

Ziihera® (zanidatamab-hrii) (Intravenous)

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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]:

- 1200 billable units (2400 mg) every 14 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**

Biliary Tract Cancers (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma) † ‡ Φ ^{1,2,2e}

- 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**
- Used as subsequent treatment for progression on or after systemic treatment for unresectable, resected gross residual (R2), or metastatic disease; **AND**
- Member received previous gemcitabine-based therapy, unless contraindicated

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

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

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Ⓢ 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 $\geq 16\%$ from pre-treatment baseline; **OR**
 - LVEF is $> 50\%$ and absolute decrease is $< 10\%$ from pre-treatment baseline

V. Dosage/Administration ¹⁻³

Indication	Dose
Biliary Tract Cancers (BTC)	Administer 20 mg/kg, administered as an intravenous infusion once every 2 weeks 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 (STANDARD)

1. Ziihera [package insert]. Palo Alto, CA; Jazz Pharm., Inc; July 2025. Accessed June 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 June 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 June 2026.
6. Hematology/Oncology Pharmacy Association. Intravenous Cancer Drug Waste Issue Brief. Updated February 2024. Available at: https://www.hoparx.org/documents/287/HOPA_Drug_Waste_Issue_Brief_-_Updated_02.22.24.pdf
7. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
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.

VIII. References (ENHANCED)

- 1e. Harding JJ, Fan J, Oh DY, et al; HERIZON-BTC-01 study group. Zanidatamab for HER2-amplified, unresectable, locally advanced or metastatic biliary tract cancer (HERIZON-BTC-01): a multicentre, single-arm, phase 2b study. *Lancet Oncol*. 2023 Jul;24(7):772-782.
- 2e. Meric-Bernstam F, Makker V, Oaknin A, et al. Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*. Published online October 23, 2023:101200JCO2302005. doi:<https://doi.org/10.1200/JCO.23.02005>
- 3e. Javle M, Borad MJ, Azad NS, et al. Pertuzumab and trastuzumab for HER2-positive, metastatic biliary tract cancer (MyPathway): a multicentre, open-label, phase 2a, multiple basket study. *Lancet Oncol*. 2021 Sep;22(9):1290-1300. doi: 10.1016/S1470-2045(21)00336-3. Epub 2021 Jul 30.
- 4e. Nakamura Y, Mizuno N, Sunakawa Y, et al. Tucatinib and Trastuzumab for Previously Treated Human Epidermal Growth Factor Receptor 2-Positive Metastatic Biliary Tract Cancer (SGNTUC-019): A Phase II Basket Study. *J Clin Oncol*. 2023 Dec 20;41(36):5569-5578. doi: 10.1200/JCO.23.00606. Epub 2023 Sep 26.
- 5e. Pant S, Fan J, Oh DY, Choi HJ, et al.; HERIZON-BTC-01 Study Group. Zanidatamab in HER2-Positive Metastatic Biliary Tract Cancer: Final Results From HERIZON-BTC-01. *JAMA Oncol*. 2026 Jan 1;12(1):106-109. doi: 10.1001/jamaoncol.2025.4736. PMID: 41264278; PMCID: PMC12635922.
- 6e. Ohba A, Morizane C, Kawamoto Y, et al. Trastuzumab Deruxtecan in Human Epidermal Growth Factor Receptor 2-Expressing Biliary Tract Cancer (HERB; NCCH1805): A Multicenter, Single-Arm, Phase II Trial. *J Clin Oncol*. 2024 Sep 20;42(27):3207-3217. doi: 10.1200/JCO.23.02010. Epub 2024 Aug 5. PMID: 39102634; PMCID: PMC11404765.
- 7e. Bernstam F, Makker V, Oakin A, et al. Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: primary results from the DESTINY-PanTumor02 phase II trial. *J Clin Oncol* 2024;42:47-58. doi: 10.1200/JCO.23.02005. Epub 2023 Oct 23.
- 8e. Prime Therapeutics Management. Ziihera Clinical Literature Review Analysis. Last updated June 2026. Accessed June 2026.

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

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Medical Necessity Criteria

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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
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

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	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
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	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC