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.

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 risk factors and signs and symptoms of infection, and manage promptly.

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.
Jakafi®
 photoshop
 If its your life, save it.

In the phase 2 COMFORT-I trial of patients with intermediate-2 risk or high-risk MF, the primary end point was the proportion of patients achieving a ≥30% reduction in spleen volume from baseline to week 24.

45% of patients receiving Jakafi achieved a ≥20% reduction in spleen volume at week 24; 0.4% of patients receiving placebo (P < 0.001).

Early dose adjustments as needed to help optimize safety and efficacy

In the phase 3 COMFORT-I trial of patients with intermediate-2–risk or high-risk MF, the primary end point was the proportion of patients achieving at least a 35% reduction in spleen volume from baseline to week 24.

45% of patients receiving Jakafi achieved a ≥20% reduction in spleen volume at week 24; 0.4% of patients receiving placebo (P < 0.001).

Starting PLT Count 50 to <100 × 10⁹/L

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

Starting PLT Count 50 to <100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

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

Starting PLT Count ≥100 × 10⁹/L

See SPECIAL POPULATIONS for dosing information in patients with renal or hepatic impairment and for information on drug interactions.
Jakafi® is a registered trademark of Incyte. Haematologica 2013;98(12):1865-1871.

**Early dose adjustments as needed to help optimize efficacy and safety**

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

- **45%** of patients receiving Jakafi achieved a ≥25% reduction in spleen volume at week 24 as compared with patients who received placebo.**

**Jakafi® is also available in 10 mg and 25 mg tablets and capsules.**

- **Starting PLT Count 50 to <100 × 10⁹/L**
  - 5 mg twice daily
  - 10 mg twice daily
  - 15 mg twice daily
  - 20 mg twice daily

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

### DECREASE DOSE

In the case of a Hematologic Toxicity including:

- **Thrombocytopenia**

Discontinuation can be avoided by reducing the dose or temporarily withholding Jakafi:

<table>
<thead>
<tr>
<th>PLT Count (× 10⁹/L)</th>
<th>20 mg</th>
<th>15 mg</th>
<th>10 mg</th>
<th>5 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 to &lt;200</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
</tr>
<tr>
<td>&gt;200</td>
<td>Hold</td>
<td>Hold</td>
<td>Hold</td>
<td>Hold</td>
</tr>
</tbody>
</table>

For patients receiving Jakafi in the COMFORT study, PLT counts and hemoglobin levels generally stabilized after 8 to 12 weeks.†

**MONITOR frequently**

Monitor CBCs every 2–4 weeks until doses are stabilized, and then on a clinically indicated basis.

### INCREASE DOSE

In the case of an insufficient response consider an increase in the dose of Jakafi to meet all these criteria:

- **Ineffective spleen reduction**

- **PLT count ≥25 × 10⁹/L at 4 weeks and >100 × 10⁹/L**

- **Absolute neutrophil count (ANC) ≥0.5 × 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 once per week. Discontinue Jakafi if there is no spleen size reduction or symptom improvement after 6 months of therapy.

**IMPORTANT NOTE:** Please see Important Safety Information on the back cover for related and other risk information.

**RISK OF BLOOD CONSOLIDATION AFTER INITIATION OF JAKAFI TREATMENT**

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

See **RESTARTING** for dose modifications.

**RESTARTING for 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 >0.5 × 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**

<table>
<thead>
<tr>
<th>PLT Count (× 10⁹/L)</th>
<th>Maximum Dose When Restarting Treatment with Jakafi®</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;200</td>
<td>20 mg twice daily</td>
</tr>
<tr>
<td>100 to &lt;200</td>
<td>15 mg twice daily</td>
</tr>
<tr>
<td>75 to &gt;75</td>
<td>10 mg twice daily for at least 2 weeks; if stable, may increase to 15 mg twice daily</td>
</tr>
<tr>
<td>&lt;75</td>
<td>5 mg twice daily for at least 2 weeks; if stable, may increase to 10 mg twice daily</td>
</tr>
</tbody>
</table>

**WARNING:** No dose reduction or interruption for an adverse event or hematological toxicity.

**At the start of treatment with Jakafi®,** patients on 5 mg once daily, maintain dose at 5 mg once daily; patients on >5 mg once daily below the largest dose in the week prior to the decrease in PLT count may increase to 10 mg twice daily for at least 2 weeks; if stable, may increase to 15 mg twice daily.

- **For patients with renal or hepatic impairment:**
  - **Non-melanoma skin cancers including basal cell, squamous cell, and Merkel cell carcinoma** have occurred. Perform a skin examination at baseline and then repeat every 2 to 4 weeks until doses are stabilized and then gradually recovered to a new steady state. If on stable dose for patients with MF:
    - **Intermediate-2–risk or high-risk MF, the primary end point was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline to study week 24.**
    - **13%** of patients receiving Jakafi achieved a ≥25% reduction in spleen volume at week 24 as measured by CT or MRI. Best available therapy until treatment with Jakafi can cause 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 and efficacy considerations.

**Risk for thrombocytopenia, anemia, and neutropenia**

- **Treatment with Jakafi may 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.**

- **Platellet transfusions may be necessary.**

- **Patients developing anemia may require blood transfusions and discontinuation of Jakafi.**

**Severe neutropenia (ANC <0.5 × 10⁹/L)** was generally reversible by withholding Jakafi until recovery.

**Please see Important Safety Information for related and other risk information.**

**Please click here for Full Prescribing Information for complete dosing recommendations.**

**Restarting dose in case of bleeding**

- **Once the bleeding event has resolved, consider resuming treatment at the prior dose level.** If the underlying cause of bleeding has been controlled. If the bleeding event has resolved but the underlying cause persists, consider treatment with Jakafi at a lower dose.
Jakafi® (ruxolitinib) is indicated for:

- Myelofibrosis (MF) for intermediate-2 or high-risk MF
- Polycythemia vera (PV) in patients who have had an inadequate response to, or who are unable to tolerate, other myeloproliferative neoplasm therapies
- Recently transformed myelofibrosis from hairy cell leukemia
- Relapsed/refractory intermediate-2–high-risk systemic myelofibrosis

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.

Early dose adjustments as needed to help optimize efficacy and safety

In the phase 3 COMFORT-I trial of patients with intermediate-2 or high-risk MF, the primary end point was the proportion of patients achieving a ≥30% reduction in spleen volume from baseline to week 24:

- 45% of patients receiving Jakafi achieved a ≥20% reduction in spleen volume at weeks 24 to 47 of patients receiving placebo (P < 0.001)

See STARTING PLT COUNT 50 to <100 to 10 mg twice daily for recommendation.

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

70% of patients receiving Jakafi at a lower dose had more improvement after 6 months of therapy compared to those receiving placebo.

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

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.

Special Populations

Renal or hepatic impairment

- 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 Coprescribed Strong CYP3A4 Inhibitors or Fluconazole Doses ≥200 mg

Starting dose for patients with MF with a PLT count:

- ≥100 to 150 × 10^9/L
- ≤100 × 10^9/L

If on stable dose for patients with MF:

- ≥5 mg twice daily
- Decrease dose by 30% (round up to the closest available tablet strength)

- 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

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.
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 × 10⁹/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. Evaluate patients prior to and while receiving Jakafi for risk factors and signs and symptoms of infection, and manage promptly.
- 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.
- 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.
- The three most frequent non-hematologic adverse reactions (incidence >10%) were bruising, dizziness and headache.
- A dose modification is recommended 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 two weeks after the final dose.

Please click here for Full Prescribing Information for Jakafi.