Jakafi®
ruxolitinib (tablets)

www.jakafi.com/HCP

Dear Dr :

We are pleased to announce FDA approval of Jakafi® (ruxolitinib) for treatment of patients with polycythemia vera (PV) who have had an inadequate response to or are intolerant of hydroxyurea (HU). This new indication makes Jakafi the **first and only FDA-approved treatment for these patients.**

The updated labeling for Jakafi includes the following new information:

- Efficacy profile of Jakafi based on data from the active-controlled, phase 3 RESPONSE trial* (N = 222)
- Adverse events occurring in patients receiving Jakafi in the RESPONSE trial
- Dosing and administration, including information on dose titration and restarting treatment
- Safety update to include a new warning regarding risk for non-melanoma skin cancers. Periodic skin examination is recommended for patients taking Jakafi

To learn more about these updates, please see the accompanying Full Prescribing Information for Jakafi and visit www.jakafi.com/HCP.

Please see the accompanying flyer for information about obtaining prior authorization for appropriate patients. If your office needs prior authorization information or support gaining access to Jakafi for your appropriate patients, please contact IncyteCARES Monday through Friday, 8 AM-8 PM ET, at 1-855-4-Jakafi (1-855-452-5234) or visit www.IncyteCARES.com.

About the RESPONSE trial

RESPONSE was a randomized, open-label trial comparing Jakafi with best available therapy (BAT)† in patients with PV who had an inadequate response to or were intolerant of HU. The composite primary end point in the RESPONSE trial was the proportion of patients achieving a response at week 32, defined as having achieved both hematocrit (Hct) control (the absence of phlebotomy eligibility‡) *and* ≥35% reduction in spleen volume. In the RESPONSE trial, 21% of patients receiving Jakafi achieved the composite primary end point, compared with 0.9% of patients in the BAT arm ($P < 0.0001$).

Important Safety Information

- 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 X 10^9/L) was generally reversible by withholding Jakafi until recovery

Important Safety Information continued on next page.

Important Safety Information (continued)

- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi® (ruxolitinib) until active serious infections have resolved. Observe patients receiving Jakafi for 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 ruxolitinib treatment for myelofibrosis. If PML is suspected, stop Jakafi and evaluate
- Advise patients about early signs and symptoms of herpes zoster and to seek early treatment
- 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
- 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 breast-feed

Please see accompanying Full Prescribing Information for Jakafi.

For more information on patient access and support, or to learn more about using Jakafi to treat your patients with PV who have had an inadequate response to or are intolerant of HU, please visit www.jakafi.com/HCP.

Respectfully,

Incyte Corporation

* The **R**andomized Study of **E**fficacy and **S**afety in **PO**lycythemia Vera with JAK I**N**hibitor Ruxolitinib Ver**S**us B**E**st Available Care (RESPONSE) was a randomized, open-label, active-controlled phase 3 trial comparing the efficacy and safety of the oral Janus kinase (JAK)1/JAK2 inhibitor ruxolitinib with best available therapy in patients with PV who had an inadequate response to or were intolerant of HU, required phlebotomy, and exhibited splenomegaly. The starting dose of ruxolitinib was 10 mg twice daily, and doses were individualized based upon tolerability and efficacy. The primary end point was the proportion of subjects achieving both Hct control without phlebotomy eligibility and ≥35% reduction in spleen volume at week 32. RESPONSE is the first phase 3 study to evaluate a JAK inhibitor for the treatment of PV.

† Best available therapy was selected by the investigator on a patient-by-patient basis and included hydroxyurea, interferon/pegylated interferon, anagrelide, pipobroman, lenalidomide/thalidomide, and observation.

‡ Phlebotomy eligibility was defined as Hct >45% that is ≥3 percentage points higher than baseline or Hct >48% (lower value).

Reference: Jakafi Prescribing Information. Wilmington, DE: Incyte Corporation.

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