

Clinical Policy: Ivosidenib (Tibsovo)

Reference Number: CP.PHAR.137

Effective Date: 08.21.18

Last Review Date: 02.24

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 old 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 \geq 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 \geq 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 \geq 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. 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 – 6 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 \geq 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 – 6 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 \geq 18 years;
 4. Member meets one of the following (a or b):
 - a. Disease is relapsed or refractory;
 - b. Disease progression, no response, or intolerance to prior systemic treatment;
 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 – 6 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 \geq 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 – 6 months

Commercial – 12 months or duration of request, whichever is less

E. Oligodendroglioma (off-label) (must meet all):

1. Diagnosis of recurrent or progressive oligodendroglioma;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Disease is positive for an IDH1 mutation;
5. Prescribed as a single agent;
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 – 6 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

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 |
|--|---|-------------------------|
| cytarabine with idarubicin or daunorubicin | <u>AML</u> <u>Age < 60 years: example of intensive induction therapy:</u> 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 | <u>AML</u> <u>Age ≥ 60 years: example of intensive induction therapy:</u> 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-fluorouracil, capecitabine, gemcitabine, FOLFOX (leucovorin, fluorouracil, oxaliplatin), FOLFIRI (leucovorin, fluorouracil, irinotecan), Stivarga [®] | <u>Cholangiocarcinoma</u> Varies | Varies |
| azacitidine, decitabine ± cedazuridine, lenalidomide, antithymocyte globulin ± cyclosporine ± eltrombopag, high-intensity chemotherapy regimens (e.g., idarubicin-, cytarabine-, fludarabine-, | <u>MDS</u> Varies | Varies |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|-------------------------------|----------------|--------------------------------|
| 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.accessdata.fda.gov/drugsatfda_docs/label/2023/211192s0111bl.pdf. Accessed November 27, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 27, 2023.
3. National Comprehensive Cancer Network Guidelines. Acute Myeloid Leukemia Version 4.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 7, 2023.

4. National Comprehensive Cancer Network Guidelines. Myelodysplastic Syndromes Version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed November 27, 2023.
5. National Comprehensive Cancer Network Guidelines. Hepatobiliary Cancers Version 2.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf. Accessed August 7, 2023.
6. National Comprehensive Cancer Network Guidelines. Bone Cancer Version 1.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed August 7, 2023.
7. National Comprehensive Cancer Network Guidelines. Central Nervous System Cancers Version 1.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed August 7, 2023.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|----------|-------------------|
| No significant changes; added HIM line of business per SDC. | 02.01.19 | |
| 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; references reviewed and updated. | 06.11.19 | 08.19 |
| 4Q 2019 annual review: FDA/NCCN dosing limitation added; induction therapy examples for patients over 60 added; 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 \geq 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 | |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|----------|-------------------|
| 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 |

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.

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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.

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