Clinical Policy Title:	fedratinib
Policy Number:	RxA.173
Drug(s) Applied:	Inrebic®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Fedratinib (Inrebic®) is a kinase inhibitor. It 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).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
fedratinib (Inrebic®)	MF	400 mg PO once daily	400 mg/day

Dosage Forms

- Capsule: 100 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (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

Commercial: 6 months

Medicaid: 6 months

B. Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes (Off label) (must meet all):

1. Diagnosis of myeloid/lymphoid neoplasms with eosinophilia and JAK2 rearrangement in chronic phase;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Treatment in combination with ALL- or AML-type induction chemotherapy followed by allogeneic HCT (if eligible) for lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and JAK2 rearrangement in blast phase;
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. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance, or member has met initial approval criteria for the covered indications and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 400 mg (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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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

Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None.

- 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® as a category 2A recommendation and the use of Inrebic® as a category 2B recommendation. Inrebic® also has a category 2A recommendation for use after failure or intolerance to Jakafi®.
- 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.

References

1. Inrebic® Prescribing Information. Summit, NJ: Celgene Corporation. August 2019. Available at http://www.inrebicpro.com. Accessed March 25, 2021.
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3. National Comprehensive Cancer Network Guidelines. Myeloproliferative Neoplasms Version 1.2020 Available at https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed March 25, 2021.
4. 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. Accessed March 25, 2021.
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6. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed March 25, 2021.
7. Fedratinib, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed March 25, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated to "fedratinib". 2. Drug(s) Applied was updated to "Inrebic®". 3. Initial Approval criteria I.B "Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes (Off label)" was added and updated. 4. Continued Therapy criteria II.A.1 was rephrased to	03/25/2021	09/14/2021

"Currently receiving medication that has been authorized by RxAdvance…". 5. References were reviewed and updated.		