# PRIOR AUTHORIZATION POLICY

**POLICY:** Oncology – Tibsovo Prior Authorization Policy
- Tibsovo® (ivosidenib tablets – Agios)

**REVIEW DATE:** 02/10/2021

---

## OVERVIEW

Tibsovo, an isocitrate dehydrogenase-1 (IDH1) inhibitor, is indicated for the following uses in patients with a susceptible IDH1 mutation as detected by an FDA-approved test:[1]

- **Acute myeloid leukemia (AML), treatment in adults with newly diagnosed disease** who are ≥ 75 years of age who have comorbidities that preclude use of intensive induction chemotherapy.
- **Acute myeloid leukemia in adults with relapsed or refractory disease**.

Data are available regarding use of Tibsovo in patients with IDH1-mutatant chemotherapy-refractory cholangiosarcinoma[2] and chondrosarcoma[3].

## Disease Overview

AML is a heterogeneous hematologic malignancy hallmarked by clonal expansion of myeloid blasts in the peripheral blood, bone marrow, and/or other tissues.[4] Undifferentiated blast cells proliferate in bone marrow instead of maturing into normal blood cells. Among adults, it is the most common form of acute leukemia and accounts for the largest number of annual deaths from leukemias in the US. An estimated 21,450 individuals will be diagnosed with AML in 2019 and 10,920 are projected to die from the condition. The median age at diagnosis is 67 years. Diagnosis occurs at ≥ 65 years of age for 54% of patients with around one-third of patients diagnosed at ≥ 75 years of age. The incidence of AML increases as the population ages. Environmental factors such as prolonged exposure to petrochemicals, solvents such as benzene, pesticides, and ionizing radiation have been established to increase the risks for AML, as well as myelodysplastic syndrome (MDS).[4] The cure rates of AML have improved with this outcome noted in 35% to 40% of adult patients who are ≤ 60 years of age and 5% to 15% for patients who are > 60 years of age.[5] However, among patients who are older and unable to receive intensive chemotherapy the survival rates are dismal with a median survival of only 5 to 10 months.[5] Various gene mutations are present in adults with AML.[4,5] The incidence of IDH1 mutations have been reported in 6% to 9% of AML cases.[6]

## Guidelines

Various guidelines by the National Comprehensive Cancer Network (NCCN) address Tibsovo.[2]

- **Acute Myeloid Leukemia:** NCCN guidelines for AML (version 2.2021 – November 12, 2020) cite Tibsovo as a preferred therapy for treatment induction for patients with the IDH1 mutation, as well as in the setting of relapsed or refractory disease (category 2A).[4]
- **Cholangiosarcinoma:** NCCN guidelines for hepatobiliary cancers (version 5.2020 – August 4, 2020) cite Tibsovo useful in certain circumstances for patients with cholangiocarcinoma with IDH1 mutations.[7]
- **Chondrosarcoma:** The NCCN guidelines for bone cancer (version 1.2021 – November 20, 2020) cite Tibsovo for conventional (grades 1 to 3) and dedifferentiated chondrosarcoma in patients with susceptible IDH1 mutations.[8]

## Safety

Tibsovo has a Boxed Warning regarding differentiation syndrome.[1] Warnings and Precautions include QTc interval prolongation and Guillain-Barre Syndrome.

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Tibsovo. All approvals are provided for the duration noted below.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tibsovo is recommended in those who meet the following criteria:

### FDA-Approved Indication

1. **Acute Myeloid Leukemia (AML).** Approve for 3 years if the patient meets the following criteria (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Disease is isocitrate dehydrogenase-1 (IDH1) mutation positive as detected by an approved test.

### Other Uses with Supportive Evidence

2. **Cholangiocarcinoma.** Approve for 3 years if the patient meets both of the following (A, B and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Disease is isocitrate dehydrogenase-1 (IDH1) mutation positive; AND
   - **C)** Patient has been previously treated with at least one chemotherapy regimen.
     Note: Examples are gemcitabine plus cisplatin; 5-fluorouracil plus oxaliplatin or cisplatin; capecitabine + oxaliplatin or cisplatin; gemcitabine + Abraxane® (paclitaxel protein-bound particles for injectable suspension) or capecitabine or oxaliplatin; and FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin).

3. **Chondrosarcoma.** Approve for 3 years if the disease is isocitrate dehydrogenase-1 (IDH1) mutation positive.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Tibsovo is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## REFERENCES

1. Tibsovo® tablets [prescribing information]. Cambridge, MA: Agios; May 2019.
2. Abou-Alfa GK, Macarulla T, Javle MM, et al. Ivosidenib in IDH1-mutation chemotherapy-refractory cholaniocarcinoma (CLARIDHy): a multicenter, randomized, double-blind, placebo-controlled, phase 3 study. *Lancet Oncol*. 2020;21(6):796-807.
3. Tap WD, Villalobos VM, Cote GM, et al. Phase I study of the mutant IDH1 inhibitor ivosidenib: safety and clinical activity in patients with advanced chondrosarcoma. *J Clin Oncol*. 2020;38(15):1693-1701.
4. The NCCN Acute Myeloid Leukemia Clinical Practice Guidelines in Oncology (version 2.2021 – November 12, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 1, 2021.
5. Dohner H, Weisdorf DJ, Bloomfield CD. Acute myeloid leukemia. *N Engl J Med*. 2015;373(12):1136-1152.
6. 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;378(25):2386-2398.

7. The NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology (version 5.2020 – August 4, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 1, 2021.
8. The NCCN Bone Cancers Clinical Practice Guidelines in Oncology (version 1.2021 – November 20, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 1, 2021.