RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	ivosidenib
Policy Number:	RxA.508
Drug(s) Applied:	Tibsovo®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Ivosidenib (Tibsovo®) is an isocitrate dehydrogenase-1 (IDH-1) inhibitor. It is indicated for:

- Treatment of newly diagnosed acute myeloid leukemia (AML) with a susceptible 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.
- Treatment of adult patients with relapsed or refractory AML with a susceptible IDH1 mutation as detected by an FDA-approved test.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ivosidenib (Tibsovo®)	AML	500 mg PO once daily until disease progression or unacceptable toxicity	500 mg/day

Dosage Forms

- Tablet: 250 mg

Clinical Policy

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

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 and (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 has relapsed after or is in remission following Tibsovo® therapy;

c. Disease has relapsed after or is refractory to induction 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 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: 6 months
Medicaid: 6 months

B. Biliary Tract Cancers (Intrahepatic and Extrahepatic Cholangiocarcinoma) (Off- label use) (must meet all)**:**

1. Diagnosis of unresectable and metastatic cholangiocarcinoma;
2. Prescribed by or in consultation with an oncologist or gastroenterologist;
3. Age ≥ 18 years;
4. Presence of an IDH1 mutation;
5. Disease has progressed on or after systemic treatment recommended by NCCN;
6. Tibsovo® will be used as a single agent for subsequent treatment;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 500 mg 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: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All indication in section I (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy 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 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: 12 months
Medicaid: 12 months

III. Appendices

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

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cytarabine with idarubicin or daunorubicin	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	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

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)
- AML without favourable cytogenetics or molecular markers
- AML secondary to prior antineoplastic therapy
- AML preceded by a hematologic disorder such as myelodysplastic syndrome

References

1. Tibsovo Prescribing Information. Cambridge, MA: Agios Pharmaceuticals, Inc.; May 2019. Available at: www.tibsovo.com. Accessed September 17, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug compendium. Accessed September 17, 2020.
3. National Comprehensive Cancer Network Guidelines. Acute Myeloid Leukemia Version 3.2020. Available at www.nccn.org. Accessed September 17, 2020.
4. National Comprehensive Cancer Network Guidelines. Hepatobiliary Cancer Version 5.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed November 05, 2020.
5. Ghassan K. Abou-Alfa, MD et al.; Ivosidenib in IDH1-mutant, chemotherapy-refractory

cholangiocarcinoma (ClarIDHy): a multicentre, randomised, double-blind, placebo-controlled, phase 3 study; Available at: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(20)30157-1/fulltext. Accessed November 05, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed 1. Clinical policy title updated 2. Line of business policy applies to was updated to All lines of business 3. Age criteria for Initial approval criteria was updated to ≥ 75 years from ≥ 60 years. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Added criteria for off-label use cholangiocarcinoma. 6. Reference reviewed and updated.	11/06/2020	12/07/2020