Inrebic® (fedratinib)
(Oral)

Document Number: IH-0492

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I. Length of Authorization

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

II. Dosing Limits

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

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]

- 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 (i.e., ruxolitinib, 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; **AND**
  - Coadministration with moderate and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's Wort, modafinil, etc.); **AND**
  - Coadministration with dual CYP3A4 and CYP2C19 inhibitors (e.g., fluconazole, fluvoxamine, etc.); **AND**

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

- Patient has intermediate-2 or high-risk disease † ; **AND**
- Patient has a baseline platelet count of ≥ 50 X 10^9/L within the previous 30 days; **AND**
- Patient has palpable splenomegaly (i.e. at least 5 cm below costal margin)

Myeloid/Lymphoid Neoplasms with Eosinophilia ‡ [4,5]

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

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

IV. Renewal Criteria [1,4,5]

Authorizations can be renewed based on the following criteria:

- Patient continues to meet 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, etc.; **AND**
- **Myelofibrosis**
  - Treatment response with a decrease in spleen size or improvements in other myelofibrosis symptoms (such as fatigue, bone pain, frequent infections, fever, night sweats, easy bruising/bleeding, etc.)
- **Myeloid/Lymphoid Neoplasms with Eosinophilia**
  - Disease response as evidenced by at least one of the following:
    - Decrease in spleen size or improvements in other myelofibrosis symptoms (such as 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	400 mg taken orally once daily

VI. Billing Code/Availability Information

HCPCS Code:

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

NDC:

- 100 mg capsules: 59572-0720-xx

VII. References

1. Inrebic [package insert]. Summit, NJ; Celgene, Corp.; August 2019. Accessed September 2020.
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 oral. National Comprehensive Cancer Network, 2020. 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 September 2020.
5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 3.2021. National Comprehensive Cancer Network, 2020. 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 September 2020.
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: http://www.cms.gov/medicare-coverage-database/search/advanced-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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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