Jakafi® (ruxolitinib)
(Oral)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed (unless otherwise specified).

- Management of CAR T-Cell-Related Toxicities may NOT be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Jakafi 5 mg tablets: 2 tablets per day
- Jakafi 10 mg tablets: 2 tablets per day
- Jakafi 15 mg tablets: 2 tablets per day
- Jakafi 20 mg tablets: 2 tablets per day
- Jakafi 25 mg tablets: 2 tablets per day

B. Max Units (per dose and over time) [HCPCS Unit]:

CAR T-Cell-Related Toxicities
- 10 mg per day

GVHD
- 20 mg per day

MDS/MPN
- 40 mg per day

All other indications
- 50 mg per day

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); AND

Universal Criteria [1]

- Therapy will not be used in combination with another JAK2-inhibitor type drug (i.e., fedratinib, pacritinib, etc.); **AND**
- Patient does not have an active infection, including clinically important localized infections; **AND**
- Patient will avoid concomitant therapy with all of the following:
  - Coadministration with fluconazole, or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented
  - Coadministration with strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole, nefazodone, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented
  - Coadministration with strong CYP3A4 inducers (e.g., rifampin, phenytoin, St. John's wort, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

Myelofibrosis (MF) (including primary, post-polycythemia vera and post-essential thrombocythemia MF) † ‡ Φ [1,4,13]

- Patient has symptomatic low- to intermediate-1-risk disease; **AND**
  - Used as a single agent; **OR**
- Patient has intermediate-2 or high-risk disease †; **AND**
  - Used as a single agent; **AND**
    - Patient has a baseline platelet count of ≥ 50 x 10^9/L within the previous 30 days; **OR**
    - Patient has splenomegaly; **OR**
- Patient has myelofibrosis (MF)-accelerated phase or MF-blast phase; **AND**
  - Used in combination with hypomethylating agents (azacitidine or decitabine); **AND**
  - Used as induction therapy or for the palliation of splenomegaly or other disease-related symptoms

Polycythemia Vera † ‡ Φ [1,4,13,25]

- Patient has had an inadequate response, loss of response, or intolerance to at least a 3 month trial of hydroxyurea or interferon therapy; **AND**
- Used as cytoreductive treatment for symptomatic low risk OR high risk disease

Essential Thrombocythemia ‡ Φ [4,13]

- Patient has had an inadequate response or loss of response to hydroxyurea, peginterferon alfa-2a therapy, or anagrelide

Graft Versus Host Disease (GVHD) † Φ [1,4,5]

- Used for disease related to allogeneic hematopoietic stem cell transplantation; **AND**

- Patient is at least 12 years of age; **AND**
- Used in combination with systemic corticosteroids for steroid-refractory disease; **AND**
  - Patient has acute graft versus host disease (aGVHD); **OR**
  - Patient has chronic graft versus host disease (cGVHD); **AND**
    - Patient has failed one or two lines of systemic therapy

Myelodysplastic/Myeloproliferative Overlap Neoplasms (MDS/MPN) ‡ [4,7,9]

- Patient has chronic myelomonocytic leukemia (CMML)-2; **AND**
  - Used in combination with a hypomethylating agent (e.g., decitabine, azacitidine, etc.); **OR**
- Patient has myelodysplastic/myeloproliferative neoplasms (MDS/MPN) with neutrophilia (e.g., atypical chronic myeloid leukemia [aCML]); **AND**
  - Used as a single agent or in combination with a hypomethylating agent (e.g., decitabine, azacitidine, etc.)

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions ‡ [4,10]

- Patient has eosinophilia with JAK2 rearrangement; **AND**
  - Patient has chronic or blast phase myeloid or lymphoid neoplasms; **AND**
    - Used as a single agent; **OR**
  - Patient has blast phase lymphoid, myeloid, or mixed lineage neoplasms; **AND**
    - Used in combination with ALL- or AML-type induction chemotherapy followed by allogeneic HCT (if eligible)

Pediatric Acute Lymphoblastic Leukemia (ALL) ‡ [4,11,12]

- Patient is at least 1 year of age; **AND**
- Patient has Philadelphia chromosome (Ph)-like B-ALL; **AND**
  - Used as induction therapy; **AND**
    - Used in combination with Total Therapy XVII regimen [prednisone, vincristine, daunorubicin, pegaspargase, cyclophosphamide, cytarabine, 6-MP, intrathecal therapy (methotrexate OR cytarabine OR methotrexate, cytarabine, and corticosteroid)]; **AND**
      - Patient has disease with mutations associated with JAK-STAT pathway activation; **OR**
  - Used as consolidation therapy; **AND**
    - Used in combination with COG AALL1521 regimen (cyclophosphamide, cytarabine, 6-MP, vincristine, pegaspargase, IT methotrexate); **AND**
      - Patient has CRLF2+ or CRLF2- with JAK2 fusions, EPOR rearrangements, SH2B3 alterations, IL7R insertions/deletions; **OR**

- Used in combination with the standard risk/high risk (SR/HR) arm of the Total Therapy XVII regimen [high-dose methotrexate, pegaspargase, 6-MP, intrathecal therapy (methotrexate OR cytarabine OR methotrexate, cytarabine, and corticosteroid)]; **AND**
    - Patient has disease with mutations associated with JAK-STAT pathway activation

Management of CAR T-Cell-Related Toxicities ‡ [4,20]

- Patient has been receiving chimeric antigen receptor (CAR) T-cell therapy (e.g., axicabtagene ciloleucel, brexucabtagene autoleucel, idecabtagene vicleucel, lisocabtagene maraleucel, tisagenlecleucel, etc.); **AND**
- Patient has grade 4 (G4) cytokine release syndrome; **AND**
- Patient is refractory to treatment with high-dose corticosteroids AND anti-IL-6 therapy (e.g., tocilizumab, sarilumab, satralizumab, etc.)

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage may be renewed based on the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious infections, severe hematologic toxicity (neutropenia, thrombocytopenia, and anemia), non-melanoma skin cancer (NMSC), lipid elevations (including total cholesterol, LDL, and triglycerides), major adverse cardiovascular events (MACE), thrombosis, secondary malignancies, etc.; **AND**

Myelofibrosis [1,4,13]

- Treatment response with a decrease in spleen size or improvements in other myelofibrosis symptoms (e.g., fatigue, bone pain, frequent infections, fever, night sweats, easy bruising/bleeding, etc.)

Polycythemia Vera [1,4,13]

- Treatment response such as hematocrit control and/or spleen volume reduction

Essential Thrombocythemia [4,13]

- Disease response as evidenced by at least one of the following:
    - Decrease in spleen size or improvements in other myelofibrosis symptoms (e.g., fatigue, bone pain, frequent infections, fever, night sweats, easy bruising/bleeding, etc.)
    - Platelet count ≤ 400 x 10^9/L, WBC count < 10 x 10^9/L, absence of leukoerythroblastosis

- Absence of any signs of progressive disease or hemorrhagic or thrombotic events

GVHD [1,4,5]

- Treatment response such as stabilization or improvement in disease; **AND**
- In patients who have had a response and have discontinued therapeutic doses of corticosteroids, tapering of ruxolitinib should be considered

Myelodysplastic/Myeloproliferative Overlap Neoplasms (MDS/MPN) [4,7-9]

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [4,10]

- Disease response as evidenced by at least one of the following:
  - Decrease in spleen size or improvements in other myelofibrosis symptoms (e.g., fatigue, bone pain, frequent infections, fever, night sweats, easy bruising/bleeding, etc.)
  - Stabilization or improvement as evidenced by a complete response [CR] (i.e., morphologic, cytogenetic or molecular complete response CR), complete hematologic response or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH

Pediatric Acute Lymphoblastic Leukemia (ALL) [4,11,12]

- Treatment response or stabilization of disease as indicated by CBC, bone marrow cytogenic analysis, QPCR, or FISH

CAR T-Cell-Related Toxicities [4,20]

- Coverage may NOT be renewed

V. Dosage/Administration [1,8,9,12,14,15,20,22-24]

Indication	Dose
Myelofibrosis & Myeloid/Lymphoid Neoplasms with Eosinophilia	• Platelets >200 x 10^9/L – Starting dose is 20 mg orally twice daily • Platelets 100 to 200 x 10^9/L – Starting dose is 15 mg orally twice daily • Platelets 50 to <100 x 10^9/L – Starting dose is 5 mg orally twice daily *Doses may be increased in 5 mg twice daily increments to a maximum of 25 mg twice daily.*
Polycythemia Vera & Essential Thrombocythemia	• Administer 10 mg orally twice daily. *Doses may be titrated based on safety and efficacy up to a maximum of 25 mg twice daily.*
aGVHD	• Starting dose is 5 mg orally twice daily.

	○ Consider increasing the dose to 10 mg orally twice daily after at least 3 days of treatment if the ANC and platelet counts are not decreased by 50% or more relative to the first day of dosing with ruxolitinib. ○ Tapering of ruxolitinib may be considered after 6 months of treatment in patients with response who have discontinued therapeutic doses of corticosteroids. Taper ruxolitinib by one dose level approximately every 8 weeks (10 mg orally twice daily to 5 mg orally twice daily to 5 mg orally once daily). If acute GVHD signs or symptoms recur during or after the taper of ruxolitinib, consider retreatment.
cGVHD	• Starting dose is 10 mg orally twice daily ○ Tapering of ruxolitinib may be considered after 6 months of treatment in patients with response who have discontinued therapeutic doses of corticosteroids. Taper ruxolitinib by one dose level approximately every 8 weeks (10 mg orally twice daily to 5 mg orally twice daily to 5mg orally once daily). If GVHD signs or symptoms recur during or after the tape of ruxolitinib, consider retreatment.
CAR T-Cell-Related Toxicities	• Administer 5 mg orally twice daily
MDS/MPN	• Platelets >200 x 10^9/L – Starting dose is 20mg orally twice daily • Platelets 100 to 200 x 10^9/L – Starting dose is 15mg orally twice daily • Platelets 50 to 100 x 10^9/L – Starting dose is 5mg orally twice daily *Doses may be titrated based on safety and efficacy up to a maximum of 20 mg twice daily.*
Pediatric ALL	• Administer up to 50 mg/m^2 orally twice daily (14-days-on/14-days-off) per 28-day cycle; OR • Administer 40 mg/m^2 orally twice daily for a 28-day cycle

VI. Billing Code/Availability Information

HCPCS Code(s):

- J8999 – Prescription drug, oral, chemotherapeutic, not otherwise specified
- C9399 – Unclassified drugs or biologicals

NDC(s):

- Jakafi 5 mg tablets: 50881-0005-xx
- Jakafi 10 mg tablets: 50881-0010-xx
- Jakafi 15 mg tablets: 50881-0015-xx
- Jakafi 20 mg tablets: 50881-0020-xx
- Jakafi 25 mg tablets: 50881-0025-xx

VII. References

1. Jakafi [package insert]. Wilmington, DE; Incyte; January 2023. Accessed October 2023.

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5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Cell Transplantation (HCT). Version 2.2023. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2023.
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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C91.00	Acute lymphoblastic leukemia not having achieved remission
C92.20	Atypical chronic myeloid leukemia, BCR/ABL-negative, not having achieved remission
C92.22	Atypical chronic myeloid leukemia, BCR/ABL-negative, in relapse
C93.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C93.11	Chronic myelomonocytic leukemia, in remission
C93.12	Chronic lymphocytic leukemia of B-cell type in relapse
C94.40	Acute panmyelosis with myelofibrosis not having achieved remission
C94.41	Acute panmyelosis with myelofibrosis in remission
C94.42	Acute panmyelosis with myelofibrosis in relapse
C94.6	Myelodysplastic disease, not classified
C94.8	Other specified leukemias
C94.80	Other specified leukemias not having achieved remission
C94.81	Other specified leukemias, in remission
C94.82	Other specified leukemias, in relapse
C95.1	Chronic leukemia of unspecified cell type
C95.10	Chronic leukemia of unspecified cell type not having achieved remission
C95.11	Chronic leukemia of unspecified cell type, in remission
C95.12	Chronic leukemia of unspecified cell type, in relapse
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
D45	Polycythemia vera
D47.1	Chronic myeloproliferative disease
D47.3	Essential (hemorrhagic) thrombocythemia
D47.4	Osteomyelofibrosis

D75.81	Myelofibrosis
D89.810	Acute graft-versus-host disease
D89.811	Chronic graft-versus-host disease
D89.812	Acute on chronic graft-versus-host disease
D89.813	Graft-versus-host disease, unspecified
D89.834	Cytokine release syndrome, grade 4
D89.839	Cytokine release syndrome, grade unspecified
T86.09	Other complications of bone marrow transplant
T80.82XA	Complication of immune effector cellular therapy, initial encounter
T80.82XS	Complication of immune effector cellular therapy, sequela
T80.89XA	Other complications following infusion, transfusion and therapeutic injection, initial encounter
T80.89XS	Other complications following infusion, transfusion and therapeutic injection, sequela

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC