Tibsovo® (ivosidenib)
(Oral)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Tibsovo 250 mg tablets: 2 tablets per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- 500 mg daily

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Will not be used in combination with other isocitrate dehydrogenase (IDH)-inhibitors (e.g., enasidenib, olutasidenib, etc.); **AND**
- Patient will have a baseline electrocardiogram (ECG) prior to start of therapy and periodically during therapy; **AND**
- Patient has a baseline QTc interval of ≤ 470 ms AND patient does not have a history of long QT syndrome; **AND**
- Patient will avoid concomitant therapy with any of the following:
  - Coadministration with strong CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
  - Coadministration with strong or moderate CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, erythromycin, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

- Coadministration with QTc prolonging drugs (e.g., amiodarone, haloperidol, tizanidine, etc.) or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

- Patient has isocitrate dehydrogenase-1 (IDH1) mutation-positive disease as detected by an FDA-approved or CLIA-compliant test❖; **AND**

Acute Myeloid Leukemia (AML) † ‡ Φ [1-4,7,9]

- Used as induction therapy †; **AND**
  - Used as single-agent therapy or in combination with azacitidine; **AND**
    - Used for newly diagnosed disease in patients ≥75 years of age; **OR**
    - Used in patients with newly diagnosed disease who are not candidates for, or have comorbidities that preclude use of, or declines intensive induction chemotherapy; **OR**
- Used as post-induction therapy ‡; **AND**
  - Used as single-agent therapy or in combination with azacitidine; **AND**
  - Used following response to a previous lower intensity therapy with the same regimen; **OR**
- Used as consolidation therapy ‡; **AND**
  - Used as single-agent therapy or in combination with azacitidine; **AND**
  - Used as continuation of low-intensity regimen used for induction in patients with poor-risk AML, therapy-related AML other than CBF-AML, antecedent MDS/CMML, or cytogenetic changes consistent with MDS (AML-MRC); **OR**
- Used for relapsed or refractory disease; **AND**
  - Used as a single agent †; **OR**
  - Used as a component of repeating the initial successful induction regimen if it has been ≥ 12 months since the induction regimen ‡; **AND**
    - Treatment has not been administered continuously; **AND**
    - Treatment was not previously stopped due to development of clinical resistance

Myelodysplastic Syndromes (MDS) † Φ [1,11]

- Used as single agent therapy; **AND**
- Patient has relapsed or refractory disease

Central Nervous System (CNS) Cancers ‡ [3,13]

- Used as single agent treatment; **AND**
  - Used as adjuvant treatment; **AND**
    - Patient has WHO grade 2 Astrocytoma or 1p19q codeleted oligodendroglioma; **AND**
      - Patient has Karnofsky Performance Status (KPS) ≥ 60 with residual or recurrent tumor after resection or biopsy and upfront treatment with radiation therapy (RT) and chemotherapy is not preferred; **OR**

- Patient has poor KPS <60; **OR**

- Used for recurrent or progressive disease; **AND**
  - Patient has Karnofsky Performance Status (KPS) ≥ 60; **AND**
    - Patient has WHO grade 2 Astrocytoma or 1p19q codeleted oligodendroglioma; **AND**
      - Used after radiation therapy plus chemotherapy; **OR**
    - Patient has WHO grade 3 1p19q codeleted oligodendroglioma

Cholangiocarcinoma (including both Intrahepatic and Extrahepatic disease) † Φ [1,3,5,6]

- Used as a single agent; **AND**
- Used as subsequent treatment for progression on or after systemic treatment for unresectable, resected gross residual (R2), locally advanced, or metastatic disease

Bone Cancer (Chondrosarcoma) ‡ [3,8]

- Used as a single agent; **AND**
- Patient has conventional (grades 1-3) or dedifferentiated (osteosarcoma) disease

❖*If confirmed using an immunotherapy assay-http://www.fda.gov/companiondiagnostics*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,3,13]

Coverage may be renewed based on the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: symptoms of differentiation syndrome (e.g., fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, and hepatic, renal, or multi-organ dysfunction), QTc interval prolongation, Guillain-Barre Syndrome, etc.; **AND**

AML

- Disease stabilization or improvement as evidenced by a complete response [CR] (i.e. morphologic, cytogenetic or molecular complete response CR), complete hematologic response or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH

MDS

- Disease stability and/or improvement as indicated by one of the following: decrease in bone marrow blasts percentage, increase in platelets, increase in hemoglobin, decrease in red

blood cell and/or platelet transfusions (if transfusion dependent), increase in WBC/ANC over pretreatment values, or reduction in abnormal cytogenetic metaphases

Cholangiocarcinoma, CNS Cancers, and Bone Cancer

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

V. Dosage/Administration [1,8,10]

Indication	Dose
AML	<u>Azacitidine Combo-therapy</u> 500 mg (2 tablets) orally once daily until disease progression or unacceptable toxicity. Start Tibsovo administration on Cycle 1 Day 1 in combination with azacitidine 75 mg/m^2 subcutaneously or intravenously once daily on Days 1-7 (or Days 1-5 and 8-9) of each 28-day cycle. <u>Monotherapy</u> 500 mg (2 tablets) orally once daily until disease progression or unacceptable toxicity. ***NOTE:** For patients with AML without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response.*
MDS	500 mg (2 tablets) orally once daily until disease progression or unacceptable toxicity. ***NOTE:** For patients with MDS without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response.*
All Other Indications	500 mg (2 tablets) orally once daily until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

<u>HCPCS Code:</u>

- J8999: Prescription drug, oral, chemotherapeutic, nos
- C9399: Unclassified drugs or biologicals

<u>NDC:</u>

- Tibsovo 250 mg tablets: 72694-0617-xx

VII. References

1. Tibsovo [package insert]. Boston, MA; Servier Pharmaceuticals, October 2023. Accessed June 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 3.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN

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3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for ivosidenib. 2024 National Comprehensive Cancer Network. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
4. DiNardo CD, Stein EM, de Botton S, et al. Durable Remissions with Ivosidenib in IDH1-Mutated Relapsed or Refractory AML. N Engl J Med. 2018 Jun 21;378(25):2386-2398. doi: 10.1056/NEJMoa1716984. Epub 2018 Jun 2.
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Biliary Tract Cancers. Version 2.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
6. Abou-Alfa GK, Macarulla T, Javle MM, et al. Ivosidenib in IDH1-mutant, chemotherapy-refractory cholangiocarcinoma (ClarIDHy): a multicentre, randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(6):796-807. doi:10.1016/S1470-2045(20)30157-1.
7. Roboz GJ, DiNardo CD, Stein EM, et al. Ivosidenib induces deep durable remissions in patients with newly diagnosed IDH1-mutant acute myeloid leukemia. Blood. 2020;135(7):463-471. doi:10.1182/blood.2019002140.
8. Tap WD, Villalobos VM, Cote GM, et al. Phase I study of the mutant IDH1 inhibitor ivosidenib: safety and clinical activity in patient with advanced chondrosarcoma. J Clin Oncol 2020;38L1693-1701.
9. Montesinos P, Recher C, Vives S, et al. Ivosidenib and Azacitidine in IDH1-Mutated Acute Myeloid Leukemia. N Engl J Med 2022; 386:1519-1531. doi: 10.1056/NEJMoa2117344
10. Mellinghoff IK, Ellingson BM, Touat M, et al. Ivosidenib in Isocitrate Dehydrogenase 1-Mutated Advanced Glioma. J Clin Oncol. 2020 Oct 10;38(29):3398-3406. doi: 10.1200/JCO.19.03327. Epub 2020 Jun 12. PMID: 32530764; PMCID: PMC7527160.
11. Sallman DA, Foran JM, Watts JM, et al. Ivosidenib in patients with IDH1-mutant relapsed/refractory myelodysplastic syndrome (R/R MDS): Updated enrollment and results of a phase 1 dose-escalation and expansion substudy. Journal of Clinical Oncology 40, no. 16_suppl (June 01, 2022) 7053-7053. DOI: 10.1200/JCO.2022.40.16_suppl.7053.

12. Cheson BD, Greenberg PL, Bennett JM, et al. Clinical application and proposal for modification of the International Working Group (IWG) response criteria in myelodysplasia. Blood. 2006 Jul 15;108(2):419-25. doi: 10.1182/blood-2005-10-4149.
13. Zeidan, AM, Platzbecker U, Bewersdorf, JP, et al. Consensus proposal for revised International Working Group 2023 response criteria for higher-risk myelodysplastic syndromes. Blood. 2023 Apr 27;141(17):2047-2061. doi: 10.1182/blood.2022018604.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C22.1	Intrahepatic bile duct carcinoma
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C40.00	Malignant neoplasm of scapula and long bones of unspecified upper limb
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.10	Malignant neoplasm of short bones of unspecified upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.20	Malignant neoplasm of long bones of unspecified lower limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.30	Malignant neoplasm of short bones of unspecified lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.80	Malignant neoplasm of overlapping sites of bone and articular cartilage of unspecified limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.90	Malignant neoplasm of unspecified bones and articular cartilage of unspecified limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb
C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx

ICD-10	ICD-10 Description
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.0	Malignant neoplasm of spinal cord
C72.9	Malignant neoplasm of central nervous system, unspecified
C92.00	Acute myeloblastic leukemia not having achieved remission
C92.01	Acute myeloblastic leukemia in remission
C92.02	Acute myeloblastic leukemia, in relapse
C92.50	Acute myelomonocytic leukemia not having achieved remission
C92.51	Acute myelomonocytic leukemia in remission
C92.52	Acute myelomonocytic leukemia, in relapse
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission
C92.61	Acute myeloid leukemia with 11q23-abnormality in remission
C92.62	Acute myeloid leukemia with 11q23-abnormality in relapse
C92.A0	Acute myeloid leukemia with multilineage dysplasia not having achieved remission
C92.A1	Acute myeloid leukemia with multilineage dysplasia in remission
C92.A2	Acute myeloid leukemia with multilineage dysplasia, in relapse
C93.00	Acute monoblastic/monocytic leukemia not having achieved remission
C93.01	Acute monoblastic/monocytic leukemia in remission
C93.02	Acute monoblastic/monocytic leukemia, in relapse
C93.10	Chronic myelomonocytic leukemia not having achieved remission
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D43.1	Neoplasm of uncertain behavior of brain, infratentorial
D43.2	Neoplasm of uncertain behavior of brain, unspecified
D43.4	Neoplasm of uncertain behavior of spinal cord
D43.9	Neoplasm of uncertain behavior of central nervous system, unspecified

ICD-10	ICD-10 Description
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.22	Refractory anemia with excess of blasts 2
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.C	Myelodysplastic syndrome with isolated del(5q) chromosomal abnormality
D46.Z	Other myelodysplastic syndromes
Z85.830	Personal history of malignant neoplasm of bone
Z85.841	Personal history of malignant neoplasm of brain

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC