ruxolitinib (Jakafi®)
EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO057

Description
Ruxolitinib (Jakafi) is an orally administered Janus Associated Kinase (JAK) inhibitor of JAK1 and JAK2.

Length of Authorization
- Initial: Six months
- Renewal: 12 months

Quantity limits

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Dosage Form</th>
<th>Indications</th>
<th>Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>ruxolitinib (Jakafi)</td>
<td>5 mg tablets</td>
<td>Intermediate or high-risk myelofibrosis</td>
<td>60 tablets/30 days</td>
</tr>
<tr>
<td></td>
<td>10 mg tablets</td>
<td>Polycythemia vera</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15 mg tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 mg tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25 mg tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 mg tablets</td>
<td>Acute Graft-Versus-Host Disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 mg tablets</td>
<td>Chronic Graft-Versus-Host disease</td>
<td></td>
</tr>
</tbody>
</table>

*Dose optimization will be required if the prescribed dose is unable to be reached at a quantity of 60/30. Use of two strengths may be necessary to reach target dose. Quantity is subject to 30/30 if multiple tablet strengths are utilized, for a maximum total allowed quantity of 60 ruxolitinib (Jakafi) tablets per 30-day supply.

Initial Evaluation

I. Ruxolitinib (Jakafi) may be considered medically necessary when the following criteria are met:
   A. Medication is prescribed by, or in consultation with, an oncologist, hematologist, dermatologist, or immunologist; AND
   B. 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 thrombocytopenia MF; OR
ruxolitinib (Jakafi®)
EOCCO POLICY

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

3. **Graft versus-host disease (GVHD), acute or chronic; AND**
   i. Member is 12 years of age or older; **AND**
   ii. Documentation of moderate-to-severe GVHD (e.g., Grade 2 to 4 GVHD, OR Grade B to D); **AND**
   iii. The member has had an inadequate response to steroids (e.g., prednisone, methylprednisolone, beclomethasone, budesonide).

II. Ruxolitinib (Jakafi) is considered **investigational** when used for all other conditions, including but not limited to:
   A. Low risk myelofibrosis
   B. Acute leukemia
   C. COVID-19
   D. Alopecia areata
   E. Vitiligo
   F. Glioma and glioblastoma
   G. Hidradenitis suppurativa
   H. Malignancy or cancer outside of myelofibrosis

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 one of the following:
   A. **Intermediate- to high-risk myelofibrosis (MF) OR polycythemia vera; AND**
      1. Documentation of reduction in spleen volume; OR
      2. Provider attestation of positive treatment response (e.g., improvement in symptoms, hematocrit control); OR
   B. **Graft versus-host disease (GVHD), acute or chronic; AND**
      1. Provider attestation of positive treatment response (e.g., reduction in symptoms associated with GVHD: gastrointestinal, ophthalmic, cutaneous, pulmonary).
ruxolitinib (Jakafi®)
EOCCO POLICY

Supporting Evidence

I. Length of authorization for initial approval is six months due to the clinical trial design, efficacy was evaluated at 24 weeks for all indications. Additionally, therapy beyond six months of treatment should be reserved for those where benefits outweigh the risks. If no treatment response is seen at six months, therapy should be tapered into discontinuation. Therapy should not be abruptly discontinued given the potential for symptom proliferation and exacerbation.

II. The FDA-approved conditions for this therapy require specialized and individualized care and monitoring; thus, a specialist prescriber, or consultation with a specialist, is required.

III. Treatment for MF is based on risk. For intermediate-to high risk MF, stem cell transplant is the recommended treatment option; however, in those ineligible for stem cell transplant, hydroxyurea, fedratinib (Inrebic), and ruxolitinib (Jakafi) are available treatment options. While hydroxurea may relieve splenomegaly and some symptoms of the condition (e.g., thrombocytosis, leukocytosis), it is thought to be less efficacious than other treatment options and may not be beneficial for major symptoms of the condition.

IV. Polycythemia vera treatment selection is also based on risk. Phlebotomy and/or low-dose aspirin are used in the management of low-risk disease. For high-risk disease, hydroxyurea is the preferred therapy given the extensive history of use, well-established safety profile, efficacy, and cost-effectiveness. Although busulfan has been used historically as a second-line therapy, because it has been associated with safety concerns such as cytopenia, pulmonary fibrosis, leukemia, and others, hydroxyurea remains the mainstay therapy. Ruxolitinib (Jakafi) is reserved for those that are not candidates for, or are refractory to, hydroxyurea, given the limited long-term safety and efficacy data. Additionally, for the treatment of polycythemia vera, ruxolitinib (Jakafi) is specifically FDA-approved after inadequate response or intolerance to hydroxyurea.

V. 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. Secondary outcomes included proportion of patients achieving a 50% or greater reduction in Total Symptom Score from baseline to week 24. This was measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF), which incorporates abdominal discomfort, pain, night sweating, itching, bone and muscle pain, and early satiety. The study met statistical significance in all outcomes. 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. This outcome was statistically significant.

VI. 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 in 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. Participants must have had a resistance or intolerance to hydroxyurea.

VII. Graft-versus-host disease is a complication of allogenic hematopoietic cell transplant. Treatment is dependent on severity and location of disease. The GVHD Grade depends on severity and location, and ranges from I-IV. Grade I is reflective of skin involvement, Grade IV is severe disease with severe skin involvement (e.g., blistering) and internal organ involvement, and Grade II-IV correlate with moderate to severe disease. The International Bone Marrow Transplant Registry Severity Index uses Grade A-D, which align with grading I-IV.

VIII. For Grade I or A, or mild disease, topical therapy is indicated. For Grade II or B or greater, or moderate-to-severe disease, systemic therapy is warranted. Glucocorticoids are the mainstay therapy; however, for those with glucocorticoid resistant disease, participation in clinical trials is recommended as there is currently no consensus on standard of care. Otherwise, therapies such as ruxolitinib (Jakafi) or ibrutinib (Imbruvica) are recommended. Therapy such as mycophenolate, rituximab, etanercept (Enbrel), everolimus, and others have been used historically, but there is lack safety and efficacy data from clinical trials to support the use of these therapies.

IX. The FDA approval of ruxolitinib (Jakafi) in the setting of acute GVHD was based on the results of an open-label, single-arm, multicenter study in participants with steroid-refractory acute GVHD Grades II to IV that were 12 years of age or older. Therapy was evaluated up to 10 mg twice daily. The 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.

X. For chronic GVHD, ruxolitinib (Jakafi) was evaluated in a Phase 3, open-label, randomized trial against best available treatment (BAT). Patients were 12 years of age or older, steroid-refractory, and had moderate-to-severe disease. Outcomes were ORR, failure-free survival (FFS), and Lee Symptom Score. Ruxolitinib (Jakafi) was superior to BAT in all outcomes. Given the availability of objective and subjective positive outcomes in this condition, and lack of standard of care beyond glucocorticoids, there is moderate confidence that ruxolitinib (Jakafi) provides clinical value for this condition.

XI. To date, ruxolitinib (Jakafi) has not been shown to improve survival for any condition.

XII. The safety and efficacy of ruxolitinib (Jakafi), or any other JAK inhibitor has not been evaluated in patients under 12 years of age.

XIII. Split fill applies to ruxolitinib (Jakafi) given the high rates of treatment discontinuation due to adverse events, and the rates of dose reduction or interruption seen in clinical trials (e.g in the pivotal trial for aGVHD the rate of treatment discontinuation due to adverse events was 31%).
Investigational or Not Medically Necessary Uses

1. Ruxolitinib (Jakafi) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Low risk myelofibrosis
   B. Acute leukemia
   C. COVID-19
   D. Alopecia areata
   E. Vitiligo
   F. Glioma and glioblastoma
   G. Hidradenitis suppurativa
   H. Cancer or malignancy outside of myelofibrosis

References


Policy Implementation/Update:

<table>
<thead>
<tr>
<th>Action and Summary of Changes</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic graft vs. host disease indication added to policy. Update of qualifying prescribers and appropriate doses and quantities per indication. Removal of infection free requirement, check of unacceptable toxicity, and requirement for previous use of hydroxyurea in myelofibrosis.</td>
<td>06/2021</td>
</tr>
<tr>
<td>Addition of acute graft vs. host disease indication to renewal section.</td>
<td>01/2020</td>
</tr>
<tr>
<td>Criteria transitioned to policy. Added newly FDA approved indication of acute graft versus host disease. Remove diagnostic questions, interaction questions, lab value questions. Added requirement for previous use of hydroxyurea prior to coverage of Jakafi for the indication of polycythemia vera.</td>
<td>07/2019</td>
</tr>
<tr>
<td>Previous reviews</td>
<td>12/2014, 12/2012, 07/2012, 05/2012</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>-----------------------------------</td>
</tr>
</tbody>
</table>

ruxolitinib (Jakafi®)