Drug Policy:

Tibsovo™ (ivosidenib)

POLICY NUMBER UM ONC_1340	SUBJECT Tibsovo™ (ivosidenib)		DEPT/PROGRAM UM Dept	PAGE 1 OF 3
DATES COMMITTEE REVIEWED 08/08/18, 07/10/19, 12/11/19, 07/08/20, 07/14/21, 10/13/21, 11/15/21, 05/11/22, 07/13/22, 06/14/23, 12/13/23, 12/12/24	**APPROVAL DATE** December 12, 2024	**EFFECTIVE DATE** December 27, 2024	**COMMITTEE APPROVAL DATES** 08/08/18, 07/10/19, 12/11/19, 07/08/20, 07/14/21, 10/13/21, 11/15/21, 05/11/22, 07/13/22, 06/14/23, 12/13/23, 12/12/24	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Evolent Specialty Services Clinical Guideline Review Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. A list of codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

I. PURPOSE

To define and describe the accepted indications for Tibsovo (ivosidenib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND

3. Additional medication(s) are not being added to the continuation request.

B. Acute Myeloid Leukemia (AML) and MDS (Myelodysplastic Syndromes)

1. The member has AML with a documented IDH1 gene-mutation as detected by an FDA approved test, e.g. Abbott RealTime IDH1 Assay, and Tibsovo (ivosidenib) may be used in ANY of the following clinical settings:
   a. As monotherapy OR in combination with Vidaza (azacitidine) for newly diagnosed AML OR
   b. As monotherapy for relapsed/refractory AML
2. MDS: Tibsovo (ivosedinib) may be used for members with relapsed/refractory MDS with a documented IDH1 mutation.

C. Cholangiocarcinoma

1. Tibsovo (ivosidenib) may be used as monotherapy for IDH1-mutation positive recurrent unresectable or metastatic cholangiocarcinoma, that has progressed on at least one prior line of therapy. Confirmation of IDH-1 mutation positivity (by any appropriate test) is required.

III. EXCLUSION CRITERIA

A. Disease progression on or following Tibsovo (ivosidenib) or Tibsovo (ivosidenib) containing regimen.

B. Lack of documentation of IDH-1 mutation positivity.

C. Dosing exceeds single dose limit of Tibsovo (ivosidenib) 500 mg.

D. Treatment exceeds the maximum limit of 60 (250 mg) tablets/month.

E. Investigational use of Tibsovo (ivosidenib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
   1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
   2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
   3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
   4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
   5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
   6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
   7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. CODING INFORMATION

HCPCS Code	Description
C9399	ivosidenib

V. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

VI. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VII. ATTACHMENTS

A. None

VIII. REFERENCES

A. Zhu AX, et al. Final Overall Survival Efficacy Results of Ivosidenib for Patients With Advanced Cholangiocarcinoma With IDH1 Mutation: The Phase 3 Randomized Clinical ClarIDHy Trial. JAMA Oncol. 2021 Nov 1;7(11):1669-1677.

B. Montesinos P, et al. Ivosidenib and Azacitidine in *IDH1*-Mutated Acute Myeloid Leukemia. N Engl J Med. 2022 Apr 21;386(16):1519-1531. doi: 10.1056/NEJMoa2117344

C. DiNardo CD, et al. Durable Remissions with Ivosidenib in IDH1-Mutated Relapsed or Refractory AML. N Engl J Med. 2018 Jun 21;378(25):2386-2398.

D. FDA approves ivosidenib for myelodysplastic syndromes (press release). Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ivosidenib-myelodysplastic-syndromes?utm_medium=email&utm_source=govdelivery. Published Oct. 24, 2023.

E. Tibsovo prescribing information. Agios Pharmaceuticals, Inc. Cambridge, MA 2023.

F. Clinical Pharmacology Elsevier Gold Standard 2024.

G. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2024.

H. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.

I. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2024.

J. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

K. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.