PHARMACY COVERAGE GUIDELINE

VONJO™ (pacritinib)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Vonjo (pacritinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** 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. Individual has 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. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. Platelet count
   b. Eastern Cooperative Oncology Group (ECOG) performance score 0-2

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

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

7. 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)

8. Individual is **NOT** on FDA-label contraindication drugs (such as concomitant use of strong CYP3A4 inhibitors or inducers) (see Definitions section)

9. Agent will **NOT** be used with other Kinase Inhibitors or other Janus Associated Kinase Inhibitors (such as Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Jakafi (ruxolitinib) or Inrebic (fedratinib), etc.)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Vonjo (pacritinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

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 with response 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. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    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

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. Agent will **NOT** be used with other Kinase Inhibitors or other Janus Associated Kinase Inhibitors (such as Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), 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**

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:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

NCCN recommendation definitions:
Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

The Child-Pugh classification system:
The Child-Pugh classification is a scoring system used to determine the prognosis of individuals with cirrhosis. Scoring is based upon several factors: albumin, ascites, total bilirubin, prothrombin time, and encephalopathy, as follows:

	Score: 1 point	Score: 2 points	Score: 3 points
Serum Albumin (g/dL)	> 3.5	3.0 - 3.5	< 3.0
Serum Bilirubin (mg/dL)	< 2.0	2.0 - 3.0	> 3.0
Prothrombin time (seconds)	1 - 4	4 - 6	> 6
Ascites	none	moderate	severe
Encephalopathy	none	mild	severe

The three classes and their scores are:
- **Class A** is score 5 – 6: Well compensated
- **Class B** is score 7 – 9: Significant functional compromise
- **Class C** is score > 9: Decompensated disease

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.

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

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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
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

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:

Vonjo prescribing information, revised by CTI BioPharma Corp. 11/2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 21, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Myeloproliferative Neoplasms Version 1.2025 – Updated February 21, 2025. Available at https://www.nccn.org. Accessed April 20, 2025.

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.