BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 5/07/15**
SECTION: DRUGS	**LAST REVIEW DATE: 5/16/19**
	LAST CRITERIA REVISION DATE: 5/16/19
	ARCHIVE DATE:

JAKAFI® (ruxolitinib phosphate) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Jakafi (ruxolitinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in Cancer or Blood diseases or is in consultation with an Oncologist or Hematologist

2. Individual is 18 years of age or older

3. A confirmed diagnosis of **ONE** of the following:
   - Primary myelofibrosis (PMF), Post-polycythemia vera myelofibrosis, or Post-essential thrombocythemia myelofibrosis for treatment of **ONE** of the following:
     - Symptomatic low-risk myelofibrosis (MF) [risk category defined by IPSS (See Definitions section)]
     - Symptomatic intermediate risk 1 (INT-1) MF [risk category defined by IPSS (See Definitions section)]
     - INT-2 MF or high-risk MF if not a transplant candidate and platelets > 50K [risk category defined by IPSS (See Definitions section)]
     - MF-accelerated phase or MF-blast phase/acute myeloid leukemia for the improvement of splenomegaly and other disease-related symptoms

   - Polycythemia vera (PV) for patients with failure, contraindication or intolerance to hydroxyurea and alfa-interferon **and** are symptomatic low-risk PV with potential indications for cytoreductive therapy **or** are high-risk PV

   - Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
   - Complete blood count with differential
   - Tuberculosis evaluation
   - Hepatitis B evaluation

5. There are **NO** unresolved active infections prior to initiation of Jakafi

6. Will not be used with other Tyrosine Kinase Inhibitors or other Janus Associated Kinase Inhibitors (such as Xeljanz (tofacitinib), Xeljanz (tofacitinib) XR, or Olumiant (baricitinib))

Initial approval duration: 6 months

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- **Criteria for continuation of coverage (renewal request):** Jakafi (ruxolitinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:
  1. Individual continues to be seen by a physician specializing in Cancer or Blood diseases or is in consultation with an Oncologist or Hematologist

  2. Individual's condition responded or has not worsened while on therapy
     - Response is defined as:
       - For MF, **BOTH** of the following:
         - At least a 35% reduction in spleen volume (by MRI or CT) **OR** at least a 50% decrease in palpable spleen length below costal margin
         - At least a 50% reduction symptoms using MPN-SAF TSS
       - For PV, **ALL** of the following:
         - Does not require phlebotomy
         - At least a 35% reduction in spleen volume (by MRI or CT) **OR** at least a 50% decrease in palpable spleen length below costal margin
         - At least a 50% reduction symptoms using MPN-SAF TSS
     - Worsening is defined as:
       - No evidence of reduction in spleen size **OR** no symptom improvement

  3. Individual has been adherent with the medication

  4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
     - Significant adverse effect such as:
       - Progressive multifocal leukoencephalopathy (PML)
       - Thrombocytopenia
       - Neutropenia

  5. There are no significant interacting drugs

  6. Will not be used with other Tyrosine Kinase Inhibitors or other Janus Associated Kinase Inhibitors (such as Xeljanz (tofacitinib), Xeljanz (tofacitinib) XR, or Olumiant (baricitinib))

  Renewal duration: 12 months

Description:

Jakafi (ruxolitinib) is indicated for patients with intermediate or high-risk myelofibrosis (MF), including primary myelofibrosis (PMF), post-polycythemia vera myelofibrosis (Post-PV MF) and post-essential thrombocythemia myelofibrosis (Post ET MF). It is also indicated for patients with polycythemia vera (PV) who have had an inadequate response to or are intolerant of hydroxyurea.

Jakafi (Ruxolitinib) is a kinase inhibitor of the Janus-associated kinases (JAK), JAK1 and JAK2. There are 4 known JAK: JAK1, JAK2, JAK3, and tyrosine kinase 2 (TyK2). JAK are intracellular enzymes that transmit signals coming from cytokine or growth factor receptor interactions on the cell membrane to influence hematopoiesis and

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immune cell function. Receptor binding of these kinases initiates intracellular signal pathways that regulate the transcription of genes for several cell products. JAK enzymes transmit signals through pairing of JAK (such as JAK1-JAK3, JAK1-JAK2, JAK1-TyK2, and JAK2-JAK2). Within the signaling pathway, JAK phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. Interruption of these signaling pathways is thought to reduce the inflammatory response. MF and PV are myeloproliferative neoplasms known to be associated with uncontrolled and overactive JAK1 and JAK2 signaling. Inhibition of this overactivity results in a decrease in the inflammatory cytokine signaling and a decrease in overproduction of cells.

Myelofibrosis (MF), a Philadelphia chromosome-negative chronic myeloproliferative disorder, is characterized by progressive anemia, bone marrow fibrosis, splenomegaly and constitutional symptoms. Up to 30% of patients are initially asymptomatic. Many patients present with symptoms from anemia, splenomegaly or constitutional symptoms (severe fatigue, low grade fever, pruritus, night sweats and weight loss). As the disease evolves, all patients become symptomatic due to marrow failure and increasing splenomegaly resulting in abdominal symptoms and early satiety.

Current drug therapy is palliative and efficacy is variable. Allogeneic stem cell transplantation is potentially curative, but is not appropriate for all patients. Treatment for MF may include androgens, corticosteroids, erythropoiesis-stimulating agents, thalidomide, lenalidomide, and hydroxyurea. Splenectomy can be considered in transfusion dependent anemia that is refractory to drug therapy.

The International Working Group (IWG) consensus for Myelofibrosis Research and Treatment has devised an international prognostic scoring system (IPSS) that uses presenting signs and symptoms to assign risk categories. Individuals with zero (low risk), one (intermediate risk-1), two (intermediate risk-2), or ≥3 (high risk) at presentation had non-overlapping median survivals of 135, 95, 48, and 27 months, respectively. The following five adverse prognostic features were noted by the IWP IPSS: age > 65 years; presence of constitutional symptoms (weight loss >10 % from baseline, night sweats, or unexplained fever); hemoglobin <10 g/dL; leukocyte count > 25 X 10^9/L; and circulating blast cells ≥ 1%.

PV is a chronic myeloproliferative disorder that causes the bone marrow to produce too many red blood cells. The median age at presentation is 60 years. Patients often present with either arterial or venous vascular occlusive events. The events are predominantly coronary and cerebral but can involve the skin and gastrointestinal tract. Over time PV may evolve to MF, acute myeloid leukemia (AML), or myelodysplastic syndrome (MDS). The mainstay of therapy for PV is phlebotomy which removes excess red blood cells and lowers blood viscosity. In general, the goal of phlebotomy is to keep the hematocrit below 45% in men and 42% in women. When patients remain symptomatic despite phlebotomy, other options include hydroxyurea (with or without phlebotomy), interferon alfa, thalidomide, lenalidomide, anagrelide (in certain circumstances) and rarely, chlorambucil, melphalan, or busulfan. It is estimated that 25% of PV patients remain uncontrolled despite the use of existing standard therapies.

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Definitions:

Myelofibrosis:

These risk stratification systems have been studied and validated only in patient with PMF, but clinically have been used for stratification of patients with Post-PV MF or Post-ET MF. Novel prognostic models are being developed for risk stratification of patients with Post-PV MF or Post-ET MF

IPSS should be used at time of diagnosis, DIPSS-PLUS is preferred during the course of treatment, DIPSS can be used if karyotyping is not available

International Working Group (IWG) International prognostic scoring system (IPSS:

Risk Stratification for Myelofibrosis (IPSS)	
	Points
Age > 65 years	1
Constitutional symptoms: Weight loss > 10 % from baseline Night sweats Unexplained fever	1
Hemoglobin <10 g/dL	1
Leukocyte count > 25 X 10^9/L	1
Circulating blast cells ≥ 1%	1
Risk Group	
Low risk	0 points
Intermediate risk-1	1 point
Intermediate risk-2	2 points
High risk	3 or more points

Dynamic International Prognostic System (DIPSS):

Prognostic Variable	Points		
	0	1	2
Age (y)	≤ 65	> 65	
Constitutional symptoms (Y/N)	N	Y	
Hemoglobin (g/dL)	≥ 10		< 10
WBC (x 10^9/L)	≤ 25	> 25	
Peripheral blood blasts (%)	< 1	≥ 1	
Risk Group	Points		
Low	0		
Intermediate-1	1 or 2		
Intermediate-2	3 or 4		
High	5 or 6		

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Dynamic International Prognostic System Plus (DIPSS-Plus):

Prognostic Variable	Points
DIPSS low risk	0
DIPSS Intermediate-1	1
DIPSS Intermediate-2	2
DIPSS high risk	3
Platelets < 100 x 10^9/L	1
Transfusion need	1
Unfavorable karyotype*	1
Risk Group	Points
Low	0
Intermediate-1	1
Intermediate-2	2 or 3
High	4 to 6
*Unfavorable karyotype: complex karyotype or sole or two abnormalities that include trisomy 8, 7/7q, i(17q), 5/5q-, 12p-, inv(3), or 11q23 rearrangement	

Assessment of Symptom Burden

MPN-SAF is recommended for assessment at baseline and MPN-SAF TSS is recommended for monitoring during the course of treatment

Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF)		
	Circle the one number that describes, **during the past week**, how much difficulty you had with each of the following symptoms	
Early satiety	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Abdominal pain	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Abdominal discomfort	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Inactivity	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Problems with headaches	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Problems with concentration compared to before Dx	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Dizziness/vertigo/lightheaded	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Numbness tingling hands/feet	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Difficulty sleeping	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Depressed or sad mood	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Problems with sexual desire or ability	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Cough	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Night sweats	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Itching	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Bone pain – not joint pain or arthritis	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Unintentional weight loss	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Fever	Absent = 0; Daily = 10	0-1-2-3-4-5-6-7-8-9-10
Overall quality of life	As good as it can be = 0; As bad as it can be = 10	0-1-2-3-4-5-6-7-8-9-10

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Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS; MPN 10)		
Rate fatigue (weariness, tiredness) that describes your worst level of fatigue **during the past 24 hours**	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Circle the one number that describes, **during the past week**, how much difficulty you had with each of the following symptoms		
Early satiety	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Abdominal discomfort	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Inactivity	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Problems with concentration compared to before Dx	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Numbness tingling hands/feet	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Night sweats	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Itching	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Bone pain – not joint pain or arthritis	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Unintentional weight loss	Absent = 0; Worst imaginable = 10	0-1-2-3-4-5-6-7-8-9-10
Fever	Absent = 0; Daily = 10	0-1-2-3-4-5-6-7-8-9-10

Polycythemia vera:

Low-risk patients
- Age < 60 years
- No history of thrombosis

High-risk patients:
- Age ≥ 60 years
- History of thrombosis

Potential indications for cytoreductive therapy:
- New thrombosis or disease related major bleeding
- Frequent and/or persistent need for phlebotomy, but with poor tolerance for phlebotomy
- Splenomegaly
- Thrombocytosis
- Leukocytosis
- Disease related symptoms (e.g., pruritus, night sweats, fatigue)

Resources:

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

Jakafi. Package Insert. Reference ID 3673218. Revised by manufacturer 12/2014. Accessed 03-23-2015.

Jakafi. Package Insert. Revised by manufacturer 12/2017. Accessed 04-13-2018, 04-27-2019

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NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative neoplasms. Version 2.2018, Sep 7, 2017. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

UpToDate: Management of primary myelofibrosis. Current through Mar, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/management-of-primary-myelofibrosis?search=myelofibrosis&source=search_result&selectedTitle=2~123&usage_type=default&display_rank=2

UpToDate: Clinical manifestations and diagnosis of myelofibrosis. Current through Mar, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-manifestations-and-diagnosis-of-primary-myelofibrosis?search=myelofibrosis&source=search_result&selectedTitle=1~123&usage_type=default&display_rank=1

UpToDate: Prognosis and treatment of polycythemia vera. Current through Mar, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/prognosis-and-treatment-of-polycythemia-vera?search=Polycythemia%20vera&source=search_result&selectedTitle=2~123&usage_type=default&display_rank=2

UpToDate: Clinical manifestations and diagnosis of polycythemia vera. Current through Mar, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-manifestations-and-diagnosis-of-polycythemia-vera?search=Polycythemia%20vera&source=search_result&selectedTitle=1~123&usage_type=default&display_rank=1

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.