09-J4000-24

Original Effective Date: 07/01/22

Reviewed: 07/12/23

Revised: 08/15/23

Subject: Pacritinib (Vonjo) Capsule

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Myelofibrosis, a myeloproliferative neoplasm, can present as a primary disease or can evolve from polycythemia vera or essential thrombocytopenia. It is characterized by marrow fibrosis, progressive anemia, and extramedullary hematopoiesis and manifests primarily as splenomegaly. Myelofibrosis debilitating symptoms (e.g., fatigue, weakness, abdominal pain, cachexia, weight loss, pruritus, night sweats, and bone pain) are thought to be the combined effects of massive splenomegaly and elevated levels of proinflammatory cytokines. Traditional therapeutic options, including splenectomy, have demonstrated only limited benefit and although allogeneic stem-cell transplant may cure myelofibrosis, few individuals are eligible for this treatment. It is hypothesized that the pathogenesis of myelofibrosis is related to direct or indirect activation of the intracellular Janus kinase (JAK) signal transducer and activator transcription (STAT) pathway. Additionally, proinflammatory cytokines that play an important role in myelofibrosis signal through JAK 1 (JAK1) AND JAK2.

Pacritinib (Vonjo™) is a kinase inhibitor with activity against Janus associated kinase 2 (JAK2) and other kinases which can be irregular in myelofibrosis. This impacts the signaling cytokines and growth factors for hematopoiesis and immune function in myelofibrosis. The FDA-approved pacritinib for the treatment of adults with 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. This indication is approved under accelerated approval based on spleen volume reduction. Continued approval for this indication is contingent upon verification and description of clinical benefit in a confirmatory trial.

In a randomized trial in 207 patients with intermediate or high-risk primary or secondary (post-polycythmia vera or post-essential thrombocythemia) MF with splenomegaly and a platelet count less than or equal to 100 x 10^9/L, pacritinib was compared to the best available therapy (BAT). BAT consisted of no treatment as a “watch and wait” approach or any treatment for MF used intermittently, in combination or sequentially (ruxolitinib, hydroxyurea, glucocorticoids, erythropoietic agents,

immunomodulatory agents, mercaptopurine, danazol, interferons, cytarabine, or melphalan). The most common BAT treatment in patients with platelets less than 50 x 10^9/L were ruxolitinib (39%), watchful waiting (32%), and hydroxyurea (26%). The efficacy was established in patients with a platelet count of less than 50 x 10^9/L (45% of patients). The efficacy endpoint evaluated the proportion of patients with a greater than or equal to 35% reduction in spleen volume reduction from baseline to week 24. In the pacritinib group 29% (9/31) of patients met the endpoint as compared to 3.1% (n=1/32) in the BAT group. The most common adverse reactions included diarrhea, thrombocytopenia, nausea, anemia, and peripheral edema.

National Comprehensive Cancer Network (NCCN) Guidelines recommend pacritinib for the treatment of myelofibrosis.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of pacritinib (Vonjo™) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Primary myelofibrosis (MF), post-polycythemia vera myelofibrosis (Post-PV-MF), or post-essential thrombocythemia myelofibrosis (Post-ET-MF) and **ALL** of the following:
    A. Member meets **ONE** of the following:
        i. When the member had an inadequate response, intolerance to, or is not a candidate for ruxolitinib (Jakafi) and pacritinib is used for improvement of clinical symptoms for **ONE** of the following:
            a. Symptomatic lower-risk MF and platelets are less than 50,000
            b. Higher-risk MF when the member is not a transplant candidate
            c. MF accelerated phase
            d. MF blast phase/AML
            e. MF-associated anemia
            f. Higher-risk MF when used for a transplant candidate near the start of conditioning therapy
        ii. Member has intermediate or high-risk MF and platelets are less than 50,000
    B. Member is not using pacritinib in combination with a strong CYP3A4 inhibitor or CYP3A4 inducer
    C. Dose does not exceed 200 mg twice per day using the fewest number of capsules per day
2. Other FDA-approved or NCCN supported diagnosis (not previously listed above)

A. **ONE** of the following is met:

   i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)

   ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation

B. Dose does not exceed the maximum FDA-approved dose

Approval duration: 180 days

Continuation of pacritinib (Vonjo™) meets the definition of medical necessity for MF, Post-PV-MF, Post-ET-MF, and other FDA-approved or NCCN supported diagnosis when **ALL** of the following criteria are met:

1. The member has been previously approved by Florida Blue or another health plan in the past 2 years for MF, Post-PV-MF, Post-ET-MF, and other FDA-approved or NCCN supported diagnosis, OR the member has previously met all indication-specific criteria for coverage
2. The member has experienced a beneficial response to therapy (e.g., reduction in spleen size, improvement in clinical symptoms)
3. The dose does not exceed 200 mg twice per day using the fewest number of capsules per day

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Treatment of adults with 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: 200 mg oral twice daily
- May be taken with or without food

Dose Adjustments

- See prescribing information for dose modifications for diarrhea, thrombocytopenia, hemorrhage, and prolonged QT interval.

Drug Availability

- 100 mg capsules

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Concomitant use of strong CYP3A4 inhibitors or inducers

Precautions/Warnings

- Hemorrhage: Avoid use in patients with active bleeding and hold prior to planned surgical procedures. May require dose interruption, dose reduction or permanent discontinuation depending on severity.
- Diarrhea: Manage significant diarrhea with anti-diarrheals, dose reduction, or dose interruption.
- Thrombocytopenia: Manage by dose reduction or interruption.
- Prolonged QT Interval: Avoid use in patients with baseline QTc >480 msec. Interrupt and reduce dosage in patients who have a QTcF >500 msec. Correct hypokalemia prior to and during administration.
- Major Adverse Cardiac Events (MACE): Risk may be increased in current/past smokers and patients with other cardiovascular risk factors. Monitor for signs, evaluate and treat promptly.
- Thrombosis: Including deep venous thrombosis, pulmonary embolism, and arterial thrombosis may occur. Monitor for signs, evaluate and treat promptly.
- Secondary Malignancies: Lymphoma and other malignancies may occur. Past/current smokers may be at increased risk.
- Risk of infection: Delay starting until active serious infections have resolved. Observe for signs and symptoms of infection and manage promptly.

BILLING/CODING INFORMATION:

HCPCS Coding

C9399	Unclassified drugs or biologicals
J8999	Prescription drug, oral, chemotherapeutic, not otherwise specified

ICD-10 Diagnosis Codes That Support Medical Necessity

C94.40 – C94.42	Acute panmyelosis with myelofibrosis
C94.6	Myelodysplastic disease, not classified
D47.1	Chronic myeloproliferative disease
D47.4	Osteomyelofibrosis
D75.81	Myelofibrosis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

Dynamic International Prognostic Scoring System (DIPSS) for myelofibrosis: mechanism for assessing a member's prognosis at the time of diagnosis; assigns a value for each prognostic variable (Table 1). A score of 0 is indicative of low risk, 1 or 2 is indicative of intermediate-1 risk, 3 or 4 intermediate-2 risk, and 5 or more points is indicative of high risk. The higher risk group corresponds to a lower median overall survival as compared to those at lower risk.

Table 1

Prognostic variable	Points
Age greater than 65	1
WBC greater than 25,000	1
Hemoglobin less than 10 g/dL	2
Peripheral blood blasts 1% or greater	1
Constitutional symptoms	1

Essential thrombocythemia: an increased number of thrombocytes (platelets) in the blood, without a known cause. Also called essential thrombocytosis.

Myelofibrosis: myeloproliferative disease in which the proliferation of an abnormal type of bone marrow stem cell results in fibrosis, or the replacement of the marrow with collagenous connective tissue fibers.

Polycythemia vera: A disease in which there are too many red blood cells in the bone marrow and blood, causing the blood to thicken. The number of white blood cells and platelets may also increase. The extra blood cells may collect in the spleen and cause it to become enlarged. They may also cause bleeding problems and make clots form in blood vessels.

Primary myelofibrosis: a progressive, chronic disease in which the bone marrow is replaced by fibrous tissue and blood is made in organs such as the liver and the spleen, instead of the bone marrow. This disease is marked by an enlarged spleen and progressive anemia. Also called agnogenic myeloid metaplasia, chronic idiopathic myelofibrosis, idiopathic myelofibrosis, and myelosclerosis with myeloid metaplasia.

Splenomegaly: enlarged spleen.

RELATED GUIDELINES:

Fedratinib (Inrebic) Tablets, 09-J3000-49

OTHER:

None

REFERENCES:

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4. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Myeloproliferative Neoplasms, v. 1.2023 [cited 2023 Jun 30]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
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6. Vonjo (pacritinib) capsules. 2022 [cited 2022 Apr 24]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 07/12/23.

GUIDELINE UPDATE INFORMATION:

07/01/22	New Medical Coverage Guideline.
08/15/23	Review and revision to guideline; consisting of updating the references.