Tibsovo

Description

Tibsovo (ivosidenib)

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 indication: Tibsovo is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated:

1. For the treatment of newly-diagnosed acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test in adult patients who are ≥75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.
2. For the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test.
Tibsovo has a boxed warning for differentiation syndrome, 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-Barre 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, parasthesias, or difficulty breathing. Permanently discontinue Tibsovo in patients who are diagnosed with Guillain-Barre syndrome (1).

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

Related policies
Idhifa

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Tibsovo may be considered medically necessary in patients with acute myeloid leukemia (AML) and if the conditions indicated below are met.

Tibsovo is considered investigational in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements
Age 18 years of age or older

Diagnosis
Section: Prescription Drugs  Effective Date: July 1, 2019
Subsection: Antineoplastic Agents  Original Policy Date: July 27, 2018
Subject: Tibsovo  Page: 3 of 5

The patient must have the following:

1. Relapsed or refractory acute myeloid leukemia (AML)
2. Newly-diagnosed acute myeloid leukemia (AML)
   a. Patient is 75 years of age or older OR patient has comorbidities that preclude the use of intensive induction chemotherapy

   AND ALL of the following:
   1. Susceptible isocitrate dehydrogenase-1 (IDH1) mutation AML detected by an FDA-approved test
   2. Prescriber agrees to monitor for signs and symptoms of differentiation syndrome
   3. Prescriber agrees to monitor electrocardiograms (ECGs) for QTc prolongation
   4. Prescriber agrees to monitor for signs and symptoms of Guillain-Barre syndrome

Prior – Approval Renewal Requirements

Age  18 years of age or older

Diagnosis

The patient must have the following:

1. Relapsed or refractory acute myeloid leukemia (AML)
2. Acute myeloid leukemia (AML)
   a. Patient is 75 years of age or older OR patient has comorbidities that preclude the use of intensive induction chemotherapy

   AND ALL of the following:
   1. NO disease progression or unacceptable toxicity
   2. Prescriber agrees to monitor for signs and symptoms of differentiation syndrome
   3. Prescriber agrees to monitor ECGs for QTc prolongation
   4. Prescriber agrees to monitor for signs and symptoms of Guillain-Barre syndrome

Policy Guidelines

Pre - PA Allowance

None
### Prior - Approval Limits

**Quantity** 180 tablets per 90 days

**Duration** 12 months

### Prior – Approval *Renewal* Limits

Same as above

### Rationale

**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) 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


### Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 2018</td>
<td>Addition to PA</td>
</tr>
<tr>
<td>September 2018</td>
<td>Annual review</td>
</tr>
<tr>
<td>November 2018</td>
<td>Annual review. Changed monitoring of ECG for QTc prolongation requirements per SME</td>
</tr>
<tr>
<td>March 2019</td>
<td>Annual review</td>
</tr>
<tr>
<td>May 2019</td>
<td>Addition of indication of newly-diagnosed AML in patients 75 years and older or in patients that have comorbidities that preclude the use of intensive induction chemotherapy</td>
</tr>
<tr>
<td>June 2019</td>
<td>Annual review</td>
</tr>
</tbody>
</table>

### Keywords
<table>
<thead>
<tr>
<th>Section:</th>
<th>Prescription Drugs</th>
<th>Effective Date:</th>
<th>July 1, 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subsection:</td>
<td>Antineoplastic Agents</td>
<td>Original Policy Date:</td>
<td>July 27, 2018</td>
</tr>
<tr>
<td>Subject:</td>
<td>Tibsovo</td>
<td>Page:</td>
<td>5 of 5</td>
</tr>
</tbody>
</table>

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.