Ziihera® (zanidatamab-hrii)
(Intravenous)

Document Number: IC-0778

Last Review Date: 10/01/2026
Date of Origin: 01/06/2025
Dates Reviewed: 01/2025, 04/2025, 06/2026, 10/2026

I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months (180 days).
- Renewal: Prior authorization validity may be renewed every 6 months (180 days) thereafter.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

Biliary Tract Cancers

- 1200 billable units (2400 mg) every 14 days

Esophageal, Esophagogastric/Gastroesophageal Junction, and Gastric Cancers

- 2700 billable units (5400 mg) every 42 days

III. Initial Approval Criteria [1]

Prior authorization validity is provided in the following conditions:

- Member is at least 18 years of age; **AND**

Universal Criteria [1]

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Females of reproductive potential must have a negative pregnancy test prior to the first dose of therapy and will use an effective contraceptive method while receiving therapy and for four months following the last dose of therapy; **AND**
- Member will be monitored for severe diarrhea and managed with antidiarrheals and supportive measures as clinically indicated when therapy is used in combination with fluoropyrimidine- and platinum-containing chemotherapy, with or without tislelizumab; **AND**

Biliary Tract Cancers (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma) † ‡ Φ [1, 2]

- Member has human epidermal growth factor receptor 2 (HER2)-positive (IHC3+) disease as determined by an FDA-approved or Clinical Laboratory Improvement Amendments (CLIA) compliant test❖; **AND**
- Used as a single agent; **AND**

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- Used as subsequent treatment for progression on or after systemic treatment for unresectable, resected gross residual (R2), or metastatic disease

Esophageal and Esophagogastric/Gastroesophageal Junction Cancers † Φ [1]

- Member has HER2 positive (IHC 3+ or IHC 2+/ISH+) disease as determined by an FDA-approved or CLIA compliant test❖; **AND**
- Member has unresectable locally advanced or metastatic adenocarcinoma; **AND**
- Used as first-line therapy in combination with fluoropyrimidine- and platinum containing chemotherapy with or without tislelizumab

Gastric Cancers † Φ [1]

- Member has HER2-positive (IHC 3+ or IHC 2+/ISH+) disease as determined by an FDA-approved or CLIA compliant test❖; **AND**
- Member has unresectable locally advanced or metastatic adenocarcinoma; **AND**
- Used as first-line therapy in combination with fluoropyrimidine- and platinum containing chemotherapy with or without tislelizumab

❖ *If confirmed using an FDA approved assay - http://www.fda.gov/companiondiagnostics*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Prior authorization validity may be renewed based upon the following criteria:

- Member continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: left ventricular dysfunction (including symptomatic congestive heart failure), severe infusion related reactions, severe diarrhea, etc.; **AND**
- Left ventricular ejection fraction (LVEF) within the previous 3 months as follows:
  - LVEF is within the normal limits, and has not had an absolute decrease of ≥ 16% from pre-treatment baseline; **OR**
  - LVEF is > 50% and absolute decrease is < 10% from pre-treatment baseline

V. Dosage/Administration [1-3]

Indication	Dose

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Biliary Tract Cancers (BTC)	Administer 20 mg/kg as an intravenous infusion once every 2 weeks until disease progression or unacceptable toxicity.
Esophageal, Esophagogastric/ Gastroesophageal Junction, and Gastric Cancers	**Body weight < 70 kg:** • Administer 1,800 mg every 3 weeks OR 1,200 mg every 2 weeks as an intravenous infusion until disease progression or unacceptable toxicity. **Body weight ≥70 kg:** • Administer 2,400 mg every 3 weeks OR 1,600 mg every 2 weeks as an intravenous infusion until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J9276 – Injection, zanidatamab-hrii, 2 mg; 1 billable unit = 2 mg

NDC:

- Ziihera 300 mg lyophilized powder in a single-dose vial: 68727-0950-xx

VII. References

1. Ziihera [package insert]. Palo Alto, CA; Jazz Pharm., Inc; August 2026. Accessed September 2026.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) zanidatamab. National Comprehensive Cancer Network, 2026. 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 April 2026.
3. Pant S, Fan J, Oh DY, et al. Zanidatamab in previously-treated HER2-positive (HER2+) biliary tract cancer (BTC): Overall survival (OS) and longer follow-up from the phase 2b HERIZON-BTC-01 study. JCO 42, 4091-4091(2024). DOI:10.1200/JCO.2024.42.16_suppl.4091
4. Pant S, Ducreux M, Harding JJ, et al. Zanidatamab in previously-treated HER2-positive (HER2+) biliary tract cancer (BTC): Overall survival (OS) and longer follow-up from the phase 2b HERIZON-BTC-01 study. JCO 42, 4091-4091(2024). DOI:10.1200/JCO.2024.42.16_suppl.4091
5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Biliary Tract Cancers, Version 1.2026. National Comprehensive Cancer Network, 2026. 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 Guidelines, go online to NCCN.org. Accessed April 2026.
6. Hematology/Oncology Pharmacy Association. Intravenous Cancer Drug Waste Issue Brief. Updated February 2024. Available at:

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8. Bartley AN, Washington MK, Colasacco C, et al. HER2 Testing and Clinical Decision Making in Gastroesophageal Adenocarcinoma: Guideline From the College of American Pathologists, American Society for Clinical Pathology, and the American Society of Clinical Oncology. J Clin Oncol. 2017 Feb;35(4):446-464. doi: 10.1200/JCO.2016.69.4836.
9. Shitara K, Elimova E, Liu T, et al. HERIZON-GEA-01 Investigators. Zanidatamab with and without Tislelizumab in HER2-Positive Gastroesophageal Cancer. N Engl J Med. 2026 May 28;394(20):2002-2014. doi: 10.1056/NEJMoa2517729. PMID: 42202319.

Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	Yes: Consider for PA
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum

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C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
C22.1	Intrahepatic bile duct carcinoma
C23	Malignant neoplasm of gallbladder
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
D37.1	Neoplasm of uncertain behavior of stomach
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.01	Personal history of malignant neoplasm of esophagus
Z85.028	Personal history of other malignant neoplasm of stomach

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied 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	Wellpoint Federal
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)

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Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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	Wellpoint Federal
15	KY, OH	CGS Administrators, LLC

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