal renal function. However, plasma AUC values of ruxolitinib metabolites increased with increasing severity of renal impairment. This was most marked in the subjects with end stage renal disease requiring hemodialysis. The change in the pharmacodynamic marker, pSTAT3 inhibition, was consistent with the corresponding increase in metabolite exposure. Ruxolitinib is not removed by dialysis; however, the removal of some active metabolites by dialysis cannot be ruled out.

When administering Jakafi to patients with moderate (CrCl 30-59 mL/min) or severe renal impairment (CrCl 15-29 mL/min) with a platelet count between 100 X 10^9/L and 150 X 10^9/L

and patients with end stage renal disease on dialysis a dose reduction is recommended [*see Dosage and Administration (2.5)*].

8.7 Hepatic Impairment

The safety and pharmacokinetics of single dose Jakafi (25 mg) were evaluated in a study in healthy subjects (N=8) and in subjects with mild [Child-Pugh A (N=8)], moderate [Child-Pugh B (N=8)], or severe hepatic impairment [Child-Pugh C (N=8)]. The mean AUC for ruxolitinib was increased by 87%, 28% and 65%, respectively, in patients with mild, moderate and severe hepatic impairment compared to patients with normal hepatic function. The terminal elimination half-life was prolonged in patients with hepatic impairment compared to healthy controls (4.1-5.0 hours versus 2.8 hours). The change in the pharmacodynamic marker, pSTAT3 inhibition, was consistent with the corresponding increase in ruxolitinib exposure except in the severe (Child-Pugh C) hepatic impairment cohort where the pharmacodynamic activity was more prolonged in some subjects than expected based on plasma concentrations of ruxolitinib.

When administering Jakafi to patients with any degree of hepatic impairment and with a platelet count between 100 X 10^9/L and 150 X 10^9/L, a dose reduction is recommended [*see Dosage and Administration (2.5)*].

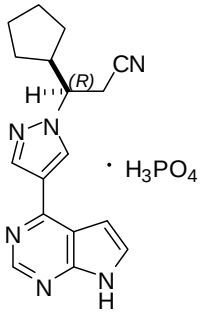
10. OVERDOSAGE

There is no known antidote for overdoses with Jakafi. Single doses up to 200 mg have been given with acceptable acute tolerability. Higher than recommended repeat doses are associated with increased myelosuppression including leukopenia, anemia and thrombocytopenia. Appropriate supportive treatment should be given.

Hemodialysis is not expected to enhance the elimination of ruxolitinib.

11. DESCRIPTION

Ruxolitinib phosphate is a kinase inhibitor with the chemical name (*R*)-3-(4-(7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl)-1*H*-pyrazol-1-yl)-3-cyclopentylpropanenitrile phosphate and a molecular weight of 404.36. Ruxolitinib phosphate has the following structural formula:



Ruxolitinib phosphate is a white to off-white to light pink powder and is soluble in aqueous buffers across a pH range of 1 to 8.

Jakafi (ruxolitinib) Tablets are for oral administration. Each tablet contains ruxolitinib phosphate equivalent to 5 mg, 10 mg, 15 mg, 20 mg and 25 mg of ruxolitinib free base together with microcrystalline cellulose, lactose monohydrate, magnesium stearate, colloidal silicon dioxide, sodium starch glycolate, povidone and hydroxypropyl cellulose.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ruxolitinib, a kinase inhibitor, inhibits Janus Associated Kinases (JAKs) JAK1 and JAK2 which mediate the signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. JAK signaling involves recruitment of STATs (signal transducers and activators of transcription) to cytokine receptors, activation and subsequent localization of STATs to the nucleus leading to modulation of gene expression.

Myelofibrosis (MF) is a myeloproliferative neoplasm (MPN) known to be associated with dysregulated JAK1 and JAK2 signaling. In a mouse model of JAK2V617F-positive MPN, oral administration of ruxolitinib prevented splenomegaly, preferentially decreased JAK2V617F mutant cells in the spleen and decreased circulating inflammatory cytokines (eg, TNF-α, IL-6).

12.2 Pharmacodynamics

Ruxolitinib inhibits cytokine induced STAT3 phosphorylation in whole blood from healthy subjects and MF patients. Jakafi administration resulted in maximal inhibition of STAT3 phosphorylation 2 hours after dosing which returned to near baseline by 10 hours in both healthy subjects and myelofibrosis patients.

12.3 Pharmacokinetics

Absorption

In clinical studies, ruxolitinib is rapidly absorbed after oral Jakafi administration with maximal plasma concentration (C_{max}) achieved within 1 to 2 hours post-dose. Based on a mass balance study in humans, oral absorption of ruxolitinib was estimated to be at least 95%. Mean ruxolitinib C_{max} and total exposure (AUC) increased proportionally over a single dose range of 5 to 200 mg. There were no clinically relevant changes in the pharmacokinetics of ruxolitinib upon administration of Jakafi with a high-fat meal, with the mean C_{max} moderately decreased (24%) and the mean AUC nearly unchanged (4% increase).

Distribution

The apparent volume of distribution of ruxolitinib at steady-state is 53 to 65 L in myelofibrosis patients. Binding to plasma proteins *in vitro* is approximately 97%, mostly to albumin.

Metabolism

In vitro studies suggest that CYP3A4 is the major enzyme responsible for metabolism of ruxolitinib. Ruxolitinib is the predominant entity in humans representing approximately 60% of the drug-related material in circulation. Two major and active metabolites were identified in

plasma of healthy subjects representing 25% and 11% of parent AUC. These two metabolites have one-fifth and one-half of ruxolitinib's pharmacological activity, respectively. The sum total of all active metabolites contributes 18% of the overall pharmacodynamics of ruxolitinib.

Elimination

Following a single oral dose of [^{14}C]-labeled ruxolitinib in healthy adult subjects, elimination was predominately through metabolism with 74% of radioactivity excreted in urine and 22% excretion via feces. Unchanged drug accounted for less than 1% of the excreted total radioactivity. The mean elimination half-life of ruxolitinib is approximately 3 hours and the mean half-life of ruxolitinib + metabolites is approximately 5.8 hours.

Effects of Age, Gender, or Race

In healthy subjects, no significant differences in ruxolitinib pharmacokinetics were observed with regard to gender and race. In a population pharmacokinetic evaluation in myelofibrosis patients, no relationship was apparent between oral clearance and patient age or race, and in women, clearance was 17.7 L/h and in men, 22.1 L/h with 39% inter-subject variability.

Drug Interactions

In vitro, ruxolitinib and its M18 metabolite are not inhibitors of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 or CYP3A4. Ruxolitinib is not an inducer of CYP1A2, CYP2B6 or CYP3A4 at clinically relevant concentrations.

In vitro, ruxolitinib and its M18 metabolite are not inhibitors of the P-gp, BCRP, OATP1B1, OATP1B3, OCT1, OCT2, OAT1 or OAT3 transport systems at clinically relevant concentrations. Ruxolitinib is not a substrate for the P-gp transporter.

12.4 Thorough QT Study

The effect of single dose ruxolitinib 25 mg and 200 mg on QTc interval was evaluated in a randomized, placebo-, and active-controlled (moxifloxacin 400 mg) four-period crossover thorough QT study in 47 healthy subjects. In a study with demonstrated ability to detect small effects, the upper bound of the one-sided 95% confidence interval for the largest placebo adjusted, baseline-corrected QTc based on Fridericia correction method (QTcF) was below 10 ms, the threshold for regulatory concern. The dose of 200 mg is adequate to represent the high exposure clinical scenario.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Ruxolitinib was not carcinogenic in the 6-month Tg.rasH2 transgenic mouse model or in a 2-year carcinogenicity study in the rat.

Ruxolitinib was not mutagenic in a bacterial mutagenicity assay (Ames test) or clastogenic in *in vitro* chromosomal aberration assay (cultured human peripheral blood lymphocytes) or *in vivo* in a rat bone marrow micronucleus assay.

In a fertility study, ruxolitinib was administered to male rats prior to and throughout mating and to female rats prior to mating and up to the implantation day (gestation day 7). Ruxolitinib had no effect on fertility or reproductive function in male or female rats at doses of 10, 30 or 60 mg/kg/day. However, in female rats doses of greater than or equal to 30 mg/kg/day resulted in increased post-implantation loss. The exposure (AUC) at the dose of 30 mg/kg/day is approximately 34% the clinical exposure at the maximum recommended dose of 25 mg twice daily.

14. CLINICAL STUDIES

Two randomized Phase 3 studies (Studies 1 and 2) were conducted in patients with myelofibrosis (either primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia-myelofibrosis). In both studies, patients had palpable splenomegaly at least 5 cm below the costal margin and risk category of intermediate 2 (2 prognostic factors) or high risk (3 or more prognostic factors) based on the International Working Group Consensus Criteria (IWG).

The starting dose of Jakafi was based on platelet count. Patients with a platelet count between 100 and 200 X 10^9/L were started on Jakafi 15 mg twice daily and patients with a platelet count greater than 200 X 10^9/L were started on Jakafi 20 mg twice daily. Doses were then individualized based upon tolerability and efficacy with maximum doses of 20 mg twice daily for patients with platelet counts between 100 to less than or equal to 125 X 10^9/L, of 10 mg twice daily for patients with platelet counts between 75 to less than or equal to 100 X 10^9/L, and of 5 mg twice daily for patients with platelet counts between 50 to less than or equal to 75 X 10^9/L.

Study 1

Study 1 was a double-blind, randomized, placebo-controlled study in 309 patients who were refractory to or were not candidates for available therapy. The median age was 68 years (range 40 to 91 years) with 61% of patients older than 65 years and 54% were male. Fifty percent (50%) of patients had primary myelofibrosis, 31% had post-polycythemia vera myelofibrosis and 18% had post-essential thrombocythemia myelofibrosis. Twenty-one percent (21%) of patients had red blood cell transfusions within 8 weeks of enrollment in the study. The median hemoglobin count was 10.5 g/dL and the median platelet count was 251 X 10^9/L. Patients had a median palpable spleen length of 16 cm below the costal margin, with 81% having a spleen length 10 cm or greater below the costal margin. Patients had a median spleen volume as measured by magnetic resonance imaging (MRI) or computed tomography (CT) of 2595 cm^3 (range 478 cm^3 to 8881 cm^3). (The upper limit of normal is approximately 300 cm^3).

Patients were dosed with Jakafi or matching placebo. The primary efficacy endpoint was the proportion of patients achieving greater than or equal to a 35% reduction from baseline in spleen volume at Week 24 as measured by MRI or CT.

Secondary endpoints included duration of a 35% or greater reduction in spleen volume and proportion of patients with a 50% or greater reduction in Total Symptom Score from baseline to Week 24 as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF) v2.0 diary.

Study 2

Study 2 was an open-label, randomized study in 219 patients. Patients were randomized 2:1 to Jakafi versus best available therapy. Best available therapy was selected by the investigator on a patient-by-patient basis. In the best available therapy arm, the medications received by more than 10% of patients were hydroxyurea (47%) and glucocorticoids (16%). The median age was 66 years (range 35 to 85 years) with 52% of patients older than 65 years and 57% were male. Fifty-three percent (53%) of patients had primary myelofibrosis, 31% had post-polycythemia vera myelofibrosis and 16% had post-essential thrombocythemia myelofibrosis. Twenty-one percent (21%) of patients had red blood cell transfusions within 8 weeks of enrollment in the study. The median hemoglobin count was 10.4 g/dL and the median platelet count was 236 X 10^9/L. Patients had a median palpable spleen length of 15 cm below the costal margin, with 70% having a spleen length 10 cm or greater below the costal margin. Patients had a median spleen volume as measured by MRI or CT of 2381 cm^3 (range 451 cm^3 to 7765 cm^3).

The primary efficacy endpoint was the proportion of patients achieving 35% or greater reduction from baseline in spleen volume at Week 48 as measured by MRI or CT.

A secondary endpoint in Study 2 was the proportion of patients achieving a 35% or greater reduction of spleen volume as measured by MRI or CT from baseline to Week 24.

Study 1 and 2 Efficacy Results

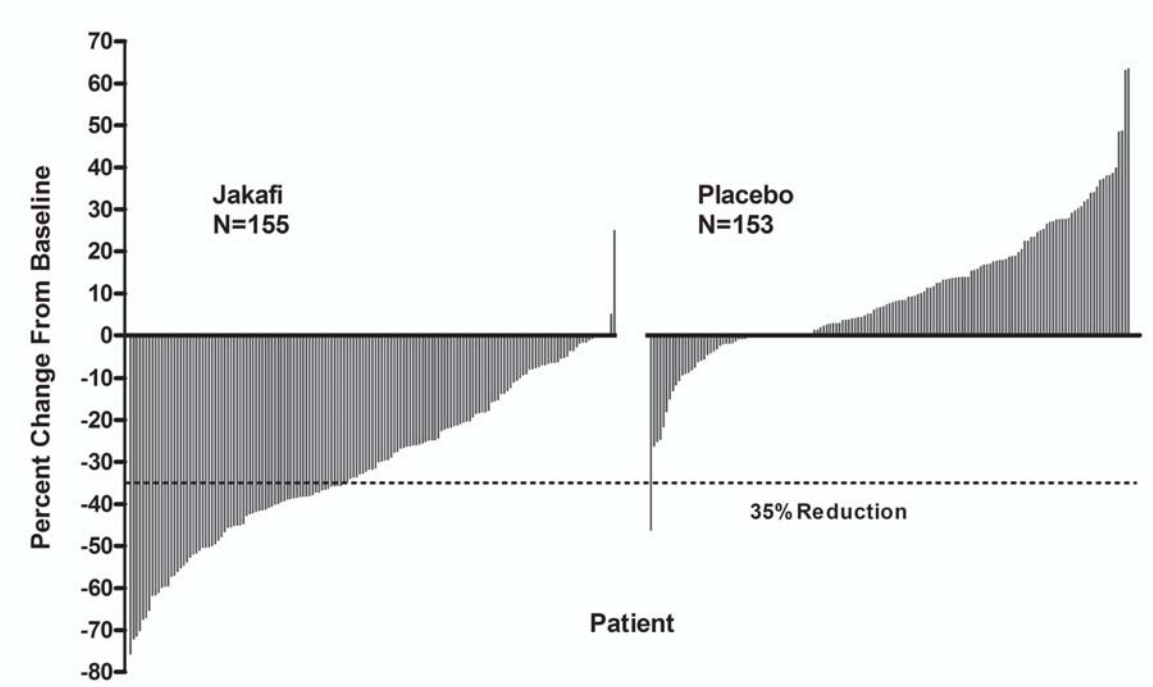
Efficacy analyses of the primary endpoint in Studies 1 and 2 are presented in Table 6 below. A significantly larger proportion of patients in the Jakafi group achieved a 35% or greater reduction in spleen volume from baseline in both studies compared to placebo in Study 1 and best available therapy in Study 2. A similar proportion of patients in the Jakafi group achieved a 50% or greater reduction in palpable spleen length.

Table 7: Percent of Patients with 35% or Greater Reduction from Baseline in Spleen Volume at Week 24 in Study 1 and at Week 48 in Study 2 (Intent to Treat)

	Study 1		**Study 2**	
	Jakafi (N=155)	**Placebo (N=154)**	**Jakafi (N=146)**	**Best Available Therapy (N=73)**
Time Points	Week 24		Week 48	
Number (%) of Patients with Spleen Volume Reduction by 35% or More	65 (41.9)	1 (0.7)	41 (28.5)	0
P-value	< 0.0001		< 0.0001	

Figure 1 shows the percent change from baseline in spleen volume for each patient at Week 24 (Jakafi N=139, placebo N=106) or the last evaluation prior to Week 24 for patients who did not complete 24 weeks of randomized treatment (Jakafi N=16, placebo N=47). One (1) patient (placebo) with a missing baseline spleen volume is not included.

Figure 1: Percent Change from Baseline in Spleen Volume at Week 24 or Last Observation for Each Patient (Study 1)



In Study 1, myelofibrosis symptoms were a secondary endpoint and were measured using the modified Myelofibrosis Symptom Assessment Form (MFSAF) v2.0 diary. The modified MFSAF is a daily diary capturing the core symptoms of myelofibrosis (abdominal discomfort, pain under left ribs, night sweats, itching, bone/muscle pain and early satiety). Symptom scores ranged from 0 to 10 with 0 representing symptoms "absent" and 10 representing "worst imaginable" symptoms. These scores were added to create the daily total score, which has a maximum of 60.

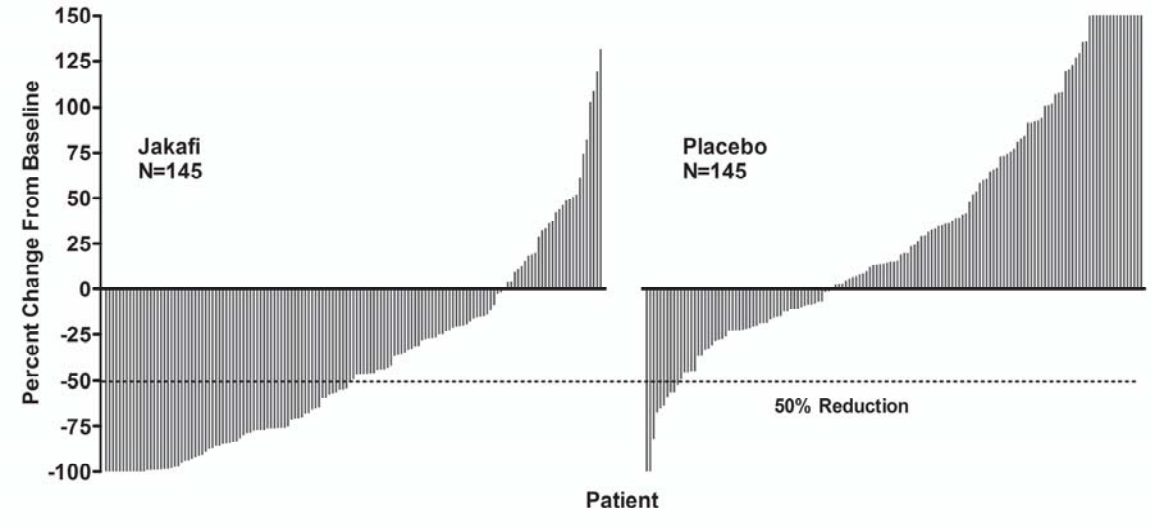
Table 7 presents assessments of Total Symptom Score from baseline to Week 24 in Study 1 including the proportion of patients with at least a 50% reduction (ie, improvement in symptoms). At baseline, the mean Total Symptom Score was 18.0 in the Jakafi group and 16.5 in the placebo group. A higher proportion of patients in the Jakafi group had a 50% or greater reduction in Total Symptom Score than in the placebo group, with a median time to response of less than 4 weeks.

Table 8: Improvement in Total Symptom Score

	Jakafi (N=148)	**Placebo (N=152)**
Number (%) of Patients with 50% or Greater Reduction in Total Symptom Score by Week 24	68 (45.9)	8 (5.3)
P-value	< 0.0001	

Figure 2 shows the percent change from baseline in Total Symptom Score for each patient at Week 24 (Jakafi N=129, placebo N=103) or the last evaluation on randomized therapy prior to Week 24 for patients who did not complete 24 weeks of randomized treatment (Jakafi N=16, placebo N=42). Results are excluded for 5 patients with a baseline Total Symptom Score of zero, 8 patients with missing baseline and 6 patients with insufficient post-baseline data.

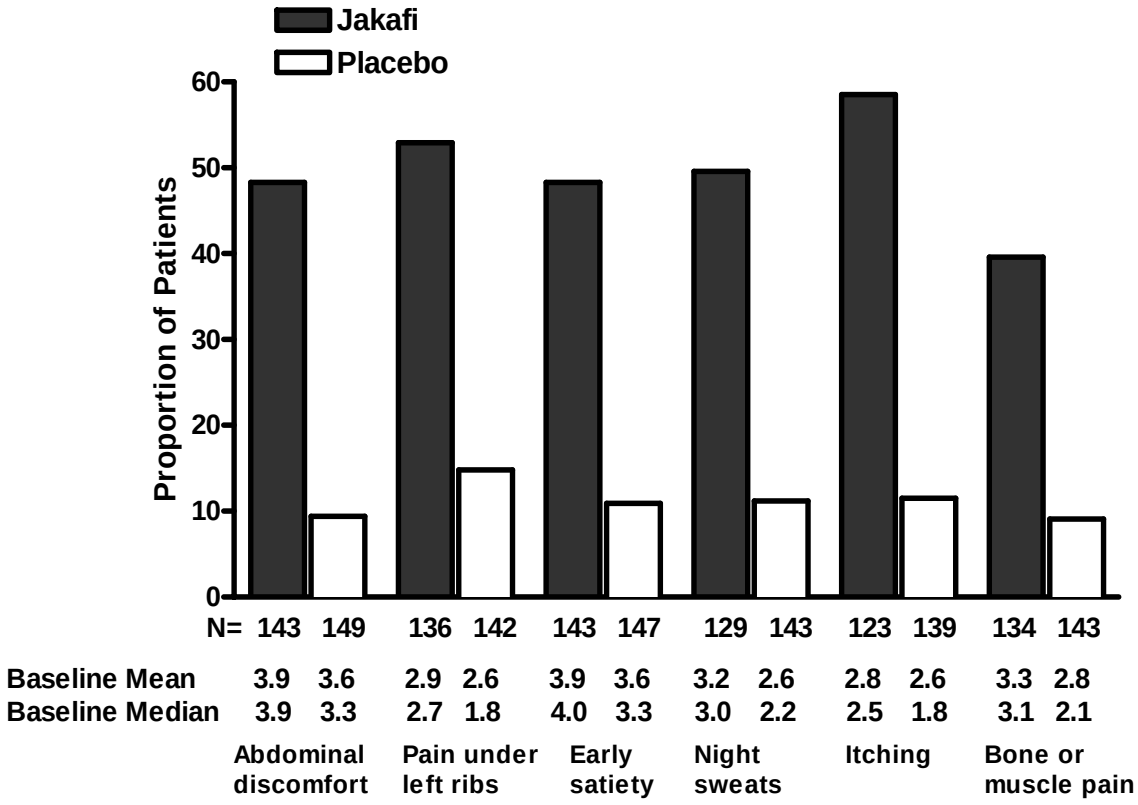
Figure 2: Percent Change from Baseline in Total Symptom Score at Week 24 or Last Observation for Each Patient (Study 1)



Worsening of Total Symptom Score is truncated at 150%.

Figure 3 displays the proportion of patients with at least a 50% improvement in each of the individual symptoms that comprise the Total Symptom Score indicating that all 6 of the symptoms contributed to the higher Total Symptom Score response rate in the group treated with Jakafi.

Figure 3: Proportion of Patients With 50% or Greater Reduction in Individual Symptom Scores at Week 24



Individual score range = 0 to 10

16. HOW SUPPLIED/STORAGE AND HANDLING

Jakafi (ruxolitinib) Tablets are available as follows:

Jakafi Trade Presentations

NDC Number	Strength	Description	Tablets per Bottle
50881-005-60	5 mg	Round tablet with "INCY" on one side and "5" on the other	60
50881-010-60	10 mg	Round tablet with "INCY" on one side and "10" on the other	60
50881-015-60	15 mg	Oval tablet with "INCY" on one side and "15" on the other	60
50881-020-60	20 mg	Capsule shaped tablet with "INCY" on one side and "20" on the other	60
50881-025-60	25 mg	Oval tablet with "INCY" on one side and "25" on the other	60

Store at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature].

17. PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information).

Discuss the following with patients prior to treatment with Jakafi:

17.1 Thrombocytopenia, Anemia and Neutropenia

Inform patients that Jakafi is associated with thrombocytopenia, anemia and neutropenia, and of the need to monitor complete blood counts before and during treatment. Advise patients to observe for and report bleeding.

17.2 Infections

Inform patients of the signs and symptoms of infection and to report any such signs and symptoms promptly.

Inform patients regarding the early signs and symptoms of herpes zoster and of progressive multifocal leukoencephalopathy, and advise patients to seek advice of a clinician if such symptoms are observed.

17.3 Drug-drug Interactions

Advise patients to inform their healthcare providers of all medications they are taking, including over-the-counter medications, herbal products and dietary supplements.

17.4 Dialysis

Inform patients on dialysis that their dose should not be taken before dialysis but only following dialysis.

17.5 Compliance

Patients should be advised to continue taking Jakafi every day for as long as their physician tells them and that this is a long-term treatment. Patients should not change dose or stop taking Jakafi without first consulting their physician. Patients should be aware that after discontinuation of treatment, myelofibrosis signs and symptoms are expected to return.

Manufactured by:
DSM Pharmaceuticals, Inc.
Greenville, NC 27834

Manufactured for:
Incyte Corporation
Wilmington, DE 19880

Patient Information

Jakafi® (JAK-ah-fye)

(ruxolitinib) Tablets

Read this Patient Information before you start taking Jakafi and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment.

What is Jakafi?

Jakafi is a prescription medicine used to treat people with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis.

It is not known if Jakafi is safe or effective in children.

What should I tell my healthcare provider before taking Jakafi?

Before taking Jakafi, tell your healthcare provider if you:

- have an infection.
- have or have had liver or kidney problems.
- are on dialysis. Jakafi should be taken after your dialysis.
- have any other medical conditions.
- are pregnant or plan to become pregnant. It is not known if Jakafi will harm your unborn baby.
- are breast-feeding or plan to breast-feed. It is not known if Jakafi passes into your breast milk. You and your healthcare provider should decide if you will take Jakafi or breast-feed. You should not do both.

Tell your healthcare provider about all the medicines you take including prescription and non-prescription medicines, vitamins and herbal supplements. Taking Jakafi with certain other medicines may affect how Jakafi works.

Especially tell your healthcare provider if you take medicine for:

- Fungal infections
- Bacterial infections
- HIV-AIDS

Ask your healthcare provider or pharmacist if you are not sure if your medicine is one listed above.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take Jakafi?

- Take Jakafi exactly as your healthcare provider tells you.
- Do not change your dose or stop taking Jakafi without first talking to your healthcare provider.
- You can take Jakafi with or without food.
- Jakafi may also be given through certain nasogastric tubes.
    - Tell your healthcare provider if you cannot take Jakafi by mouth. Your healthcare provider will decide if you can take Jakafi through a nasogastric tube.
    - Ask your healthcare provider to give you specific instruction on how to properly take Jakafi through a nasogastric tube.
- Do not drink grapefruit juice while taking Jakafi. Grapefruit juice can affect the amount of Jakafi in your blood.
- If you take too much Jakafi call your healthcare provider or go to the nearest hospital emergency room department right away. Take the bottle of Jakafi with you.
- If you miss a dose of Jakafi, take your next dose at your regular time. Do not take 2 doses at the same time.
- You will have regular blood tests during your treatment with Jakafi. Your healthcare provider may change your dose of Jakafi or stop your treatment based on the results of your blood tests.

What are the possible side effects of Jakafi?

Jakafi can cause serious side effects including:

Low blood cell counts: Jakafi may cause low platelet counts (thrombocytopenia), low red blood cell counts (anemia), and low white blood cell counts (neutropenia). If you develop bleeding, stop Jakafi and call your doctor. Your healthcare provider will do a blood test to check your blood cell counts before you start Jakafi and regularly during your treatment with Jakafi. Tell your healthcare provider right away if you develop any of these symptoms:

- unusual bleeding
- bruising
- fatigue
- shortness of breath
- fever

Infection: You may be at risk for developing a serious infection while taking Jakafi. Tell your healthcare provider if you have:

- chills
- aches
- fever
- nausea
- vomiting
- weakness
- painful skin rash or blisters

The most common side effects of Jakafi include:

- dizziness
- headache

Tell your healthcare provider about any side effect that bothers you or that does not go away.

These are not all the possible side effects of Jakafi. Ask your healthcare provider or pharmacist for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Jakafi?

- Store Jakafi at room temperature between 68°F and 77°F (20°C and 25°C).

Keep this and all medicines out of the reach of children.

General information about the safe and effective use of Jakafi:

Medicines are sometimes prescribed for purposes other than those listed in Patient Information. Do not use Jakafi for a condition for which it is not prescribed. Do not give Jakafi to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet summarizes the most important information about Jakafi. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information that is written for healthcare professionals.

For more information call 1-855-463-3463 or go to www.jakafi.com.

What are the ingredients in Jakafi?

Active ingredient: ruxolitinib.

Inactive ingredients: microcrystalline cellulose, lactose monohydrate, magnesium stearate, colloidal silicon dioxide, sodium starch glycolate, povidone and hydroxypropyl cellulose.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Issued: May 2013