Ruxolitinib (JAKAFI)

Criteria for Use

November 2017

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or http://vaww.pbm.va.gov for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive ruxolitinib.*

- ☐ Active bacterial, mycobacterial, fungal and viral infections requiring therapy (see issues for consideration for patients with active or latent tuberculosis and chronic hepatitis B virus)
- ☐ Known active hepatitis A, B, or C (untreated or uncontrolled) or known HIV infection
- ☐ Subjects with impairment of gastrointestinal function or GI disease that may significantly alter the absorption of ruxolitinib
- ☐ Patient receiving fluconazole doses of greater than 200 mg/day orally
- ☐ Breastfeeding
- ☐ ECOG performance status >3

Inclusion Criteria *The answers to the following must be fulfilled in order to meet criteria.*

☐ Patient's cancer care is being managed by a VA authorized oncology provider

☐ Diagnosis of intermediate or high-risk myelofibrosis (as defined by the International Working Group for Myeloproliferative Neoplasms Research and Treatment International Prognostic Scoring System[1,2,3])*, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis

--- OR---

☐ Diagnosis of polycythemia vera who have had an inadequate response to or are intolerant of hydroxyurea**

**Dynamic International Prognostic Scoring System (DIPSS)*

	Value		
Prognostic variable	0	1	2
Age	≤65	>65	
White Blood Count x10^9/L	≤25	>25	
Hemoglobin g/dL	≥10		<10
Peripheral blood blast %	<1	≥1	
Constitutional symptoms	N	Y	

Obtain risk category by adding values for each variable.
Risk categories: Low: 0; intermediate-1: 1 or 2; intermediate 2: 3 or 4; high: 5 or 6

***Definition of Resistance/Intolerance to Hydroxyurea[4,5]*

1. Intolerance to phlebotomy to keep hematocrit < 45% (men) or <42% (women) on at least 2 g/day of hydroxyurea OR
2. Failure to reduce massive splenomegaly (organ extending by > 10 cm from the costal margin) by 50% as measured by palpation or failure to completely relieve symptoms related to splenomegaly after 3 months of at least 2 g/day of hydroxyurea OR
3. Absolute neutrophil count <1 × 10^9/L or platelets < 100 × 10^9/L or hemoglobin < 10 g/dL at the lowest dose of hydroxyurea required to achieve a complete or partial response OR
4. Presence of leg ulcers or other unacceptable hydroxyurea-related nonhematologic toxicities, such as mucocutaneous manifestations, GI symptoms, pneumonitis, or fever at any dose of hydroxyurea

For women of childbearing potential, please see issues for consideration

Dosage and Administration

Recommended starting doses of ruxolitinib are based on platelet counts, renal and hepatic function and are adjusted for use with strong 3A4 inhibitors and fluconazole doses less than 200 mg per day. Doses are titrated based on safety and efficacy. Please refer to the prescribing information for additional dosing and administration information.

Monitoring

Baseline (see Issues for Consideration for patients with chronic hepatitis B)

- A complete blood count (CBC) must be completed before initiating therapy
- Symptom assessment (consider use of the Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score: MPN-SAF TSS[6])

- Spleen size by palpation or imaging
- Tuberculin skin test patients at high risk for TB

During Therapy

- CBC after 1 week, then every 2-4 weeks until dose stabilizes, then as clinically necessary. Closely monitor platelet count and ANC and if platelets drop to <50 x 10^9/L or ANC to < 0.5 x 10^9/L hold dose and restart as per label instructions depending on baseline platelet values.
- Monitoring patient's symptom response utilizing standard symptom assessment form is recommended (consider use of the Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score: MPN-SAF TSS[6])
- Monitor patient's spleen size by palpation or imaging
- Consider utilization of the response criteria of the International Working Group- Myeloproliferative Neoplasms Research (IWG-MRT) and Treatment and European LeukemiaNet (ELN) for evaluation of clinical response[7,8]
- Monitor patient for serious anemia and thrombocytopenia, serious infections (particularly monitoring for signs/symptoms of tuberculosis and herpes zoster), non-melanoma skin cancers, and hepatic enzymes.
- Monitor patient for bleeding events and interrupt therapy if bleeding requiring intervention occurs regardless of platelet count
- Assess lipid levels lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides at 8-12 weeks after initiation of ruxolitinib and manage per clinical guidelines for hyperlipidemia[9]

Issues for Consideration

- **Transplant Candidates:** In the COMFORT-II trial of ruxolitinib in myelofibrosis patients, patients who were candidates for allogeneic transplant were excluded from the trial. Transplant is an option for intermediate-2 or high-risk myelofibrosis patients given the potential curative benefit in these patients. Risk and benefits should be weighed individually for myelofibrosis patients who are transplant candidates.
- **Tuberculosis:** Prior to initiating patients should be evaluated for tuberculosis risk factors, and those at higher risk should be tested for latent infection. For patients with evidence of active or latent tuberculosis, consult a physician with expertise in the treatment of tuberculosis before starting ruxolitinib. The decision to continue ruxolitinib during treatment of active tuberculosis should be based on the overall risk-benefit determination.
- **Chronic Hepatitis B (HBV):** Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections while taking ruxolitinib. Patients should be treated and monitoring per clinical guidelines for HBV.[10]
- **Pregnancy**: Ruxolitinib is pregnancy Category C. Administration during pregnancy should only be considered when potential benefits outweigh risks to fetus. For more information on embryofetal toxicity, see prescribing information.

Discontinuation Criteria

- Following discontinuation of therapy, dose interruption or taper, patients may experience an exacerbation or return of myeloproliferative symptoms and some patients have experienced one or more of the following adverse events after discontinuing: fever, respiratory distress, hypotension, DIC, or multi-organ failure. When discontinuing or interrupting therapy with ruxolitinib for reasons other than thrombocytopenia or neutropenia, consider tapering the dose gradually rather than discontinuing abruptly by 5 mg twice daily each week.
- Therapeutic trial (typically 6 months of therapy) has been completed without documented evidence of clinical benefit (spleen reduction or symptom improvement)- consider utilization of the response criteria of the International Working Group- Myeloproliferative Neoplasms Research (IWG-MRT) and Treatment and European LeukemiaNet (ELN) for evaluation of clinical response.[7.8]
- Non-compliance with therapy, laboratory or follow-up visits.
- Patient declines further therapy.
- Permanently discontinue for significant drug-related toxicity

References:
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3. Gangat N, Caramazza D, Vaidya R, et al. DIPSS plus: a refined Dynamic International Prognostic Scoring System for primary myelofibrosis that incorporates prognostic information from karyotype, platelet count, and transfusion status. J Clin Oncol. 2011;29(4):392-7.
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6. Scherber R, Deuck AC, Johansson P, et al. The myeloproliferative neoplasm symptom assessment form (MPN-SAF): international prospective validation and reliability trial in 402 patients. Blood. 2011; 118: 401-8.
7. Tefferi A, Cervantes F, Mesa R, et al. Revised response criteria for myelofibrosis: International working group myeloproliferative neoplasms research and treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus report. Blood. 2013; 122(8):1395-8.
8. Barosi G, Mesa R, Finazzi G, et al. Revised response criteria for polycythemia vera and essential thrombocytopenia: an ELN and IWG-MRT consensus project. Blood. 2013; 121(23): 4778-81.
9. Stone NJ, Robinson JG, Lichtenstein AH et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults. Circulation. 2014;129:S1-S45.
10. Terrault NA, Bzowej NH, Chang K, et al. AASLD guidelines for treatment of chronic hepatitis B. Hepatology. 2016; 63(1): 261-83.

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