ruxolitinib (Jakafi®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO057

Description

Ruxolitinib (Jakafi) is an orally administered Janus associated kinase (JAK) inhibitor. JAK signaling mediates the signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function.

Length of Authorization

- Initial: six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indications	Quantity Limit
ruxolitinib (Jakafi)	5 mg tablets	Intermediate or high-risk myelofibrosis	60 tablets/30 days
	10 mg tablets		60 tablets/30 days
	15 mg tablets	Polycythemia vera	60 tablets/30 days
	20 mg tablets	Acute Graft Versus-Host disease	60 tablets/30 days
	25 mg tablets		60 tablets/30 days

Initial Evaluation

I. Ruxolitinib (Jakafi) may be considered medically necessary when the following criteria below are met:
   A. Medication is prescribed by, or in consultation with, an oncologist or endocrinologist; **AND**
   B. Member does <u>not</u> have an active infection, including clinically important localized infections; **AND**
   C. A diagnosis of one of the following:
      1. **Intermediate- to high-risk myelofibrosis (MF)** which includes: primary MF, post-polycythemia vera MF, or post essential thrombocythemia MF; **AND**
         i. Treatment with hydroxyurea has been ineffective, contraindicated, or not tolerated; **OR**
      2. **Polycythemia vera**; **AND**

i. Treatment with hydroxyurea has been ineffective, contraindicated, or not tolerated; **OR**

3. Acute Graft Versus-Host Disease (GVHD); AND

i. Member is 12 years of age or older; **AND**

ii. Documentation that member has Grades 2 to 4 GVHD; **AND**

iii. Member is steroid refractory

II. Ruxolitinib (Jakafi) is considered investigational when used for all other conditions, including but not limited to:

A. Low risk myelofibrosis

B. Acute leukemia

Renewal Evaluation

I. The member has an absence of unacceptable toxicity from the medication; **AND**

II. A diagnosis of one of the following:

A. **Intermediate- to high-risk myelofibrosis (MF)**; **AND**

1. Documentation of reduction in spleen volume; **AND**
2. Documentation of improvement in symptoms; **OR**

B. **Polycythemia vera**; **AND**

1. Documentation of reduction in spleen volume; **AND**
2. Does not require phlebotomy

C. **Acute Graft Versus-Host Disease (GVHD); AND**

1. Member has responded to therapy with ruxolitinib (Jakafi) (e.g. decreased GVHD symptoms)

Supporting Evidence

I. Length of authorization for initial approval has been extended to six months due to the clinical trial design, efficacy was not evaluated until 24 weeks.

II. Serious bacterial, mycobacterial (including tuberculosis), fungal, or viral infections have occurred. Active serious infections should be resolved prior to treatment initiation. Continual monitoring for infections (including signs/symptoms of active tuberculosis and herpes zoster) should be performed while on treatment ruxolitinib (Jakafi).

III. The FDA approval of ruxolitinib (Jakafi) in the setting of intermediate- to high-risk myelofibrosis was based on the results of two randomized Phase 3 trials. In Study 1, the primary endpoint was the proportion of participants achieving greater than, or equal to, a 35% reduction from baseline

in spleen volume at Week 24; while in Study 2, the primary endpoint was the proportion of participants achieving greater than, or equal to, a 35% reduction from baseline in spleen volume at Week 48. In both studies, a significantly larger proportion of participants in the ruxolitinib (Jakafi) arm (Study 1 = 41.9%, Study 2 = 28.5%) achieved a 35% or greater reduction in spleen volume from baseline compared to placebo (Study 1 = 0.7% and Study 2 = 0%).

- Available therapies for intermediate- to high-risk MF include: hydroxyurea, busulfan, 6-mercaptopurine, anagrelide, thalidomide, lenalidomide, interferon, corticosteroids, androgens, erythropoiesis stimulating agents, or growth factors. Although there are many "available therapies" for intermediate- to high-risk MF, the most robust evidence – and the majority of the patients in the clinical trials – were previously on hydroxyurea.

IV. The FDA approval of ruxolitinib (Jakafi) in the setting of polycythemia vera was based on the result of a randomized, open-label, active-controlled Phase 3 study. The primary endpoint was the proportion of participants at Week 32 achieving hematocrit control (the absence of phlebotomy) and spleen volume reduction. In the ruxolitinib (Jakafi) arm, 60% of the participants met the primary endpoint compared to 19% in the placebo arm.

- The inclusion criteria in this trial was that participants must have had a resistance or intolerance to hydroxyurea.

V. The FDA approval of ruxolitinib (Jakafi) in the setting of acute graft versus host disease (GVHD) was based on the results of an open-label, single-arm, multicenter study in participants with steroid-refractory acute GVHD Grades 2 to 4. The primary efficacy of ruxolitinib (Jakafi) was based on a Day-28 overall response rate (ORR) by the Center for International Blood and Marrow Transplant Research (CIBMTR) criteria, and the duration of response. The ORR was 57.1% with a median duration response of 16 days.

Investigational or Not Medically Necessary Uses

I. Ruxolitinib (Jakafi) is and has been studied in a variety of other conditions; however, there is currently insufficient evidence to support the use of ruxolitinib (Jakafi) outside of the FDA approved indications.

References

1. Jakafi [Prescribing Information]. Wilmington, DE: Incyte Corporation. May 2019.
2. Verstovsek, S, Mesa, RA, Gotlib, J, et al. Efficacy, safety and survival with ruxolitinib in patients with myelofibrosis: results of a median 2-year follow-up of COMFORT-I. Italy, 2013. p. 1865-71.

3. Verstovsek, S, Mesa, RA, Gotlib, J, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. The New England journal of medicine. 2012 Mar 1;366(9):799-807. PMID: 22375971
4. Vannucchi AM, Kiladjian JJ, Griesshammer M, et al. Ruxolitinib versus standard therapy for the treatment of polycythemia vera. N Engl J Med. 2015;372(5):426-435. [PubMed 25629741]
5. Mesa RA, Gotlib J, Gupta V, et al. Effect of ruxolitinib therapy on myelofibrosis-related symptoms and other patient-reported outcomes in COMFORT-I: a randomized, double-blind, placebo-controlled trial. J Clin Oncol. 2013;31(10):1285-1292. [PubMed 23423753]

Policy Implementation/Update:

Date Created	February 2012
Date Effective	February 2012
Last Updated	January 2020
Last Reviewed	05/2012, 07/2012, 12/2012, 12/2014, 07/2019, 01/2020

Action and Summary of Changes	**Date**
Criteria update: added acute graft versus host disease to renewal evaluation section with renewal criterion to assess for response.	01/2020
Transitioned Jakafi criteria into policy. Added newly FDA approved indication of acute graft versus host disease, the route to approval is per label. Remove diagnostic questions for intermediate to high-risk myelofibrosis since provider is a specialist that will be diagnosing members. Remove the following assessment: CYP3A4 inhibitor drug-drug interactions, creatinine clearance and platelet count as the providers will already be assessing for treatment appropriateness. For the diagnosis of polycythemia vera, the requirement of trial and failure of hydroxyurea has been added as that is standard of practice.	07/2019