BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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VONJO™ (pacritinib)

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.**

VONJO™ (pacritinib)

Criteria:

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

1. Prescriber is a physician specializing in the patient's diagnosis 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:
   a. Intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50 x 10^9/L

   b. 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:
   a. Platelet count
   b. Eastern Cooperative Oncology Group (ECOG) performance score 0-2

5. Individual does **NOT** have ANY of the following:
   a. Prolonged QT interval (greater than 480msec)
   b. Unresolved active infection
   c. Significant renal impairment (eGFR <30ml/min)
   d. Moderate (Child-Pugh B) or severe hepatic impairment (Child-Pugh C)

6. There are **NO** significant interacting drugs such as CYP3A4 inhibitors, moderate CYP3A4 inducers, and sensitive substrates of P-gp, BCRP, or OCT1 (See Definitions Section)

7. There are **NO** FDA-label contraindications, such as:
   a. Concomitant use of strong CYP3A4 inhibitors or inducers (See Definitions Section)

8. Will **NOT** be used with other Kinase Inhibitors or other Janus Associated Kinase Inhibitors (such as Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadactinib), Jakafi (ruxolitinib) or Inrebic (fedratinib), etc.)

Initial approval duration: 6 months

VONJO™ (pacritinib)

- **Criteria for continuation of coverage (renewal request):** Vonjo (pacritinib) 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 the patient's diagnosis or is in consultation with an Oncologist or Hematologist

  2. Individual's condition has responded while on therapy, defined as **TWO** of the following:
     a. No evidence of disease progression
     b. At least a 35% reduction in spleen volume (measured by MRI or CT)
     c. At least a 50% decrease in total symptoms (tiredness, early satiety, abdominal discomfort, night sweats, itching, bone pain, and pain under ribs on left side).

  3. Individual has been adherent with the medication

  4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
     a. Contraindications as listed in the criteria for initial therapy section
     b. Significant adverse effect such as:
        i. Prolonged QT interval (greater than 500msec)
        ii. Active serious infection
        iii. Hemorrhage
        iv. Major adverse cardiac event
        v. Thrombosis

  5. There are **NO** significant interacting drugs such as CYP3A4 inhibitors, moderate CYP3A4 inducers, and sensitive substrates of P-gp, BCRP, or OCT1 (See Definitions Section)

  6. Will **NOT** be used with other Kinase Inhibitors or other Janus Associated Kinase Inhibitors (such as Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadactinib), Jakafi (ruxolitinib) or Inrebic (fedratinib), etc.)

  Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

VONJO™ (pacritinib)

Description:

Vonjo (pacritinib) is indicated for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia myelofibrosis (MF) with a platelet count below 50 × 10 /L. This indication is approved under accelerated approval based on spleen volume reduction. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Pacritinib is an oral kinase inhibitor with activity against wild type Janus associated kinase 2 (JAK2), mutant JAK2, and FMS-like tyrosine kinase 3 (FLT3), which contribute to signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. MF is often associated with dysregulated JAK2 signaling. Pacritinib has higher inhibitory activity for JAK2 compared to JAK3 and TYK2. At clinically relevant concentrations, pacritinib does not inhibit JAK1.

Primary myelofibrosis (PMF) is a myeloproliferative neoplasm associated with bone marrow fibrosis, cytopenias, constitutional symptoms, hepatosplenomegaly, and/or extramedullary hematopoiesis. Myelofibrosis that arises after a previous diagnosis of polycythemia vera (PV) or essential thrombocytopenia (ET) is referred to as secondary myelofibrosis. The treatment for secondary MF is the same as primary MF.

Myelofibrosis is stratified by risk through various risk modeling systems. In higher risk MF, allogeneic hematopoietic cell transplantation can offer the possibility of cure and prolong survival for those that are eligible. For those that are not candidates, clinical trials or oral therapy may be an option including ruxolitinib, fedratinib pacritinib or hydroxyurea.

Pacritinib was studied intermediate and high-risk primary or secondary MF in individuals with splenomegaly and a baseline platelet count less than 100 x 10^9/L. However, the FDA indication is for those with baseline platelets less than 50 x 10^9/L due to the reported outcome found in this subset of individuals. Individuals treated with pacritinib had a ≥ 35% decrease in spleen volume in 29% of patients compare to 3% in the best available therapy treatment group. Pacritinib has not been studied to determine clinical benefit such as progression free survival or overall survival in MF.

Definitions:

Myelofibrosis:
The 3 most common risk stratification systems in MF are the International Prognostic Scoring System (IPSS), DIPSS, and DIPSS-Plus. They are studied and validated in primary MF. More recently, the novel Myelofibrosis Secondary to PV and ET-Prognostic Model (MYSEC)-PM has been validated to stratify post-PV and post-ET MF into four risk groups.

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. Other risk stratification models incorporate cytogenetic information and mutational status, but further validation is needed before they can be widely adopted.

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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		

Dynamic International Prognostic System Plus (DIPSS-Plus):

Prognostic Variable	Points
DIPSS low risk	0
DIPSS Intermediate-1	1

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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	

Myelofibrosis Secondary to PV and ET-Prognostic Model (MYSEC-PM):

Prognostic Variable	Points
Age at diagnosis	0.15 per patient's year of age
Hemoglobin < 11g/dl	2
Circulating blasts ≥3%	2
Absence of *CALR* type 1 mutation	2
Constitutional symptoms	1
Transfusion need	1
Risk Group	Points
Low	<11
Intermediate-1	≥11
Intermediate-2	≥14 and <16
High	≥16

VONJO™ (pacritinib)

Potential Drug Interactions:

Enzyme or Transporter Mechanism	Potential Interaction with Vonjo
Moderate CYP3A4 Inhibitor (avoid combination or adjust dose)	aprepitant, ciprofloxacin, conivaptan, crizotinib, cyclosporine, diltiazem, dronedarone, erythromycin, fluconazole, fluvoxamine, imatinib, verapamil
Strong CYP3A4 Inhibitor (Contraindication)	boceprevir, cobicistat, grapefruit juice, itraconazole, ketoconazole, posaconazole, ritonavir, telaprevir, telithromycin, voriconazole
Moderate CYP3A4 Inducer (avoid combination or adjust dose)	bosentan, efavirenz, etravirine, phenobarbital, primidone
Strong CYP3A4 Inducer (Contraindication)	apalutamide, carbamazepine, enzalutamide, mitotane, phenytoin, rifampin, St. John's wort
P-glycoprotein substrate (avoid combination, adjust dose or monitor)	digoxin, quinidine
BCRP substrate (avoid combination, adjust dose or monitor)	dantrolene, prazosin, sulfasalazine
OCT1 substrate (avoid combination, adjust dose or monitor)	cimetidine, imatinib

Resources:

Ayalew T. Prognosis of primary myelofibrosis. In: UpToDate, Larson RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated March 15, 2021. Accessed May 16, 2022.

Ayalew T. Clinical manifestations and diagnosis of primary myelofibrosis. In: UpToDate, Larson RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated August 13, 2020. Accessed May 16, 2022.

Ayalew T. Management of primary myelofibrosis. In: UpToDate, Larson RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated December 6, 2021. Accessed May 16, 2022.

Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. March 10, 2020. Accessed May 17, 2022. https://www.fda.gov/drugs/drug-interactions-labeling/drug-development-and-drug-interactions-table-substrates-inhibitors-and-inducers

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Myeloproliferative Neoplasms Version 2.2022 – Updated April 13, 2022. Available at https://www.nccn.org. Accessed May 16, 2022.

Vonjo prescribing information, revised by CTI BioPharma Corp. 02/22. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 16, 2022.

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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.