BlueCross BlueShield Federal Employee Program

TIBSOVO (ivosidenib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Tibsovo (ivosidenib) is an oral cancer agent that inhibits isocitrate dehydrogenase-1 (IDH1). Susceptible IDH1 mutations are defined as those leading to increased levels of 2-hydroxyglutarate (2-HG) in the leukemia cells and where efficacy is predicted by 1) clinically meaningful remissions with the recommended dose of ivosidenib and/or 2) inhibition of mutant IDH1 enzymatic activity at concentrations of ivosidenib sustainable at the recommended dosage according to validated methods. The most common of such mutations are R132H and R132C substitutions. Inhibition of the mutant IDH1 enzyme by ivosidenib led to decreased 2-HG levels and induced myeloid differentiation in vitro and in vivo in mouse xenograft models of IDH1-mutated AML (1).

Regulatory Status

FDA-approved indications: Tibsovo is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated for patients with a susceptible IDH1 mutation as detected by an FDA-approved test with: (1)

1. Newly Diagnosed Acute Myeloid Leukemia (AML)
    a. In combination with azacitidine or as monotherapy for the treatment of newly diagnosed AML in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.
2. Relapsed or refractory AML
    a. For the treatment of adult patients with relapsed or refractory AML.
3. Relapsed or refractory Myelodysplastic Syndromes (MDS)
    a. For the treatment of adult patients with relapsed or refractory MDS.
4. Locally Advanced or Metastatic Cholangiocarcinoma
    a. For the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma who have been previously treated.

Tibsovo has a boxed warning for differentiation syndrome in AML and MDS, which can be fatal if not treated. Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells. While there is no diagnostic test for differentiation syndrome, symptoms in patients treated with Tibsovo included noninfectious leukocytosis, peripheral edema, pyrexia, dyspnea, pleural effusion, hypotension, hypoxia, pulmonary edema, pneumonitis, pericardial effusion, rash, fluid overload, tumor lysis syndrome and increased creatinine. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution

(1).

Patients treated with Tibsovo can develop QT (QTc) prolongation and ventricular arrhythmias. Monitor electrocardiograms and electrolytes. If QTc interval prolongation occurs, dose reduce or withhold, then resume dose or permanently discontinue Tibsovo (1).

Guillain-Barré syndrome occurred in <1% of patients treated with Tibsovo. Monitor patients for signs and symptoms of motor and/or sensory neuropathy such as unilateral or bilateral weakness, sensory alterations, paresthesias, or difficulty breathing. Permanently discontinue Tibsovo in patients who are diagnosed with Guillain-Barré syndrome (1).

The safety and effectiveness of Tibsovo in pediatric patients have not been established (1).

Summary

Tibsovo (ivosidenib) is an oral cancer agent that inhibits isocitrate dehydrogenase-1 (IDH1). Tibsovo is indicated for the treatment of adult patients with acute myeloid leukemia (AML), myelodysplastic syndromes (MDS), and locally advanced or metastatic cholangiocarcinoma with a susceptible IDH1 mutation as detected by an FDA-approved test. The safety and effectiveness of Tibsovo in pediatric patients have not been established (1).

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

References

1. Tibsovo [package insert]. Boston, MA: Servier Pharmaceuticals, Inc.; October 2023.
2. NCCN Drugs & Biologics Compendium® Ivosidenib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 9, 2025.