CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Ziihera Utilization Management Medical Policy
- Ziihera® (zanidatamab-hrii intravenous infusion – Jazz)

REVIEW DATE: 09/02/2026

OVERVIEW

Ziihera, a bispecific human epidermal growth factor receptor 2 (HER2)-directed antibody, is indicated for the following uses:[1]

- **Biliary Tract Cancer:** Treatment of adults with previously treated, unresectable or metastatic HER2-positive (immunohistochemistry [IHC] 3+) disease, as detected by an FDA-approved test. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.
- **Gastroesophageal Adenocarcinoma:**
  - In combination with fluoropyrimidine- and platinum-containing chemotherapy and Tevimbra (tislelizumab-jsgr intravenous infusion) as first-line treatment for adults with human epidermal growth factor receptor 2 (HER2)-positive (immunohistochemistry [IHC] 3+ or IHC 2+/in situ hybridization [ISH]+) unresectable locally advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma, as detected by an FDA-approved test.
  - In combination with fluoropyrimidine-, and platinum-containing chemotherapy, as first-line treatment for adults with HER2-positive (IHC 3+) unresectable locally advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma, as detected by an FDA-approved test.

Dosing Information

The recommended dose of Ziihera in biliary tract cancer 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] For gastroesophageal adenocarcinoma, Ziihera is dosed as per the patient's body weight. For patients < 70 kg the dosage is 1,800 mg every 3 weeks or 1,200 mg every 2 weeks. For patients ≥ 70 kg, the dosage is 2,400 mg every 3 weeks or 1,600 mg every 2 weeks.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines have the following recommendations:

- **Biliary Tract Cancer:** Guidelines (version 1.2026 – March 10, 2026) have 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].[3]
- **Gastroesophageal Adenocarcinoma:** Guidelines for gastric cancer (version 3.2026 - June 3, 2026) and esophageal and esophagogastric junction cancers (version 3.2026 - June 3, 2026) have the same recommendations for HER2 positive unresectable locally advanced, recurrent, or metastatic disease in the first-line setting.[4,5] Ziihera is not addressed in the current guidelines. The "Preferred" regimens for HER2-positive disease are as follows: fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and trastuzumab (category 2A); fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, trastuzumab, and Keytruda (pembrolizumab intravenous infusion) for PD-L1 CPS ≥ 1 (category 1); fluoropyrimidine (fluorouracil or capecitabine), cisplatin, and

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trastuzumab (category 1); and fluoropyrimidine (fluorouracil or capecitabine), cisplatin, trastuzumab, and Keytruda for PD-L1 CPS ≥ 1 (category 1). The guidelines note that oxaliplatin is preferred over cisplatin due to lower toxicity.

Safety

Ziihera has a Boxed Warning for diarrhea and 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 one of the following criteria:

FDA-Approved Indications

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 ≥ 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.

2. **Gastroesophageal Adenocarcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   Note: Examples of gastroesophageal cancer are gastric cancer, gastroesophageal junction cancer, and esophageal cancers.
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has unresectable locally advanced or metastatic disease; AND
   - **C)** The tumor is human epidermal growth factor receptor 2 (HER2) positive; AND
   - **D)** The medication is used in combination with fluoropyrimidine- and platinum-containing chemotherapy; AND

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Note: Examples of fluoropyrimidine include fluorouracil or capecitabine. Examples of platinum-containing chemotherapy include cisplatin, carboplatin, or oxaliplatin.

E) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) Patient weighs < 70 kg and meets ONE of the following regimens (i or ii):
- **i.** 1,800 mg as an intravenous infusion administered not more frequently than once every 3 weeks; OR
- **ii.** 1,200 mg as an intravenous infusion administered not more frequently than once every 2 weeks; OR

B) Patient weighs ≥ 70 kg and meets ONE of the following regimens (i or ii):
- **i.** 2,400 mg as an intravenous infusion administered not more frequently than once every 3 weeks; OR
- **ii.** 1,600 mg as an intravenous infusion administered not 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; August 2026.
2. The NCCN Drugs & Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 26, 2026. Search term: zanidatamab.
3. The NCCN Biliary Tract Cancers Clinical Practice Guidelines in Oncology (version 1.2026 – March 10, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 26, 2026.
4. The NCCN Esophageal and Esophagogastric Junction Cancers Clinical Practice Guidelines in Oncology (version 3.2026 – June 3, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 26, 2026.
5. The NCCN Gastric Cancers Clinical Practice Guidelines in Oncology (version 3.2026 – June 3, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 26, 2026.

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
Early Annual Revision	**Gastroesophageal Adenocarcinoma:** This was added as a new condition for approval.	09/02/2026

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