

**Clinical Policy: Zanidatamab-hrii (Ziihera)**

Reference Number: LA.PHAR.709

Effective Date:

Last Review Date: 05.09.25

Line of Business: Medicaid

[Coding Implications](#)[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**\*\*Please note: This policy is for medical benefit\*\***

**Description**

Zanidatamab-hrii (Ziihera®) is a bispecific HER2-directed antibody.

**FDA Approved Indication(s)**

Ziihera is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (immunohistochemistry [IHC] 3+) biliary tract cancer (BTC), 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 a confirmatory trial(s).

**Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of Louisiana Healthcare Connections® that Ziihera is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria****A. Biliary Tract Cancer** (must meet all):

1. Diagnosis of BTC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is HER2-positive (IHC 3+);
5. Disease is unresectable, resected gross residual (R2), or metastatic;
6. Failure of at least one prior systemic treatment (*see Appendix B for examples*);
7. Prescribed as a single agent;
8. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 20 mg/kg every 2 weeks;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

**B. Other diagnoses/indications** (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

**II. Continued Therapy**

**A. Biliary Tract Cancer** (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connections, or documentation supports that member is currently receiving Ziihera for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Prescribed as a single agent;
4. Dose requested is  $\geq 15$  mg/kg;
5. If request is for a dose increase, request meets one of the following (a or b):\*
  - a. New dose does not exceed 20 mg/kg every 2 weeks;
  - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 12 months**

**B. Other diagnoses/indications** (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

BTC: biliary tract cancer

FDA: Food and Drug Administration

HER2: human epidermal growth factor  
receptor 2

IHC: immunohistochemistry (assay)

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<p>Examples of systemic therapies include:</p> <ul style="list-style-type: none"> <li>• Imfinzi<sup>®</sup> + gemcitabine + cisplatin</li> <li>• Keytruda<sup>®</sup> + gemcitabine + cisplatin</li> <li>• gemcitabine + cisplatin/oxaliplatin</li> <li>• capecitabine (Xeloda<sup>®</sup>) + oxaliplatin</li> <li>• FOLFOX (5-fluorouracil, leucovorin, oxaliplatin)</li> <li>• gemcitabine + Abraxane<sup>®</sup> (paclitaxel, protein-bound)</li> <li>• gemcitabine + capecitabine (Xeloda)</li> <li>• Single agents: 5-fluorouracil, capecitabine (Xeloda), gemcitabine</li> </ul>	Varies	Varies

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): none reported
- Boxed warning(s): embryo-fetal toxicity

*Appendix D: General Information*

- A HER2 IHC test determines HER2 protein levels using scores that range from 0 to 3+. The higher the score, the more HER2 is overexpressed. The efficacy of Zihera was established in 62 patients with HER2-positive (IHC 3+) BTC in the HERIZON-BTC-302 trial.
- Ziihera should be permanently discontinued in patients who cannot tolerate 15 mg/kg per the product labeling.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
BTC	20 mg/kg IV once every 2 weeks until disease progression or unacceptable toxicity	20 mg/kg every 2 weeks

**VI. Product Availability**

Lyophilized powder in single-dose vial for injection: 300 mg

**VII. References**

1. Ziihera Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; November 2024. Available at: <https://www.ziihera.com/>. Accessed December 5, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed December 6, 2024.
3. National Comprehensive Cancer Network. Biliary Tract Cancers 5.2024. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/btc.pdf](https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf). Accessed December 6, 2024.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPSC Codes	Description
C9302	Injection, zanidatamab-hrii, 2 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted from Corporate Policy to Local Policy	05.09.25	

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing

this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

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This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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