Pharmacy Policy Bulletin: J-0899 JAK Inhibitors – Commercial and Healthcare Reform	
Number: J-0899	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes with Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0899-012	**Original Date:** 06/04/2003
Effective Date: 02/14/2025	**Review Date:** 01/29/2025

Drugs Product(s):	• Jakafi (ruxolitinib) • Inrebic (fedratinib) • Vonjo (pacritinib) • Ojjaara (momelotinib)

FDA-Approved Indication(s):	• Jakafi (ruxolitinib)
	  ○ Treatment of intermediate or high-risk myelofibrosis, including primary myelofibrosis (MF), post-polycythemia vera (PV) myelofibrosis and post-essential thrombocythemia (ET) MF in adults.
	  ○ Treatment of PV in adults who have had an inadequate response to or are intolerant of hydroxyurea.
	  ○ Treatment of steroid-refractory acute graft-versus-host disease (aGVHD) in adult and pediatric patients 12 years and older.
	  ○ Treatment of chronic graft-versus-host disease (cGVHD) after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older.
	• Inrebic (fedratinib)
	  ○ Treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-PV or post-ET) MF.
	• Vonjo (pacritinib)
	  ○ Treatment of adults with intermediate or high-risk primary or secondary (post-PV or post-ET) MF with a platelet count below 50 x 10^9/L.
	• Ojjaara (momelotinib)
	  ○ Treatment of intermediate or high-risk MF, including primary MF or secondary MF (post-PV and post-ET), in adults with anemia.

Background:	• Jakafi and Ojjaara inhibit dysregulated Janus Associated Kinase (JAK) 1 and JAK2 signaling. JAK1 and JAK2 recruit signal transducers and activators of transcription (STATs) to cytokine receptors leading to modulation of gene expression. Ojjaara also has a metabolite, M21, that inhibits the activin A receptor type 1 (ACVR1). This reduces liver hepcidin expression and increases iron availability, resulting in increased blood cell production.

	• Vonjo and Inrebic selectively inhibit dysregulated JAK2, but not JAK1. Vonjo also inhibits FMS-like tyrosine kinase 3 (FLT3), which contributes to hematopoiesis.
	• MF is a myeloproliferative neoplasm characterized by dysfunctional hematopoiesis and fibrosis in the bone marrow. This leads to spleen enlargement, anemia, cytopenia, and an increased production of abnormal white blood cells. MF affects approximately 21,000 individuals in the United States; over half are anemic and one-third are cytopenic. Anemia and cytopenia in MF are associated with an increased risk of mortality.
	• For management of symptomatic, lower-risk MF, the National Comprehensive Cancer Network (NCCN) guidelines recommend participation in a clinical trial, ruxolitinib, peginterferon alfa-2a, hydroxyurea (if cytoreduction would be symptomatically beneficial), pacritinib (if platelets < 50 x 10^9/L), or momelotinib (category 2B). For higher-risk MF, if the patient is not a transplant candidate/transplant is not currently feasible, recommendations differ based on platelet counts. For patients with platelets < 50 x 10^9/L, participation in a clinical trial, pacritinib (category 1), or momelotinib (category 2B) is recommended. For patients with platelets ≥ 50 x 10^9/L and presence of symptomatic splenomegaly and/or constitutional symptoms, participation in a clinical trial, ruxolitinib (category 1), fedratinib (category 1), momelotinib, or pacritinib (category 2B) is recommended. All recommendations are category 2A, unless stated otherwise.
	• For MF-associated anemia and presence of symptomatic splenomegaly and/or constitutional symptoms, NCCN recommendations include: participation in a clinical trial, ruxolitinib combination (for example, add luspatercept-aamt, add danazol [category 2B]), momelotinib, or pacritnib. For anemia and no symptomatic splenomegaly and/or constitutional symptoms, participation in a clinical trial, luspatercept-aamt, erythropoiesis-stimulating agents (ESAs) (if serum erythropoietin < 500 mU/mL), danazol, momelotinib (category 2B), pacritinib (category 2B), or lenalidomide + prednisone for del(5q) (category 2B) is recommended. All recommendations are category 2A, unless stated otherwise.
	• PV is a rare, chronic myeloproliferative neoplasm caused by somatic mutations in the *JAK2* gene and overproduction of JAK proteins. PV causes overproduction of red blood cells in the bone marrow, leading to thrombosis, bleeding, myelofibrosis, and acute leukemia.
	• GVHD is an immunologic complication of allogenic stem cell transplant in which transplanted stem cells attack healthy hosts cells, resulting in systemic complications, including fibrosis, and an increase in morbidity and mortality. GVHD generally occurs after the first 100 days post-transplant.
	• GVHD can be classified as acute or chronic. When studied in clinical trials, aGVHD was defined as GVHD which progressed after 3 days or had not improved after 7 days of primary treatment with methylprednisolone ≥ 2 mg/kg/day (or equivalent); development of GVHD in another organ after receiving ≥ 1 mg/kg/day methylprednisolone for skin or skin plus upper gastrointestinal GVHD; or inability to tolerate a corticosteroid taper.
	• For the treatment of cGVHD, clinical trials utilized NIH Consensus Criteria to define moderate cGVHD as at least one organ (not lung) with a score of 2, 3 or more organs involved with a score of 1 in each organ, or lung score of 1; or severe cGHVD as at least 1 organ with a score of 3, or lung score of 2 or 3. In this study, patients were steroid-refractory defined as:
	  ○ A lack of response or disease progression after administration of minimum prednisone 1 mg/kg/day for at least 1 week, OR
	  ○ Disease persistence without improvement despite continued treatment with prednisone at > 0.5 mg/kg/day or 1 mg/kg/every other day for at least 4 weeks, OR
	  ○ Increase to prednisolone dose to > 0.25 mg/kg/day after 2 unsuccessful attempts to taper the dose

	• Accepted risk stratification tools for MF include International Prognostic Scoring System (IPSS), Dynamic International Prognostic Scoring System (DIPSS, or DIPSS-PLUS), and Mutation-Enhanced Prognostic System for Transplant-Age Patients (MIPSS70).
	• Unlike Inrebic, Jakafi does not have a black box warning for encephalopathy. Additionally, NCCN guidelines include fedratinib as an option in intermediate-risk 2 or high-risk MF patients who are not a transplant candidate and platelets ≥ 50 x 10^9/L.
	• Prescribing Considerations:
	  ○ Jakafi
	  ▪ Discontinue Jakafi if there is no spleen size reduction or symptom improvement after 6 months of therapy.
	  ▪ The starting dose of Jakafi is based on baseline platelet count.
	  ▪ Interrupt Jakafi treatment for platelet counts less than 50 X 10^9/L or absolute neutrophil count (ANC) less than 0.5 X 10^9/L.
	  ○ Inrebic
	  ▪ Do not start Inrebic in patients with thiamine deficiency. Replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue and initiate parenteral thiamine.
	  ▪ Dose reductions for Inrebic are recommended for patients when the following is experienced during treatment: anemia and thrombocytopenia, gastrointestinal toxicities, severe renal impairment, hepatic toxicities, amylase and lipase elevation.
	  ○ Vonjo
	  ▪ Dose modifications are made for adverse reactions, thrombocytopenia, hemorrhage, and prolonged QT interval.
	  ○ Ojjaara
	  ▪ According to NCCN guidelines, Ojjaara is preferred over other JAK inhibitors for patients with anemia. Other JAK inhibitors may increase the risk of anemia.
	  ▪ Dose may be adjusted between 100 mg, 150 mg, and 200 mg if thrombocytopenia, neutropenia, hepatotoxicity, or other adverse reactions occur.

Approval Criteria

I. Initial Authorization

A. Jakafi

1. Polycythemia vera (ICD-10: D45)
When a benefit, coverage of Jakafi may be approved when all of the following criteria are met **(a., b., and c.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of polycythemia vera.
c. The member has had a therapeutic failure, contraindication, or intolerance to hydroxyurea.

2. Myelofibrosis (ICD-10: D75.81)
When a benefit, coverage of Jakafi may be approved when all of the following criteria are met **(a., b., and c.)**:
a. The member is 18 years of age or older.

b. The member has a diagnosis of myelofibrosis that is intermediate or high-risk.
c. If the member is a new start to therapy, baseline platelet count is ≥ 50 x 10^9/L.

3. Acute Graft-Versus-Host Disease (ICD-10: D89.813)
When a benefit, coverage of Jakafi may be approved when all of the following criteria are met **(a., b., and c.)**:
a. The member is 12 years of age or older.
b. The member has a diagnosis of steroid-refractory acute graft-versus-host disease.
c. The member has experienced therapeutic failure, contraindication, or intolerance to one (1) systemic corticosteroid.

4. Chronic Graft-Versus-Host Disease (ICD-10: D89.811)
When a benefit, coverage of Jakafi may be approved when all of the following criteria are met **(a., b., and c.):**
a. The member is 12 years of age or older.
b. The member has a diagnosis of chronic graft-versus-host disease.
c. The member has experienced therapeutic failure or intolerance to at least one (1) systemic therapy.

B. Inrebic

1. Myelofibrosis (ICD-10: D75.81)
When a benefit, coverage of Inrebic may be approved when all of the following criteria are met **(a., b., and c.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of myelofibrosis that is intermediate-2 or high-risk.
d. If the member is a new start to therapy, the member meets all of the following criteria **(i. and ii.)**:
i. The member's baseline platelet count is ≥ 50 x 10^9/L.
ii. The member has experienced therapeutic failure, contraindication, or intolerance to plan-preferred product Jakafi.

C. Vonjo

1. Myelofibrosis (ICD-10: D75.81)
When a benefit, coverage of Vonjo may be approved when all of the following criteria are met **(a., b., and c.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of myelofibrosis that is intermediate or high-risk.
c. The member has a platelet count of < 50 x 10^9/L.

D. Ojjaara

1. Myelofibrosis (ICD-10: D75.81)
When a benefit, coverage of Ojjaara may be approved when all of the following criteria are met **(a., b., and c.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of myelofibrosis that is intermediate or high-risk.
c. The prescriber attests that the member is anemic.

II. Reauthorization

A. Jakafi

1. **Polycythemia Vera (ICD-10: D45) or Myelofibrosis (ICD-10: D75.81)**
   When a benefit, reauthorization of Jakafi may be approved when one (1) of the following criteria are met **(a. or b.)**:
   a. The prescriber attests that the member has experienced a reduction in spleen size.
   b. The prescriber attests that the member has experienced improvement in symptoms.

2. **Graft-Versus-Host Disease (ICD-10: D89.813, D89.811)**
   When a benefit, reauthorization of Jakafi may be approved when the following criterion is met **(a.)**:
   a. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(i. or ii.)**:
      i. Disease improvement
      ii. Delayed disease progression

B. Inrebic

1. **Myelofibrosis (ICD-10: D75.81)**
   When a benefit, reauthorization of Inrebic may be approved when one (1) of the following criteria are met **(a. or b.)**:
   a. The prescriber attests that the member has experienced a reduction in spleen size.
   b. The prescriber attests that the member has experienced improvement in symptoms.

C. Vonjo

1. **Myelofibrosis (ICD-10: D75.81)**
   When a benefit, reauthorization of Vonjo may be approved when one (1) of the following criteria are met **(a. or b.)**:
   a. The prescriber attests that the member has experienced a reduction in spleen size.
   b. The prescriber attests that the member has experienced improvement in symptoms.

D. Ojjaara

1. **Myelofibrosis (ICD-10: D75.81)**
   When a benefit, reauthorization of Ojjaara may be approved when one (1) of the following criteria are met **(a. or b.)**:
   a. The prescriber attests that the member has experienced a reduction in spleen size.
   b. The prescriber attests that the member has experienced improvement in symptoms.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drugs addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

For previous versions please see J-699 & J-1200.

References:

1. Jakafi [package insert]. Wilmington, Delaware: Incyte Corporation; January 2023.
2. Inrebic [package insert]. Summit, New Jersey: Celgene Corporation; July 2024.
3. Vonjo [package insert]. Seattle, Washington: CTI BioPharma Corporation; August 2023.
4. Ojjaara [package insert]. Durham, North Carolina: GlaxoSmithKline; September 2023.
5. NCCN Guidelines. Myeloproliferative Neoplasms v.2.2024. National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed October 1, 2024.
6. Jagasia M, Ali H, Schroeder MA, et al. Ruloxitinib in Combination with Corticosteroids for the Treatment of Steroid-Refractory Acute Graft-Vs-Host Disease: Results from the Phase 2 REACH1 Trial. *Biology of Blood and Marrow Transplantation*. March 2019:25(3);S52.
7. Passamonti F, Cervantes F, Vannucchi AM, et al. A dynamic prognostic model to predict survival in primary myelofibrosis: a study by the IWG-MRT (International Working Group for Myeloproliferative Neoplasms Research and Treatment). *Blood*. 2010;115(9):1703-8.
8. Gangat N, Caramazza D, Vaidya R, et al. DIPSS plus: a refined Dynamic International Prognostic Scoring System for primary myelofibrosis that incorporates prognostic information from karyotype, platelet count, and transfusion status. *J Clin Oncol*. 2011;29(4):392-7.
9. National Comprehensive Cancer Network. NCCN Guidelines Version 2.2024 Myeloproliferative Neoplasms. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed January 15, 2025.