PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 9/20/2018**
SECTION: DRUGS	**LAST REVIEW DATE: 8/19/2021**
	LAST CRITERIA REVISION DATE: 8/19/2021
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Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Tibsovo (ivosidenib) is considered ***medically necessary*** and will be approved when **ALL** of 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. 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)

     c. 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. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring 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. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Tibsovo (ivosidenib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  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 responded while on therapy
     a. Response is defined as:
        i. No evidence of disease progression
        ii. 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

a. Significant adverse effect such as:
   i. QTc interval prolongation with signs and symptoms of life-threatening arrhythmia
   ii. Development of Guillain-Barre syndrome
   iii. Any severe or life-threatening toxicity that has recurred

5. There are no significant interacting drugs

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 a Non-cancer Medications**

2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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. 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

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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	

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.

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Resources:

Tibsovo (ivosidenib) product information, revised by Agios Pharmaceuticals, Inc. 05-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on June 28, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 3.2021 – Updated March 02,2021. Available at https://www.nccn.org. Accessed on June 28, 2021.

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.