Clinical Policy: Fedratinib (Inrebic)

Reference Number: CP.PHAR.442
Effective Date: 12.01.19
Last Review Date: 11.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Fedratinib (Inrebic®) is a kinase inhibitor.

FDA Approved Indication(s)

Inrebic is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera (post-PV) or post-essential thrombocythemia (post-ET)) myelofibrosis (MF).

Policy/Criteria

Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Inrebic is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Myelofibrosis (must meet all)**:**

1. Diagnosis of intermediate-2 or high-risk primary MF, post-PV MF, or post-ET MF;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Documentation of a recent (within the last 30 days) thiamine level of ≥ 70 nmol/L (3 mcg/dL);
5. Documentation of a recent (within the last 30 days) platelet count of ≥ 50,000/mcL;
6. Failure of Jakafi®, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Jakafi*
7. For brand Inrebic requests, member must use generic fedratinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 400 mg per day;
      ii. 4 capsules per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Myeloid/Lymphoid Neoplasms with Eosinophilia and Janus Kinase 2 arrangement (off-label) (must meet all):

1. Diagnosis of myeloid or lymphoid neoplasm with eosinophilia and Janus kinase 2 arrangement;
2. Documentation that disease is in the chronic or blast phase;
3. Prescribed by or in consultation with a hematologist or oncologist;
4. Age ≥ 18 years;
5. Documentation of a recent (within the last 30 days) thiamine level of ≥ 70 nmol/L (3 mcg/dL);
6. Documentation of a recent (within the last 30 days) platelet count of ≥ 50,000/mcL;
7. Failure of Jakafi, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Jakafi*
8. For brand Inrebic requests, member must use generic fedratinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
9. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 400 mg per day;
      ii. 4 capsules per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Inrebic for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Inrebic requests, member must use generic fedratinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed both of the following (i and ii):
      i. 400 mg per day;
      ii. 4 capsules per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration	MF: myelofibrosis

NCCN: National Comprehensive Cancer Network
Post-ET: post-essential thrombocythemia
Post-PV: post-polycythemia vera

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Jakafi (ruxolitinib)	MF: 5 mg to 25 mg PO BID	50 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): serious and fatal encephalopathy, including Wernicke's

Appendix D: General Information

- NCCN recommendations for the initial treatment of intermediate-2 or high-risk MF include the use of Jakafi® and Inrebic as a category 1 recommendation after clinical trial therapies and allogeneic hematopoietic cell transplantation.
- The Inrebic Prescribing Information and NCCN guidelines for myeloproliferative neoplasms recommend a baseline platelet count of ≥ 50,000/mcL before initiation of Inrebic. The Jakafi Prescribing Information also recommends the same baseline platelet count for Jakafi, but NCCN guidelines include support for use of Jakafi for low- or intermediate-1 risk MF without regard to baseline platelet counts.
- Examples of positive response to therapy for myelofibrosis include: reduction in spleen size or improvement in symptoms such as pruritus, fatigue, night sweats, bone pain since initiation of therapy.
- Intermediate-2 or high-risk disease is defined as having two or more of the following risk factors:
  - Age > 65
  - Constitutional symptoms (weight loss greater than 10 percent from baseline and/or unexplained fever, or excessive sweats persisting for more than 1 month)
  - Hemoglobin less < 10 g/dL
  - White blood cell count ≥ 25 x10^9/L
  - Peripheral blood blasts ≥ 1 %
  - Platelets < 100 x 10^9/L
  - Red Cell Transfusion
  - Unfavorable karyotype (i.e., complex karyotype or sole or two abnormalities that include trisomy 8, -7/7q-, i(17q),-5/5q-, 12p-, inv(3), or 11q23 rearrangement)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MF	400 mg PO QD	400 mg/day

VI. Product Availability

Capsule: 100 mg

VII. References

1. Inrebic Prescribing Information. Summit, NJ: Celgene Corporation; May 2023. Available at http://www.inrebicpro.com. Accessed July 15, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 1, 2024.
3. National Comprehensive Cancer Network. Myeloproliferative Neoplasms Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed August 1, 2024.
4. National Comprehensive Cancer Network. Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf. Accessed August 1, 2024.
5. 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;1(5): 643-51.
6. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed August 1, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: no significant changes; references reviewed and updated.	07.15.20	11.20
4Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; added legacy WCG initial auth duration (WCG.CP.PHAR.442 to be retired); WCG.CP.PHAR.442: removed requirement for failure of HCT, hydroxyurea, and concurrent tx with Jakafi within 14 days; references reviewed and updated.	06.22.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
4Q 2022 annual review: added off-label criteria for myeloid or lymphoid neoplasm with eosinophilia and Janus kinase 2 arrangement per NCCN category 2A recommendation; for brand name requests added requirement for generic alternative if available; WCG-specific policy was retired and 12-month approval duration was consolidated to 6 months for initial auth and 12 months for continued therapy; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.28.22	11.22
4Q 2023 annual review: COC applied to continuation of therapy section; added definition of intermediate-2 or high-risk disease to Appendix D; references reviewed and updated.	06.30.23	11.23
4Q 2024 annual review: no significant changes; references reviewed and updated.	07.15.24	11.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.