

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Ziihera Utilization Management Medical Policy

- Ziihera® (zanidatamab-hrii intravenous infusion – Jazz)

REVIEW DATE: 12/10/2025

OVERVIEW

Ziihera, a bispecific human epidermal growth factor receptor 2 (HER2)-directed antibody, is indicated for the treatment of previously treated, unresectable or metastatic HER2-positive (immunohistochemistry [IHC] 3+) **biliary tract cancer**, as detected by an FDA-approved test in adults.¹

Dosing Information

The recommended dose of Ziihera is up to 20 mg/kg administered by intravenous infusion no more frequently than once every 2 weeks, until disease progression or unacceptable adverse events.¹

Guidelines

The National Comprehensive Cancer Network (NCCN) biliary tract cancers (version 2.2025 – July 2, 2025) guidelines recommended Ziihera as “Useful in Certain Circumstances” for the subsequent treatment of unresectable, resected gross residual, or metastatic gallbladder cancer, intrahepatic cholangiocarcinoma, and extrahepatic cholangiocarcinoma that is HER2-positive (IHC3+) [category 2A].^{2,3}

Safety

Ziihera has a Boxed Warning for embryo-fetal toxicity.¹

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Ziihera. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Ziihera as well as the monitoring required for adverse events and long-term efficacy, approval requires Ziihera to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

-
1. **Biliary Tract Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
 - A) Patient is \geq 18 years of age; AND
 - B. Patient has unresectable, resected gross residual, or metastatic disease; AND

- C. The medication is used for subsequent therapy; AND
- D. The tumor is human epidermal growth factor receptor 2 (HER2) positive with immunohistochemistry score of 3+ (IHC3+); AND
- E. The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 20 mg/kg administered by intravenous infusion no more frequently than once every 2 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Ziihera 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. Ziihera® intravenous infusion [prescribing information]. Palo Alto, CA: Jazz; November 2024.
2. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 3, 2025. Search term: zanidatamab.
3. The NCCN Biliary Tract Cancers Clinical Practice Guidelines in Oncology (version 2.2025 – July 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 3, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	12/04/2024
Annual Revision	Biliary Tract Cancer: The requirement that the patient has gallbladder cancer, intrahepatic cholangiocarcinoma or extrahepatic cholangiocarcinoma was removed. The requirement that the medication is used as a single agent was removed. The requirement that the tumor is human epidermal growth factor receptor 2 (HER2) positive with immunohistochemistry score of 3+ (IHC3+) as determined by an approved test was modified to the tumor is human epidermal growth factor receptor 2 (HER2) positive with immunohistochemistry score of 3+ (IHC3+).	12/10/2025