Tibsovo® (ivosidenib)
(Oral)

Document Number: IC-0374

Last Review Date: 09/01/2021
Date of Origin: 08/06/2018
Dates Reviewed: 08/2018, 07/2019, 07/2020, 07/2021, 09/2021

I. Length of Authorization

Coverage will be provided for six 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

- Patient will avoid concomitant use with strong CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
- Patient will avoid concomitant use 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; **AND**
- Patient will avoid concomitant use with QTc prolonging drugs (e.g., amiodarone, haloperidol, tizanidine, etc.); **AND**
- Patient has an isocitrate dehydrogenase-1 (IDH1) mutation, as detected by any FDA-approved of CLIA-compliant test❖; **AND**

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

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

- Used as induction therapy in patients ≥ 60 years of age who are not candidates for or decline intensive therapy; **OR**
- Used as post-remission therapy following response to a previous lower intensity therapy with the same regimen in patients ≥ 60 years of age ‡; **OR**

- Used as a component of repeating the initial successful induction regimen for relapsed or refractory disease in patients experiencing a late relapse (≥ 12 months after induction regimen); **AND**
  - Treatment has not been administered continuously; **AND**
  - Treatment was not previously stopped due to development of clinical resistance

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

- Used as a single agent; **AND**
- Used as subsequent treatment for disease progression on or after systemic treatment for unresectable, locally advanced, or metastatic disease

Bone Cancer (Chondrosarcoma) ‡ [3,8]

- Used as a single agent; **AND**
- Patient has conventional (stages 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]

Coverage may be renewed based on the following criteria:

- Patient continues to meet 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

Cholangiocarcinoma 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]

Indication	Dose
All indications	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.*

VI. Billing Code/Availability Information

HCPCS Code:

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

NDC:

- Tibsovo 250 mg tablets: 72694-0617-xx

VII. References

1. Tibsovo [package insert]. Cambridge, MA; Servier Pharmaceuticals, August 2021. Accessed August 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 3.2021. National Comprehensive Cancer Network, 2021. 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 August 2021.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for ivosidenib. 2021 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 August 2021.
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®) Hepatobiliary Cancers. Version 3.2021. National Comprehensive Cancer Network, 2021. 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 August 2021.

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.

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

ICD-10	ICD-10 Description
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
C41.9	Malignant neoplasm of bone and articular cartilage, 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
C94.00	Acute erythroid leukemia not having achieved remission
C94.01	Acute erythroid leukemia in remission
C94.02	Acute erythroid leukemia, in relapse
C94.20	Acute megakaryoblastic leukemia not having achieved remission
C94.21	Acute megakaryoblastic leukemia in remission
C94.22	Acute megakaryoblastic leukemia, in relapse
Z85.830	Personal history of malignant neoplasm of bone

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

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at:

http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered 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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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