BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

TIBSOVO® (ivosidenib) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Tibsovo (ivosidenib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual has a confirmed diagnosis of **ONE** of the following:
    a. In combination with azacitidine or as monotherapy 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 adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy

b. Adult 18 years of age or older with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test

c. Adult 18 years of age or older with relapsed or refractory myelodysplastic syndromes (MDS) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test

d. Adult 18 years of age or older with previously treated, locally advanced or metastatic cholangiocarcinoma with an isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test

e. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

3. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. A susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test
   b. Electrocardiogram (ECG)
   c. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as use with strong CYP3A inducers (e.g. carbamazepine, phenobarbital, phenytoin, rifampin, others)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Tibsovo (ivosidenib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual's condition has responded while on therapy with response defined as there is no evidence of disease progression or unacceptable toxicity

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any other significant adverse drug effects that recurs after dose adjustment that may exclude continued use such as:
    a. Differentiation syndrome with severe pulmonary symptoms and/or renal dysfunction
    b. Noninfectious leukocytosis
    c. QTc interval prolongation with signs and symptoms of life-threatening arrhythmia
    d. Development of Guillain-Barre syndrome
    e. Any severe or life-threatening toxicity that has recurred

6. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as use with strong CYP3A inducers (e.g. carbamazepine, phenobarbital, phenytoin, rifampin, others)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Tibsovo (ivosidenib) is an isocitrate dehydrogenase-1 (IDH1) enzyme inhibitor indicated for patients with a susceptible IDH1 mutation as detected by an FDA-approved test with: newly diagnosed acute myeloid leukemia (AML) 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; for the treatment of adult patients with relapsed or refractory AML; for the treatment of adult patients with relapsed or refractory myelodysplastic syndromes (MDS); for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma who have been previously treated.

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 leads to decreased 2-HG levels, reduced blast counts, and increased percentages of mature myeloid cells.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Co-morbidities that precluded the use of intensive induction chemotherapy based on at least **ONE** of the following criteria:

- Baseline Eastern Cooperative Oncology Group (ECOG) performance status of ≥ 2
- Severe cardiac disease
- Severe pulmonary disease
- Hepatic impairment with bilirubin > 1.5 times the upper limit of normal
- Creatinine clearance < 45 mL/min

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Acute Myeloid Leukemia:

Therapy for AML with FLT3-ITD mutation
Hypomethylating agents (5-azacytidine or decitabine) + sorafenib
Therapy for AML with IDH2 mutation
Enasidenib
Therapy for AML with IDH1 mutation
Ivosidenib
Therapy for CD33-positive AML
Gemtuzumab ozogamicin

Response criteria for AML:

CR (complete remission) was defined as <5% blasts in the bone marrow, no evidence of disease, and full recovery of peripheral blood counts (platelets >100,000/microliter and absolute neutrophil counts [ANC] >1,000/microliter).

CRh (complete remission with partial hematological recovery) was defined as <5% of blasts in the bone marrow, no evidence of disease, and partial recovery of peripheral blood counts (platelets >50,000/microliter and ANC >500/microliter).

DOR (duration of response) was defined as time since first response of CR or CRh to relapse or death, whichever is earlier.

Resources:

Tibsovo (ivosidenib) product information, revised by Servier Pharmaceutical, LLC. 10-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 01, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 3.2024. Updated May 17, 2024. Available at https://www.nccn.org. Accessed July 01, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Biliary Tract Cancers Version 2.2024. Updated April 19, 2024. Available at https://www.nccn.org. Accessed July 01, 2024.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.