BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

TIBSOVO® (ivosidenib) oral

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 precertification 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:** [**Agent Name]** 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 is 18 years of age or older.

  3. Individual has a confirmed diagnosis of **ONE** of the following:
     a. Relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH-1) mutation

b. Newly diagnosed AML with a susceptible isocitrate dehydrogenase-1 (IDH-1) mutation in an adult patient who is ≥ 75 years old or who has comorbidities that preclude use of intensive induction chemotherapy (See Definitions section) used in combination with azacytidine or as monotherapy

c. Previously treated, locally advanced or metastatic cholangiocarcinoma with an isocitrate dehydrogenase-1 (IDH1) mutation

d. 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

4. The 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 in the blood or bone marrow as detected by an FDA-approved test
   b. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2

5. Individual is not using strong CYP3A inducers (ex. carbamazepine, phenobarbital, phenytoin, rifampin, others)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Tibsovo (ivosidenib) 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:
   a. No evidence of disease progression
   b. Documented evidence of efficacy, disease stability and/or improvement

3. Individual has been adherent with the medication

4. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
   a. QTc interval prolongation with signs and symptoms of life-threatening arrhythmia
   b. Development of Guillain-Barre syndrome
   c. Any severe or life-threatening toxicity that has recurred

5. Individual is not using strong CYP3A inducers (ex. carbamazepine, phenobarbital, phenytoin, rifampin, others)

Renewal duration: 12 months

PHARMACY COVERAGE GUIDELINE

TIBSOVO® (ivosidenib) oral

- 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 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 (ivosidenib) is also indicated 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:

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	

PHARMACY COVERAGE GUIDELINE

TIBSOVO® (ivosidenib) oral

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. 05-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 06, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 2.2022 – Updated June 14, 2022. Available at https://www.nccn.org. Accessed August 06, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Hepatobiliary Cancers Version 2.2022 – Updated July a5, 2022. Available at https://www.nccn.org. Accessed August 06, 2022.

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.