Ziihera® (zanidatamab-hrii)
(Intravenous)

Document Number: IC-0778

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

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

- 1200 billable units every 21 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient 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 during treatment; **AND**
- Patient doesn't have untreated or symptomatic central nervous system (CNS) metastases; **AND**
- Females of childbearing 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) † [1]

- Patient has human epidermal growth factor receptor 2 (HER2)-positive (IHC3+) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used as a single agent; **AND**
- Used for unresectable or metastatic disease; **AND**
- Used as subsequent treatment after at least one prior line of therapy containing a gemcitabine containing regimen.

❖*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]

Coverage may be renewed based upon the following criteria:

- Patient 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 has an absolute decrease of < 16% from baseline; **OR**
    - LVEF is > 50% and absolute decrease is < 10% from baseline

V. Dosage/Administration [1,11-13,16,21,23,25,26-28]

Indication	Dose
Biliary Tract Cancer (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:

- C9302 – Injection, zanidatamab-hrii, 2 mg; 1 billable unit = 2 mg *(Effective 04/01/2025)*
- J9999 – Not otherwise classified, antineoplastic drugs

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; November 2024. Accessed December 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) zanidatamab. National Comprehensive Cancer Network, 2024. 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 December 2024.

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 5.2024. National Comprehensive Cancer Network, 2024. 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 December 2024.
6. Hematology/Oncology Pharmacy Association (2019). *Intravenous Cancer Drug Waste Issue Brief*. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.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.

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 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)
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