Drug Coverage Policy

Effective Date 10/1/2026
Coverage Policy Number.....IP0318
Policy Title.....Jakafi/Jakafi XR

Oncology – Jakafi/Jakafi XR

- Jakafi® (ruxolitinib tablets – Incyte)
- Jakafi XR™ (ruxolitinib extended release tablets – Incyte)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Jakafi, an inhibitor of Janus Associated Kinases (*JAKs*) *JAK1* and *JAK2*, is indicated for the following uses:[1]

- **Graft-versus-host disease**, acute treatment of steroid-refractory disease, in patients ≥ 12 years of age.
- **Graft-versus-host disease**, chronic treatment, after failure of one or two lines of systemic therapy in patients ≥ 12 years of age.
- **Myelofibrosis**, intermediate or high risk, including primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis in adults.

- **Polycythemia vera**, in adults who have had an inadequate response to or are intolerant of hydroxyurea.

Guidelines

Jakafi is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):[2]

- **Graft-Versus-Host Disease:** NCCN guidelines for hematopoietic cell transplantation discuss graft-versus-host disease (version 3.2025 – September 24, 2025) and include Jakafi.[3] Jakafi is recommended as additional therapy in conjunction with systemic corticosteroids for adults and pediatric patients ≥ 12 years old with steroid-refractory acute graft-versus-host disease, or chronic graft-versus-host disease, after failure of one or two lines of systemic therapy (both category 1).
- **Myelodysplastic Syndromes:** NCCN guidelines (version 3.2026 – January 12, 2026) recommend Jakafi for patients with chronic myelomonocytic leukemia-2, with hypomethylating agents (HMA) for symptom management or splenomegaly (category 2A).[4] Jakafi ± HMA is also recommended for myelodysplastic syndrome/myeloproliferative neoplasm with neutrophilia (atypical chronic myeloid leukemia); there is a footnote, which states that rare patients with *CSF3R* or *JAK2* mutations may respond to Jakafi due to their JAK-STAT pathway activation (category 2A).
- **Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions**: NCCN guidelines (version 1.2026 – October 3, 2025) recommend Jakafi for treatment of myeloid/lymphoid neoplasms with eosinophilia and *JAK2* rearrangement in chronic or blast phase (category 2A).[5] The guidelines also recommend Jakafi for treatment in combination with acute lymphocytic leukemia or acute myeloid leukemia type induction chemotherapy followed by allogeneic hematopoietic stem cell transplantation (if eligible) for lymphoid, myeloid, or mixed phenotype neoplasms with eosinophilia and *JAK2* rearrangement in blast phase (category 2A).
- **Myeloproliferative Neoplasms:** NCCN guidelines (version 1.2026 – January 22, 2026) recommend Jakafi among patients with lower- or higher-risk myelofibrosis (category 2A; category 1 for the initial treatment of higher-risk myelofibrosis).[6] It is also recommended as "other recommended regimens" for the management of myelofibrosis associated anemia with the presence of symptomatic splenomegaly and/or constitutional symptoms in combination with other medications (category 2A). It is also a recommended as "useful in certain circumstances" for high-risk polycythemia vera as initial treatment (category 2A) and as "preferred regimen" for patients with hydroxyurea resistance or intolerance (category 1). There is a footnote that states Jakafi may have activity after inadequate response or loss of response to other agents besides hydroxyurea. The guidelines also recommend Jakafi for treatment of essential thrombocythemia for inadequate response or loss of response to hydroxyurea, Pegasys® (peginterferon alfa-2a subcutaneous injection), or anagrelide as "useful in certain circumstances" (category 2A). JAK inhibitors are also recommended for accelerated or blast phase myeloproliferative neoplasms for the palliation of splenomegaly or other disease-related symptoms (category 2A). Some examples of disease-related symptoms of myeloproliferative neoplasms include fatigue, fever, night sweats, weight loss, abdominal discomfort, splenomegaly, thrombocytosis, or leukocytosis.
- **Pediatric Acute Lymphoblastic Leukemia:** NCCN guidelines (version 1.2026 – August 11, 2025) recommend Jakafi in a variety of regimens for pediatric patients and young adults with acute lymphoblastic leukemia as induction or consolidation therapy (category 2A).[7] The utility of Jakafi is described primarily in patients in which the mutation/pathway is *JAK*-related, but it Jakafi can be used for other mutations as well, such as *EPOR* rearrangements, *SH2B3* alterations, and *IL7R* insertions/deletion.
- **T-Cell Lymphoma**: NCCN guidelines (version 1.2026 – December 9, 2025) recommend Jakafi as a single-agent for symptomatic disease as second-line or subsequent therapy for T-cell prolymphocytic leukemia as "other recommended regimen" (category 2A) and T-cell large granular lymphocytic leukemia (category 2A).[8] Jakafi is also recommended as "other

recommended regimens" for peripheral T-cell lymphomas as initial therapy and second-line and subsequent therapy (category 2B), for breast implant-associated anaplastic large cell lymphoma as second-line and subsequent therapy for relapsed/refractory disease (category 2B), and for hepatosplenic T-cell lymphoma for refractory disease after two first-line therapy regimens (category 2B).

Jakafi is also discussed in American College of Rheumatology (ACR) [2025] guidelines for the diagnosis and management of Vacuoles E1 Enzyme X-linked Autoinflammatory Somatic (VEXAS) Syndrome.[9] VEXAS is an adult-onset autoinflammatory condition caused by somatic mutations in the *UBA1* gene, which disrupts the function of the E1 enzyme responsible for protein cleanup inside cells. This leads to a buildup of damaged proteins, triggering widespread inflammation. It presents with a combination of systemic inflammation and hematologic abnormalities. Regarding diagnosis, ACR notes that the majority of patients with typical VEXAS have missense or splice site mutations at exon 3 of *UBA1*. For patients that are negative with genetic testing for mutations in *UBA1*, clinicians should ensure that testing covers the complete gene and consider testing a bone marrow sample. For treatment of inflammatory manifestations, corticosteroids are recommended.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for prescription benefit coverage of Jakafi and Jakafi XR. All approvals are provided for the duration noted below.

Certain indications and/or approval conditions that are delegated to EviCore by Evernorth will follow Oncology Medications (1403) coverage policy for prior authorization medically necessity criteria. Note: Any listed preferred product requirements in this coverage policy, inclusive of oncology and/or oncology-related uses, are applicable as noted.

Jakafi and Jakafi XR is considered medically necessary when ONE of the following is met:

FDA-Approved Indication

1. **Graft versus Host Disease, Acute.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 12 years of age; AND
   B) Patient has tried one systemic corticosteroid

2. **Graft versus Host Disease, Chronic.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 12 years of age; AND
   B) Patient has tried one conventional systemic treatment for graft-versus-host disease.
   Note: Examples include systemic corticosteroids (methylprednisolone, prednisone), cyclosporine, tacrolimus, mycophenolate mofetil, Imbruvica (ibrutinib capsules, tablets, and oral solution), Rezurock (belumosudil tablet), Niktimvo (axatilimab-csfr intravenous infusion), pentostatin, rituximab, Orencia (abatacept intravenous infusion), hydroxychloroquine, and imatinib.

3. **Myelofibrosis (MF), including Primary MF, Post-Polycythemia Vera MF, and Post-Essential Thrombocythemia MF.** Approve for 1 year if the patient is ≥ 18 years of age.

4. **Polycythemia Vera.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried hydroxyurea, Pegasys (peginterferon alfa-2a subcutaneous injection), or Besremi (ropeginterferon alfa-2b-njft subcutaneous injection).

Other Uses with Supportive Evidence

5. **Accelerated or Blast Phase Myeloproliferative Neoplasm**. Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has at least one disease-related symptom.
      Note: Examples of disease-related symptoms include: fatigue, fever, night sweats, weight loss, abdominal discomfort, splenomegaly, thrombocytosis, or leukocytosis.

6. **Acute Lymphoblastic Leukemia.** Approve for 1 year if the patient meets BOTH of the following (A and B)
   A) Patient is < 21 years of age; AND
   B) Patient meets ONE of the following (i or ii):
      i. The mutation/pathway is Janus Associated Kinase (*JAK*)-related ; OR
      ii. The disease has a *EPOR* rearrangement, *SH2B3* alterations, or *IL7R* insertion/deletion.

7. **Atypical Chronic Myeloid Leukemia.** Approve for 1 year if the patient meets ONE of following (A or B):
   Note: This includes a patient who has myelodysplastic syndrome/myeloproliferative neoplasm with neutrophilia.
   A) Patient has a *CSF3R* mutation; OR
   B) Patient has a Janus Associated Kinase 2 (*JAK2*) mutation.

8. **Chronic Myelomonocytic Leukemia-2.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient is also receiving a hypomethylating agent.
      Note: Examples of hypomethylating agents include azacitidine and decitabine.

9. **Essential Thrombocythemia.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried hydroxyurea, Pegasys (peginterferon alfa-2a subcutaneous injection), or anagrelide.

10. **Myeloid or Lymphoid Neoplasms.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
    A) Patient is ≥ 18 years of age; AND
    B) Patient has eosinophilia; AND
    C) The tumor has a Janus Associated Kinase 2 (*JAK2)* rearrangement.

11. **T-Cell Lymphoma**. Approve for 1 year if the patient meets BOTH of the following (A and B):
    A) Patient is ≥ 18 years of age; AND
    B) Patient meets ONE of the following (i or ii):
       i. Patient has peripheral T-cell lymphoma; OR
       ii. Patient meets BOTH of the following: (a and b):
          a) Patient has ONE of the following [(1), (2), (3), or (4)]:
          (1)T-cell prolymphocytic leukemia; OR

(2)T-cell large granular lymphocytic leukemia; OR
(3) Hepatosplenic T-cell lymphoma; OR
(4) Breast implant-associated anaplastic large cell lymphoma; AND

b) Patient has tried at least one systemic regimen.
Note: Examples of a systemic regimen include one or more of the following products: methotrexate, corticosteroids, cyclosporine, Lemtrada (alemtuzumab intravenous infusion), fludarabine, mitoxantrone, or cyclophosphamide.

12. **Vacuoles E1 Enzyme X-linked Autoinflammatory Somatic (VEXAS) Syndrome.** Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient is ≥ 18 years of age; AND
ii. Patient has a molecular genetic test demonstrating pathogenic or likely pathogenic *UBA1* gene variant; AND
iii. Patient meets ONE of the following (a or b):
a) Patient has tried or is currently taking a systemic corticosteroid; OR
b) Systemic corticosteroids are contraindicated; AND
iv. The medication is prescribed by or in consultation with a rheumatologist, hematologist, dermatologist, immunologist, or specialist in the treatment of autoinflammatory conditions; OR

B) Patient is Currently Receiving Jakafi. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on the requested medication for at least 6 months; AND
Note: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.
ii. Patient meets at least ONE of the following (a or b):
a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include resolution of fever, improvement in skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.
b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased joint pain, decreased fatigue, decreased cough and/or dyspnea, improved ocular symptoms, and/or improved function or activities of daily living.

Conditions Not Covered

Jakafi and Jakafi XR for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

References

1. Jakafi® tablets and Jakafi XR tablets [prescribing information]. Wilmington, DE: Incyte; May 2026.
2. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 17, 2025. Search term: ruxolitinib.

3. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 2.2024 – August 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 7, 2025.
4. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 2.2025 – January 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 17, 2025.
5. The NCCN Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions Clinical Practice Guidelines in Oncology (version 2.2024 – June 19, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 7, 2025.
6. The NCCN Myeloproliferative Neoplasms Clinical Practice Guidelines in Oncology (version 2.2024 – August 8, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 7, 2025.
7. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 2.2025 – December 16, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 17, 2025.
8. The NCCN T-Cell Lymphoma Clinical Practice Guidelines in Oncology (version 1.2025 – November 11, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 17, 2025.
9. Mekinian AM, Georgin-Lavaille S, Ferrada MA, et al. American College of Rheumatology Guidance Statement for Diagnosis and Management of VEXAS Developed by the International VEXAS Working Group Expert Panel. *Arthritis Rheumatol*. 2025 Aug 11. doi: 10.1002/art.43287 [Online ahead of print].

Revision Details

Summary of Changes	Review Date	Effective Date
Updated title from "Jakafi (ruxolitinib) for Non-Oncology Indications " **to** "Oncology – Jakafi" **Graft versus Host Disease, Acute.** **Updated from** "Documentation of failure, contraindication, or intolerance to ONE systemic corticosteroid" **to** "Patient has tried one systemic corticosteroid" **Graft versus Host Disease, Chronic.** **Updated from** "Documentation of failure, contraindication, or intolerance to ONE conventional systemic treatment for grapft-versus-host-disease" **to "**Patient has tried one conventional systemic treatment for graft-versus-host disease.Note: Examples include systemic corticosteroids (methylprednisolone, prednisone), cyclosporine, tacrolimus, mycophenolate mofetil, Imbruvica (ibrutinib capsules, tablets, and oral solution), Rezurock (belumosudil tablet), Niktimvo (axatilimab-csfr intravenous infusion), pentostatin, rituximab, Orencia (abatacept intravenous infusion), hydroxychloroquine, and imatinib."	03/13/2025	05/15/2025

Added criteria for: Myelofibrosis (MF), including Primary MF, Post-Polycythemia Vera MF, and Post-Essential Thrombocythemia MF, Polycythemia Vera, Accelerated or Blast Phase Myeloproliferative Neoplasm, Acute Lymphoblastic Leukemia, Atypical Chronic Myeloid Leukemia, Chronic Myelomonocytic Leukemia-2, Essential Thrombocythemia, Myeloid or Lymphoid Neoplasms, T-Cell Lymphoma.		
Vacuoles E1 Enzyme X-linked Autoinflammatory Somatic Syndrome (VEXAS): This was added as condition of approval under Other Uses with Supportive Evidence.	12/18/2026	2/1/2026
Acute Lymphoblastic Leukemia: An option of approval was added when the disease has a *EPOR* rearrangement, *SH2B3* alterations, or *IL7R* insertion/deletion.	2/26/2026	5/1/2026
The policy name was changed to as listed. Previously, it was Oncology – Jakafi. Jakafi XR was added to the policy with the same criteria as Jakafi.	8/13/2026	10/1/2026

The policy effective date is in force until updated or retired.

"Cigna Companies" refers to operating subsidiaries of The Cigna Group. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc., and HMO or service company subsidiaries of The Cigna Group. © 2026 The Cigna Group.