Inrebic® (fedratinib)
(Oral)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

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

- Inrebic 100 mg capsule: 4 capsules per day

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

- 400 mg per day

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient must have tried and failed treatment with Jakafi or a contraindication exists; **AND**

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Therapy will not be used in combination with another JAK2-inhibitor type drug (e.g., ruxolitinib, pacritinib, etc.); **AND**
- Baseline thiamine (vitamin B1), amylase, and lipase levels are within normal limits prior to initiating of therapy and will continue to be monitored periodically while on treatment; **AND**
- Patient will avoid concomitant therapy with all of the following:
  - 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 moderate and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's Wort, efavirenz, etc.)

- Coadministration with dual CYP3A4 and CYP2C19 inhibitors (e.g., fluconazole, fluvoxamine, 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 or secondary post-polycythemia vera and post-essential thrombocythemia MF) † ‡ Φ [1,4]

- 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

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions ‡ [4,5]

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

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

IV. Renewal Criteria [1,4,5]

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: encephalopathy (including Wernicke's encephalopathy), anemia, thrombocytopenia, hepatotoxicity (elevated AST/ALT), gastrointestinal toxicity (severe nausea, vomiting, diarrhea), amylase/lipase elevations, Major Adverse Cardiac Events (MACE), thrombosis, secondary malignancies, etc.; **AND**

Myelofibrosis [1,4]

- 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.)

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes [4,5]

- 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

V. Dosage/Administration [1,5]

Indication	Dose
All Indications	Administer 400 mg (4 capsules) orally once daily until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code(s):

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

NDC:

- Inrebic 100 mg capsules: 59572-0720-xx

VII. References

1. Inrebic [package insert]. Princeton, NJ; Bristol-Myers Squibb Company; May 2023. Accessed October 2023.
2. Tefferi A. Primary myelofibrosis: 2013 update on diagnosis, risk-stratification, and management. Am J Hematol. 2013 Feb; 88(2):141-50.
3. Reilly JT, McMullin MF, Beer PA, et al. Guideline for the diagnosis and management of myelofibrosis. Br J Haematol 2012; 158:453.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) fedratinib. 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.

5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions, Version 2.2023. National Comprehensive Cancer Network, 2023. 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 Guidelines, go online to NCCN.org. Accessed October 2023.
6. Pardanani A, Harrison C, Cortes JE, et al. Safety and Efficacy of Fedratinib in Patients With Primary or Secondary Myelofibrosis: A Randomized Clinical Trial. JAMA Oncol. 2015 Aug;1(5):643-51.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
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
D47.1	Chronic myeloproliferative disease
D47.4	Osteomyelofibrosis
D75.81	Myelofibrosis

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