Clinical Policy: Ivosidenib (Tibsovo)

Reference Number: ERX.SPA.294
Effective Date: 12.01.18
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Ivosidenib (Tibsovo®) is an isocitrate dehydrogenase-1 (IDH-1) inhibitor.

FDA Approved Indication(s)
Tibsovo is indicated for the treatment of adult 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, in adults ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy
- Relapsed or refractory AML
- Locally advanced or metastatic cholangiocarcinoma who have been previously treated.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Tibsovo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Myeloid Leukemia (must meet all)**:**

1. Diagnosis of AML;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a, b, or c):
   a. Disease is newly diagnosed, prescribed in combination with azacitidine or as monotherapy, and one of the following (i or ii):
      i. Age ≥ 75 years;
      ii. Medical justification supports inability to use intensive induction chemotherapy (*see Appendices B and D for examples*);*
   b. Disease is relapsed or refractory;
   c. Age ≥ 60 years and one of the following (i or ii):
      i. Member is not a candidate for intensive induction therapy;
      ii. Used for post-induction therapy with previous lower-intensity therapy (*see Appendix B for examples*);*

   **Prior authorization may be required.*
5. Presence of an IDH1 mutation;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 500 mg (2 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Commercial – Length of Benefit
Medicaid – 6 months

B. Cholangiocarcinoma (must meet all)**:**
1. Diagnosis of locally advanced or metastatic cholangiocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is positive for an IDH1 mutation;
5. Prescribed as a single agent for disease progression on or after systemic treatment;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 500 mg (2 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

C. Chondrosarcoma (off-label) (must meet all)**:**
1. Diagnosis of conventional (grade 1-3) or dedifferentiated chondrosarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is positive for an IDH1 mutation;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 500 mg (2 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

D. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Tibsovo for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 500 mg (2 tablets) per day;
   b. New dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: acute myeloid leukemia
FDA: Food and Drug Administration
IDH1: isocitrate dehydrogenase-1
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cytarabine with idarubicin or daunorubicin	AML Age < 60 years: example of intensive induction therapy: cytarabine 100 – 200 mg/m^2 continuous IV infusion x 7 days with idarubicin 12 mg/m^2 IV or daunorubicin 60-90 mg/m^2 IV x 3 days	Varies
cytarabine with idarubicin or daunorubicin or mitoxantrone	AML Age ≥ 60 years: example of intensive induction therapy: cytarabine 100 – 200 mg/m^2 continuous IV infusion x 7 days with idarubicin 12 mg/m^2 IV or daunorubicin 60-90 mg/m^2 IV x 3 days or mitoxantrone 12 mg/m^2 x 3 days	Varies
gemcitabine+cisplatin, 5-fluorouracil+ oxaliplatin, capecitabine+cisplatin, 5-fluoruracil, capecitabine, gemcitabine, FOLFOX (leucovorin, fluorouracil, oxaliplatin), FOLFIRI (leucovorin, fluorouracil, irinotecan), Stivarga®	Cholangiocarcinoma Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): differentiation syndrome

Appendix D: General Information

Patient or disease state characteristics that may preclude use of intensive induction therapy include but are not limited to the following examples:

- Limited functional status as indicated by an Eastern Cooperative Oncology Group (ECOG) performance status of ≥ 2
- Significant comorbidity (e.g., severe cardiac, pulmonary or renal disease)
- Adverse features (e.g., AML without favorable cytogenetics or molecular markers, therapy-related AML, antecedent hematologic disorder)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AML, cholangiocarcinoma	500 mg PO QD until disease progression or unacceptable toxicity	500 mg/day

VI. Product Availability

Tablet: 250 mg

VII. References

1. Tibsovo Prescribing Information. Cambridge, MA: Agios Pharmaceuticals, Inc.; May 2022. Available at: www.tibsovo.com. Accessed July 28, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 28, 2022.
3. National Comprehensive Cancer Network Guidelines. Acute Myelogenous Leukemia Version 1.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed July 28, 2022.
4. National Comprehensive Cancer Network Guidelines. Hepatobiliary Cancers Version 2.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed July 28, 2022.
5. National Comprehensive Cancer Network Guidelines. Bone Cancer Version 2.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed July 28, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.21.18	11.18
Added new FDA labeled indication for newly diagnosed AML (was previously presented as an NCCN recommended use); criteria revised to include patient or disease state characteristics that may preclude intensive induction therapy; added NCCN recommended uses for relapsed disease or disease in remission post-Tibsovo therapy; removed requirement for FDA-approved testing; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	06.11.19	08.19
4Q 2019 annual review: no significant changes; FDA/NCCN dosing limitation added; induction therapy examples for patients over 60 added; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	08.27.19	11.19
4Q 2020 annual review: added criteria for biliary tract cancer per NCCN 2A off label indication; references reviewed and updated.	08.17.20	11.20
4Q 2021 annual review: added coverage for age ≥ 60 with either not candidate for induction therapy or used for post-induction therapy with previous lower intensity therapy as per NCCN; updated Appendix D: General Information; RT4: updated new FDA labeled indication for locally advanced or metastatic cholangiocarcinoma (previously off-label supported indication) who have been previously treated; references reviewed and updated.	07.14.21	11.21
RT4: revised criteria per updated FDA approved indication to include combination therapy with azacitidine or monotherapy for treatment of AML.	06.13.22	
4Q 2022 annual review: per NCCN, added chondrosarcoma as a coverable off-label diagnosis; references reviewed and updated.	07.28.22	11.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of

physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.