Clinical Policy: Ivosidenib (Tibsovo)

Reference Number: CP.PHAR.137
Effective Date: 08.21.18
Last Review Date: 11.25
Line of Business: Commercial, HIM, 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 (IDH1) 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 or older, or who have comorbidities that preclude use of intensive induction chemotherapy
- Relapsed or refractory AML
- Relapsed or refractory myelodysplastic syndromes (MDS)
- 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.

It is the policy of health plans affiliated with Centene Corporation® 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 or b):
   a. Tibsovo is prescribed for induction, post-induction, or consolidation therapy and both of the following (i and ii):
      i. Tibsovo is prescribed in combination with azacitidine or as monotherapy;
      ii. One of the following (1 or 2):
         1) Age ≥ 75 years and disease is newly diagnosed;
         2) Member is not a suitable candidate for or declines intensive induction chemotherapy;
   b. Disease is relapsed or refractory and Tibsovo is prescribed as a single agent;
5. Presence of an IDH1 mutation;
6. For Tibsovo requests, member must use generic ivosidenib, if available, unless contraindicated or clinically significant adverse effects are experienced;

7. 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/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

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. For Tibsovo requests, member must use generic ivosidenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. 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/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Myelodysplastic Syndromes (must meet all)**:**

1. Diagnosis of MDS;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. One of the following (a, b, or c):
   a. Disease is relapsed or refractory;
   b. Disease progression, no response, or intolerance to prior systemic treatment;
   c. Disease is higher-risk (i.e., IPSS-R [intermediate, high, or very high]);
5. Presence of an IDH1 mutation;
6. For Tibsovo requests, member must use generic ivosidenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. 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/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

D. 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. For Tibsovo requests, member must use generic ivosidenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
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/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

E. Glioma (off-label) (must meet all)**:**

1. Diagnosis of oligodendroglioma or astrocytoma;
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;
6. Member is unable to tolerate Voranigo®;
7. For Tibsovo requests, member must use generic ivosidenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. 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/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

F. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, 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. For Tibsovo requests, member must use generic ivosidenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. 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:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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
IPSS-R: revised International Prognostic Scoring System
MDS: myelodysplastic syndromes
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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of induction therapy: cytarabine with idarubicin or daunorubicin, cytarabine with idarubicin or daunorubicin or mitoxantrone	AML Varies	Varies
gemcitabine+cisplatin ± Imfinzi® (durvalumab), gemcitabine+cisplatin ± Keytruda® (pembrolizumab), 5-fluorouracil+ oxaliplatin, capecitabine+cisplatin, 5-fluoruracil, capecitabine, gemcitabine, FOLFOX (leucovorin, fluorouracil, oxaliplatin), FOLFIRI (leucovorin, fluorouracil, irinotecan), Stivarga®	Cholangiocarcinoma Varies	Varies
azacitidine, decitabine ± cedazuridine, lenalidomide, antithymocyte globulin ± cyclosporine ± eltrombopag, high-intensity chemotherapy regimens (e.g., idarubicin-,	MDS Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cytarabine-, fludarabine-, and topotecan-based regimens)		

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 in AML and MDS

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, hepatic, 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, MDS	500 mg PO QD until disease progression or unacceptable toxicity For patients with AML or MDS without disease progression or unacceptable toxicity, continue Tibsovo for a minimum of 6 months to allow time for clinical response	500 mg/day

VI. Product Availability

Tablet: 250 mg

VII. References

1. Tibsovo Prescribing Information. Boston, MA: Servier Pharmaceuticals, LLC.; October 2023. Available at: https://www.tibsovopro.com/pdf/prescribinginformation.pdf. Accessed July 7, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 28, 2025.
3. National Comprehensive Cancer Network Guidelines. Acute Myeloid Leukemia Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 28, 2025.

4. National Comprehensive Cancer Network Guidelines. Myelodysplastic Syndromes Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed August 28, 2025.
5. National Comprehensive Cancer Network Guidelines. Hepatobiliary Cancers Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf. Accessed August 28, 2025.
6. National Comprehensive Cancer Network Guidelines. Bone Cancer Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed August 28, 2025.
7. National Comprehensive Cancer Network Guidelines. Central Nervous System Cancers Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed August 28, 2025.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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 per NCCN; updated Appendix D: General Information; modified reference from HIM.PHAR.21 to HIM.PA.154; added legacy WCG auth durations (WCG.CP.PHAR.137 to be retired); RT4: updated new FDA labeled indication for locally advanced or metastatic cholangiocarcinoma (previously off-label supported indication) who have been previously treated; added requirement for use of generic if available; references reviewed and updated.	07.14.21	11.21
Corrected last review date in header from 02.22 to 11.21.	12.15.21	
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
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; consolidated legacy WCG auth duration to standard Medicaid auth duration; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.28.22	11.22
4Q 2023 annual review: per NCCN, added oligodendroglioma as a coverable off-label diagnosis; references reviewed and updated.	08.07.23	11.23
RT4: added newly approved MDS indication; for Appendix B, added therapeutic alternative examples of initial systemic therapies for MDS; updated boxed warning as differentiation syndrome applies to AML and MDS per prescriber information.	11.27.23	02.24
4Q 2024 annual review: renamed section I.E. from "Oligodendroglioma" to "Glioma," removed qualifiers of	07.11.24	11.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
"recurrent or progressive" from oligodendroglioma, and added astrocytoma as potential diagnosis per NCCN; references reviewed and updated.		
4Q 2025 annual review: revised Medicaid and HIM initial approval durations to 12 months; for AML, removed the age ≥ 60 years pathway, removed requirement that disease is newly diagnosed, added requirement for monotherapy use in relapsed/refractory disease, and replaced medical justification requirement for inability to use intensive induction chemotherapy with option to either be unsuitable candidate or decline per NCCN; for MDS, added option for higher-risk disease per NCCN; for glioma indication, added requirement for lack of Voranigo tolerability per NCCN; references reviewed and updated.	07.07.25	11.25

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.