





## JOURNEY TO THE JAK PATHWAY

Janus kinases, or JAKs, are enzymes that reside within the cells and control specific biological functions including production of new blood cells and functioning of immune system. Over-activation or dysregulation of the JAK pathway as a result of genetic mutations and/or elevated cytokine levels, can result in abnormal numbers or function of blood cells. Incyte's discovery and development of Jakafi™ (ruxolitinib) was founded on the proven association between abnormal JAK signaling and a group of blood disorders referred to as MPNs, which include myelofibrosis (MF), polycythemia vera (PV) and essential thrombocythemia (ET).

The JAK family of proteins is comprised of JAK1, JAK2, JAK3, and TYK2. Jakafi is an oral treatment that inhibits JAK1 and JAK2 resulting in the down-modulation of overactive JAK signaling. Over-active or dysregulated JAK 1 and JAK 2 has been linked to the splenomegaly and debilitating symptoms seen in the majority of patients with MF.



“During clinical trials, Jakafi provided significant reductions in spleen size and significant improvements in symptoms in patients with myelofibrosis. Importantly, many of these benefits were achieved early on and were sustained during treatment.”

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## 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 INFORMATION

- Treatment with Jakafi can cause hematologic adverse reactions, including thrombocytopenia, anemia and neutropenia, which are each dose-related effects, with the most frequent being thrombocytopenia and anemia. A complete blood count must be performed before initiating therapy with Jakafi. Complete blood counts should be monitored as clinically indicated and dosing adjusted as required
- The three most frequent non-hematologic adverse reactions were bruising, dizziness and headache
- Patients with platelet counts  $<200 \times 10^9/L$  at the start of therapy are more likely to develop thrombocytopenia during treatment. Thrombocytopenia was generally reversible and was usually managed by reducing the dose or temporarily withholding Jakafi. If clinically indicated, platelet transfusions may be administered
- Patients developing anemia may require blood transfusions. Dose modifications of Jakafi for patients developing anemia may also be considered
- Neutropenia ( $ANC < 0.5 \times 10^9/L$ ) was generally reversible and was managed by temporarily withholding Jakafi
- Patients should be assessed for the risk of developing serious bacterial, mycobacterial, fungal and viral infections. Active serious infections should have resolved before starting Jakafi. Physicians should carefully observe patients receiving Jakafi for signs and symptoms of infection (including herpes zoster) and initiate appropriate treatment promptly
- A dose modification is recommended when administering Jakafi with strong CYP3A4 inhibitors or in patients with renal or hepatic impairment [see *Dosage and Administration*]. Patients should be closely monitored and the dose titrated based on safety and efficacy
- There are no adequate and well-controlled studies of Jakafi in pregnant women. 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 breast-feed. Discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother

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