Original Effective Date: 09/01/2019
Current Effective Date: 06/20/2025
Last P&T Approval/Version: 04/30/2025
Next Review Due By: 04/2026
Policy Number: C17941-A

Inrebic (fedratinib)

PRODUCTS AFFECTED

Inrebic (fedratinib)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Myelofibrosis (MF)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. MYELOFIBROSIS:
1. Documented diagnosis of primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis
   AND
2. Documented GIPSS (genetically inspired prognostic scoring system) of 2 points or greater (int-2

or high risk) OR MIPSS70+ v2.0 (mutation- enhanced international prognostic scoring system plus karyotype, version 2.0) score of 3 points or greater (intermediate, high, or very high risk) [DOCUMENTATION REQUIRED] See Appendix for scoring information
AND

3. Documentation that member is ineligible for allogeneic hematopoietic cell transplantation (HCT)
AND
4. Documentation of baseline assessment of disease (e.g., spleen size, symptoms, Total Symptom Score as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF)) [DOCUMENTATION REQUIRED]
AND
5. Documentation that baseline platelet count is ≥ 50,000/mm^3 (labs dated within the last 4 weeks)
AND
6. Documentation that member has tried and failed or has a labeled contraindication to Jakafi (ruxolitinib)

CONTINUATION OF THERAPY:

A. MYELOFIBROSIS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member's medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation, or held for toxicity
AND
2. Documentation of a positive response to treatment 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.) or reduction in the Total Symptom Score from baseline as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF) [DOCUMENTATION REQUIRED]

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified hematologist or oncologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

400 mg orally once daily

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

Janus Associated Kinase (JAK) Inhibitors

FDA-APPROVED USES:

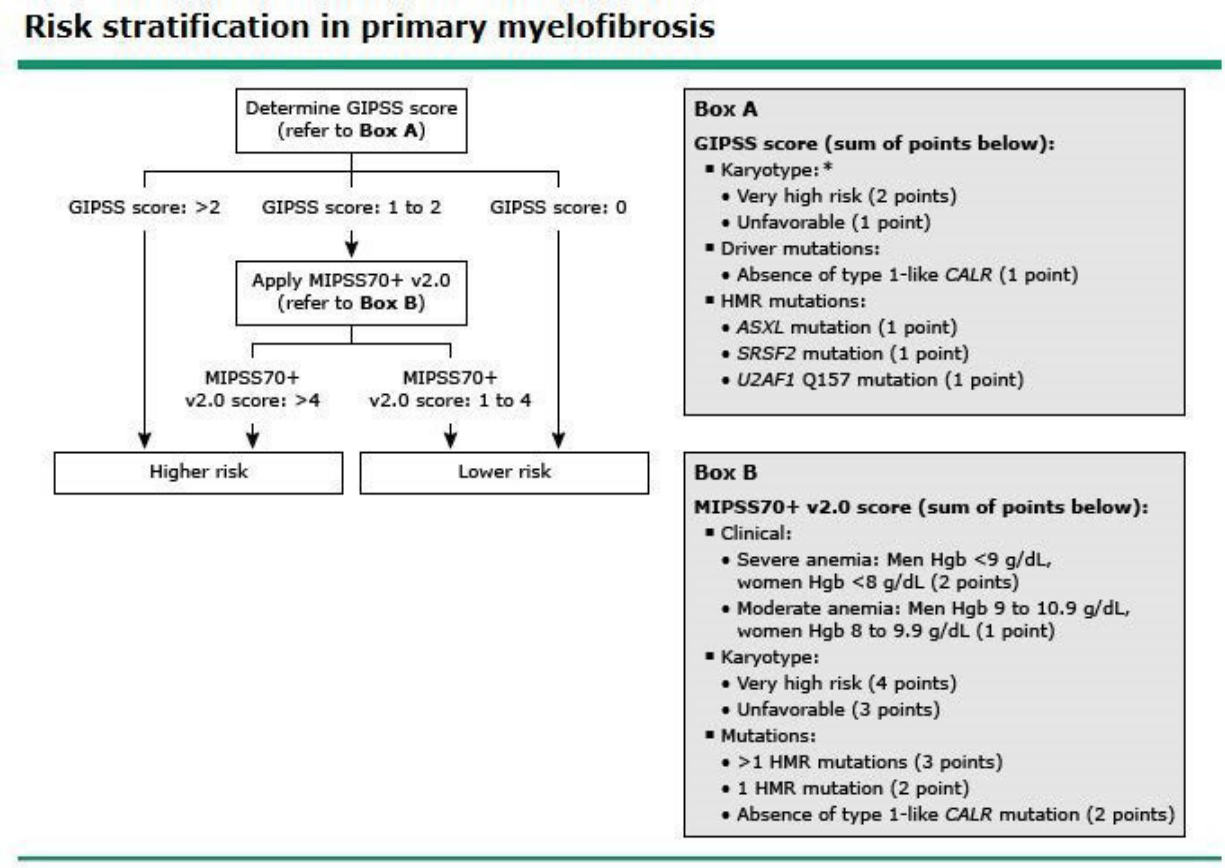
Indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF)

COMPENDIAL APPROVED OFF-LABELED USES:

Myeloid/lymphoid neoplasms with eosinophilia and JAK2 rearrangement (NCCN Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions Version 2.2025 MLNE-8)

APPENDIX

APPENDIX:



BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Myelofibrosis (MF) is a serious and rare bone marrow disorder that disrupts the body's normal production of blood cells. It is classified as a myeloproliferative neoplasm, a group of rare blood cancers that are derived from blood forming stem cells. Myelofibrosis occurs when bone marrow is gradually replaced with fibrous scar tissue, which limits the ability of the bone marrow to make blood cells. The disorder can lead to anemia, weakness, fatigue, and enlargement of the spleen and liver, among other symptoms. In the U.S., between 16,000 and 18,500 are living with myelofibrosis, and 1.5 of every 100,000 people will be diagnosed with myelofibrosis each year. Both men and women are affected, and while the disease can affect people of all ages, the median age at diagnosis ranges from 60 to67 years. Myelofibrosis can cause extreme fatigue, shortness of breath, pain under the ribs, fever, night sweats, itching, and bone pain. The most common presenting complaint in MF is that of severe fatigue, occurring in 50–70% of patients. Symptoms due to an enlarged spleen have been described in 25–50% of patients, while a smaller number note weight loss, and 5– 20% experience low grade fever, bone pain, and night sweats. Approximately 15–30% of patients are asymptomatic, with the diagnosis being made during investigation of splenomegaly (occurring in at least 90% of patients), hepatomegaly (40–70%), or abnormal blood findings. Other findings include but are not limited to pulmonary hypertension, pruritus, thrombotic events, portal vein thrombosis, extramedullary hematopoiesis, bone and joint involvement, and secondary gout. Relief of symptoms and improved quality of life are important goals for all patients with MF. Allogenic hematopoietic cell transplantation can prolong survival with the potential for cure. Up until the approval of Inrebic, therapy consisted of Jakafi or hydroxyurea for patients with symptomatic MF. Selection of therapy is informed by the nature and severity of symptoms, blood counts, kidney and liver function, clinician experience, and member preference. Jakafi and hydroxyurea can provide symptomatic relief, but neither agent has been proven to prolong survival or reduce the risk of leukemic transformation. Jakafi is generally considered to be more effective for relieving MF-related symptoms, but it cannot be used in patients with active infections, and it should be used with care in patients with thrombocytopenia, impaired liver or kidney function, or concurrent use of medications that are strongCYP3A4 inhibitors. In addition, it cannot be abruptly discontinued due to risk of full relapse of disease symptoms. Hydroxyurea is thought to be less effective than Jakafi, but it can relieve moderate splenomegaly and other proliferative manifestations.

Inrebic (fedratinib) is indicated for the treatment of adult patients with intermediate-2 or high- risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) MF. Approval of Inrebic is based on findings from the double-blind, placebo-controlled Phase 3 JAKARTA trial, which included 289 patients with intermediate-2 or high-risk primary myelofibrosis, post-polycythemia vera (PV) myelofibrosis, or post-essential thrombocytopenia (ET) myelofibrosis randomized to receive Inrebic orally at 400 (n = 96) or 500 mg daily (n = 97), or placebo (n = 96), for at least 6 consecutive 4-week cycles. The primary endpoint was spleen response, specifically a ≥35% reduction in spleen volume from baseline; a key secondary endpoint was symptom response, determined as ≥50% reduction in total symptom score assessed via the modified Myelofibrosis Symptom Assessment Form. The results demonstrated a reduction in splenomegaly and symptom burden in patients with MF. The study found that 35 of 96 patients (36%) treated with the Inrebic 400-mg daily dose experienced a 50% or greater reduction in MF related symptoms compared to 1% of patients on placebo. Additionally, Inrebic improved the Total Symptom Score by ≥50% when assessed from baseline to the end of cycle 6 in 40% of patients treated with the 400-mg dose of Inrebic versus 9% of those on the placebo arm.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Inrebic (fedratinib) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Inrebic (fedratinib) include: avoid use with strong and

moderate CYP3A4 inducers.

Exclusions/Discontinuation:
Coadministration of Inrebic with a strong or moderate CYP3A4 inducer (E.G., efavirenz, rifampin) can decrease fedratinib exposure. Decreased exposure may reduce the effectiveness of Inrebic. Avoid Inrebic with strong and moderate CYP3A4 inducers.
Do not start Inrebic in patients with thiamine (vitamin B1) deficiency. However, if thiamine levels are low, replete thiamine prior to starting treatment. While on treatment all patients should receive prophylaxis with oral thiamine and should have thiamine levels assessed as clinically indicated.
Patients that are on treatment with (Jakafi) ruxolitinib before the initiation of Inrebic must taper and discontinue according to the ruxolitinib prescribing information.

OTHER SPECIAL CONSIDERATIONS:
Inrebic (fedratinib) has a Black Box Warning for ENCEPHALOPATHY INCLUDING WERNICKE'S. Serious and fatal encephalopathy, including Wernicke's, has occurred in patients treated with Inrebic. Wernicke's encephalopathy is a neurologic emergency. Assess thiamine levels in all patients prior to starting Inrebic, periodically during treatment, and as clinically indicated. Do not start Inrebic in patients with thiamine deficiency, replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue Inrebic and initiate parenteral thiamine.

Obtain the following blood tests prior to starting treatment with Inrebic, periodically during treatment, and as clinically indicated: thiamine (Vitamin B1) level, complete blood count with platelets, creatinine and BUN, hepatic panel, amylase and lipase.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:
Inrebic CAPS 100MG

REFERENCES

1. Inrebic (fedratinib) capsules, for oral use [prescribing information]. Summit, NJ: Celgene;July 2024.
2. Harrison CN, Schaap N, Vannucchi AM, et al: Janus kinase-2 inhibitor fedratinib in patients with myelofibrosis previously treated with ruxolitinib (JAKARTA-2): a single-arm, open-label, non-randomized, phase 2, multicenter study. Lancet Haematol 2017;4(7):e317-e324

3. Deeg HJ, Bredeson C, Farnia S, et al. Hematopoietic Cell Transplantation as Curative Therapy for Patients with Myelofibrosis: Long-Term Success in all Age Groups. Biol Blood Marrow Transplant 2015; 21:1883.
4. Deeg HJ, Gooley TA, Flowers ME, et al. Allogeneic hematopoietic stem cell transplantation for myelofibrosis. Blood 2003; 102:3912.
5. Harrison C, Kiladjian JJ, Al-Ali HK, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med 2012; 366:787.
6. Verstovsek S, Mesa RA, Gotlib J, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. N Engl J Med 2012; 366:799.
7. Passamonti F, Caramazza D, Maffioli M. JAK inhibitor in CALR-mutant myelofibrosis. N Engl J Med 2014; 370:1168
8. Emanuel RM, Dueck AC, Geyer HL, et al. Myeloproliferative neoplasm (MPN) symptom assessment form total symptom score: prospective international assessment of an abbreviated symptom burden scoring system among patients with MPNs. J Clin Oncol 2012; 30:4098.
9. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms (Version 3.2019). Retrieved 9 October 2019, from https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf
10. National Comprehensive Cancer Network. 2023. Myeloproliferative Neoplasms (Version 3.2022). [online] Available at: < mpn.pdf (nccn.org) > [Accessed 2 April 2023].
11. National Comprehensive Cancer Network. 2024. Myeloproliferative Neoplasms (Version 1.2024). [online] Available at: < mpn.pdf (nccn.org) > [Accessed 10 April 2024].
12. National Comprehensive Cancer Network. 2025. Myeloproliferative Neoplasms (Version 1.2025). [online] Available at: < mpn.pdf (nccn.org) > [Accessed 8 April 2025].

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Compendial Approved Off-Labeled Uses Contraindications/Exclusions/Discontinuation References	Q2 2025
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Background References	Q2 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q2 2023
Q2 2022 Established tracking in new format	Historical changes on file