pacritinib (Vonjo™)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO256

Description

Pacritinib (Vonjo) is a Janus associated kinase 2 (JAK2) inhibitor.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
pacritinib (Vonjo)	Intermediate- or high-risk myelofibrosis with severe thrombocytopenia (platelet count below 50 x 10^9/L)	100 mg capsules	120 capsules/30 days

Initial Evaluation

I. **Pacritinib (Vonjo)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a hematologist or oncologist; **AND**
   C. A diagnosis of **intermediate- or high-risk myelofibrosis** when the following are met:
      1. Splenomegaly is present and spleen volume is documented; **AND**
      2. Member has severe thrombocytopenia (defined as platelet counted below 50 x 10^9/L); **AND**
      3. Documentation of disease-related symptoms (e.g., fatigue, shortness of breath, bruising, bleeding, fever, bone pain)

II. Pacritinib (Vonjo) is considered <u>not medically necessary</u> when criteria above are not met and/or when used for:
   A. Myelofibrosis without severe thrombocytopenia (i.e., platelet count is ≥ 50 x 10^9/L)

III. Pacritinib (Vonjo) is considered <u>investigational</u> when used for all other conditions, including but <u>not limited to</u>:
   A. Low risk myelofibrosis
   B. Polycythemia vera
   C. Graft versus host disease

D. Lymphoproliferative neoplasms
E. Solid tumors (e.g., prostate, colorectal, lung)
F. Acute myeloid leukemia (AML)
G. Chronic lymphocytic leukemia, small lymphocytic lymphoma
H. COVID-19

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. A diagnosis of intermediate- or high-risk myelofibrosis (has not transformed to AML); **AND**
IV. Member has exhibited improvement in or stability of spleen volume; **AND**
V. Member has exhibited improvement in or stability of disease-related symptoms (e.g., fatigue, shortness of breath, bruising, bleeding, fever, bone pain).

Supporting Evidence

I. Myelofibrosis (MF) is a cancer of the bone marrow. Symptoms are non-specific (e.g., fatigue, shortness of breath, bleeding) and splenomegaly is common. Over time MF may progress to acute myeloid leukemia (AML). There are five risk levels of disease that correlate with prognosis, and treatment is based on risk. When patients are not eligible for allogeneic stem cell transplant, symptom targeted therapy may be used in those with intermediate or higher risk MF. Symptomatic therapies include hydroxyurea and JAK inhibitors: ruxolitinib (Jakafi), fedratinib (Inrebic), pacritinib (Vonjo). JAK inhibitors have only been sufficiently evaluated in patients with at least intermediate-risk MF and have unknown clinical value for lower risk disease. JAK inhibitors do not reverse fibrosis or prolong survival but may reduce spleen size and improve disease-related symptoms. In absence of splenomegaly and symptoms, these medications have unknown application. Given the specialized diagnosis, treatment, and monitoring, prescribing by or in consultation with a specialist is required.
II. Ruxolitinib (Jakafi) and fedratinib (Inrebic) are approved for MF in those with a platelet count ≥ 50 x 10^9/L. These medications are known to cause thrombocytopenia and are recommended to be discontinued if the platelet count drops below 50 x 10^9/L. Pacritinib (Vonjo), has a unique approval, and was approved under the accelerated approval pathway based on spleen volume reduction (SVR) when platelet count is under 50 x 10^9/L (severe thrombocytopenia). Pacritinib

(Vonjo) has been evaluated in adults; use in pediatrics or adolescents has unknown value or consequences. Outside of a clinical trial setting, therapy should only be utilized in adults.

III. Pacritinib (Vonjo) was evaluated in two Phase 3 trials, PERSIST1 and PERSIST2. The accelerated approval was based on results from PERSIST2, a randomized, open-label trial vs. best available therapy (BAT) (included 39% of patients on ruxolitinib [Jakafi]) for 24 weeks (n=311). Patients had platelets < 100 x 10^9/L (45% had < 50 x 10^9/L). Regimens of 400 mg once daily and 200 mg twice daily were evaluated. Outcomes included spleen volume reduction (SVR) of ≥ 35%, and daily symptom score reduction of at least 50% via the MPN-SAF TSS tool. The trial indicated a statistically significant improvement in SVR for both treatment arms compared to BAT, and the 200 mg twice daily arm showed an improvement in daily symptoms scores over BAT. Subgroup analyses for the specific FDA-approved population (i.e., platelet count <50 x 10^9/L) were not statistically evaluated. PERSIST1 was a randomized, open-label trial evaluating 400 mg once daily vs. BAT for 24 weeks (n=327). For pacritinib (Vonjo), 148 patients (67%) had platelets > 100 x 10^9/L, 37 (17%) had < 100x10^9/L, and 35 (16%) had < 50 x10^9/L. There was statistical significance over BAT for SVR ≥ 35%, and reduction in TSS ≥ 50%.

IV. There is positive evidence to indicate clinical value of pacritinib (Vonjo) in patients with MF with severe thrombocytopenia; however, given lack of clinical trials focused solely on this specific population, as well as other trials with various doses and conflicting results, the FDA has granted accelerated approval based on SVR, and continued approval is contingent upon verification of clinical benefit in the PACIFICA3 Phase 3 clinical trial. Results are due in 2025. Of note, this therapy is only FDA approved given the already seen impact on SVR and a condition of the accelerated approval, is that the manufacturer confirms that SVR and this therapy leads to a clinical benefit. Until confidence in the clinical benefit is determined, therapy is reserved for those that have reduction in spleen volume and also experience symptom improvement.

V. Given the limited approval of pacritinib (Vonjo), coverage consideration is limited to MF with severe thrombocytopenia and disease-related symptoms. There is unknown clinical value in those without symptoms. Coverage consideration is also limited to those with severe thrombocytopenia as other treatment options with full FDA-approval, stronger evidence for efficacy, and more developed safety profiles are available; ruxolitinib (Jakafi) and fedratinib (Inrebic). Pacritinib (Vonjo) has some evidence for efficacy in patients that have platelet counts above 50 x 10^9/L and could be considered as a treatment option for patients with trial and failure or contraindication to ruxolitinib (Jakafi) and fedratinib (Inrebic); however, when possible, therapy should be reserved for the FDA-approved population as the efficacy and safety profile of pacritinib (Vonjo) continues to develop. In 2016 the FDA put a hold on the trials due to noted deaths from hemorrhage, cardiac failure and arrest. The hold was later lifted in 2017 after evaluation of all clinical trial evidence; however, the safety profile of pacritinib (Vonjo) is not fully understood. One unique black box warning for fedratinib (Inrebic) is encephalopathy, and in those that experience signs/symptoms or are at an increased risk may not be appropriate for

fedratinib (Inrebic) use. This has not yet been noted for pacritinib (Vonjo) or ruxolitinib (Jakafi); however, comparative safety and efficacy data for these therapies are not available.

VI. Pacritinib (Vonjo) outcomes of SVR and improvement in daily symptoms were evaluated by week 24; a six-month initial approval is granted to allow sufficient time for and evaluation of symptom response. There is lack of strong evidence to indicate treatment response will occur if not reached by this time. Pacritinib (Vonjo) has shown clinical value in reducing spleen size and improving disease-related symptoms; thus, continuation of therapy is reasonable when both of these are stable or have improved. Reduction in spleen size without improvement in disease-related symptoms has unknown clinical value at this time. Of note, spleen volume or size may be assessed or examined by physical examination (i.e., palpation); however, if the spleen is not palpable, imaging is appropriate for determining spleen size or volume. This is done when there is a need to determine the spleen size or changes when physical examination is insufficient (e.g., for determining response to therapy).

Investigational or Not Medically Necessary Uses

I. Pacritinib (Vonjo) is considered not medically necessary in patients with MF with platelet counts greater than 50 x 10^9/L when patients are eligible for the two JAK inhibitors that are FDA-approved in that population; ruxolitinib (Jakafi) and fedratinib (Inrebic). Ruxolitinib (Jakafi) and fedratinib (Inrebic) have established safety and efficacy profiles for patients with platelets greater than 50 x 10^9/L. In the event of treatment failure or contraindication to these two JAK inhibitors, pacritinib (Vonjo) could be considered a fair treatment option; however, when patients do not have failure or contraindication to ruxolitinib (Jakafi) and fedratinib (Inrebic), use of pacritinib (Vonjo) should be reserved for patients with severe thrombocytopenia.

II. Pacritinib (Vonjo) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
    A. Low risk myelofibrosis
    B. Polycythemia vera
    C. Graft vs. host disease
    D. Lymphoproliferative neoplasms
    E. Solid tumors (e.g., prostate, colorectal, lung)
    F. Acute myeloid leukemia (AML)
    G. Chronic lymphocytic leukemia, small lymphocytic lymphoma
    H. COVID-19

References

1. Mesa RA, Vannucchi AM, Mead A, et al. Pacritinib versus best available therapy for the treatment of myelofibrosis irrespective of baseline cytopenias (PERSIST-1): an international, randomised, phase 3 trial. *Lancet Haematol*. 2017;4(5):e225-e236.
2. Mascarenhas J, Hoffman R, Talpaz M, et at. Pacritinib vs best available therapy, including ruxolitinib, in patients with myelofibrosis. A randomized clinical trial. *JAMA Oncol*. 2018;4(5):652-659.
3. Vonjo [Prescribing Information]. CTI Biopharma Corp. Seattle, WA. February 2022.
4. National Comprehensive Cancer Network. NCCN Guidelines: Myeloproliferative Neoplasms. V1.2022, updated 02/28/2022.
5. Jakafi [Prescribing Information]. Incyte Corporation. Wilmington, DE. September 2021.
6. Inrebic [Prescribing Information]. Celgene Corporation. Summit, NJ. August 2019.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
ruxolitinib (Jakafi, Opzelura) Policy	Intermediate or high-risk myelofibrosis
fedratinib (Inrebic) Policy	Myelofibrosis

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	05/2022