BlueCross BlueShield Federal Employee Program

INREBIC (fedratinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Inrebic (fedratinib) is an oral kinase inhibitor with activity against wild type and mutationally activated Janus Associated Kinase 2 (JAK2) and FMS-like tyrosine kinase 3 (FLT3). Abnormal activation of JAK2 is associated with myeloproliferative neoplasms (MPNs), including myelofibrosis and polycythemia vera. Inrebic is thought to inhibit cell proliferation and induce apoptotic cell death when JAK2 or FLT3 is mutationally active (1).

Myelofibrosis is a disease in which the bone marrow is replaced by scar tissue resulting in blood cells being made in organs such as the liver and the spleen. This disease is marked by an enlarged spleen, anemia, decreased white blood cells and platelets, and myelofibrosis-related symptoms (2).

Polycythemia vera occurs when too many red blood cells are made in the bone marrow. Patients may also experience an increase in white blood cells and platelets. An overabundance of blood cells can cause the spleen to swell, bleeding problems and blood clots in the veins near the skin surface (phlebitis). In addition, it puts patients at increased risk of stroke or heart attack (2).

Regulatory Status

FDA-approved indication: Inrebic is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocytopenia) myelofibrosis (MF) (1).

Inrebic contains a boxed warning regarding encephalopathy. Serious and fatal encephalopathy, including Wernicke's, has occurred in patients treated with Inrebic. Wernicke's encephalopathy is a neurologic emergency. Thiamine levels should be assessed in all patients prior to starting Inrebic, periodically throughout treatment, and as clinically indicated. Inrebic should not be started in patients with thiamine deficiency; thiamine should be repleted prior to treatment initiation. If encephalopathy is suspected, Inrebic should be discontinued immediately, and parenteral thiamine initiated. Patient should be monitored until symptoms resolve or improve and thiamine levels normalize (1).

The recommended dose of Inrebic is 400 mg taken orally once daily for patients with a baseline

platelet count of greater than or equal to 50 x 10^9/L (1).

Treatment with Inrebic can cause anemia and thrombocytopenia. A complete blood count (CBC) should be obtained at baseline, periodically during treatment, and as clinically indicated. For Grade 3 thrombocytopenia with active bleeding or Grade 4 thrombocytopenia, Inrebic should be interrupted until the thrombocytopenia is resolved to less than or equal to Grade 2 or baseline and the dose restarted at 100 mg daily below the last given dose (1).

The safety and effectiveness of Inrebic in pediatric patients less than 18 years of age have not been established (1).

Summary

Inrebic (fedratinib) is an oral kinase inhibitor with activity against wild type and mutationally activated Janus Associated Kinase 2 (JAK2) and FMS-like tyrosine kinase 3 (FLT3). Abnormal activation of JAK2 is associated with myeloproliferative neoplasms (MPNs), including myelofibrosis and polycythemia vera. Inrebic is thought to inhibit cell proliferation and induce apoptotic cell death when JAK2 or FLT3 is mutationally active. The safety and effectiveness of Inrebic in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Inrebic while maintaining optimal therapeutic outcomes.

References

1. Inrebic [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2023.
2. Clinical manifestations and diagnosis of primary myelofibrosis. UpToDate. Accessed on April 24, 2024.
3. NCCN Drugs & Biologics Compendium® Fedratinib 2024. National Comprehensive Cancer Network, Inc. Accessed on April 24, 2024.