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 ≥ 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
Examples of systemic therapies include: • Imfinzi® + gemcitabine + cisplatin • Keytruda® + gemcitabine + cisplatin • gemcitabine + cisplatin/oxaliplatin • capecitabine (Xeloda®) + oxaliplatin • FOLFOX (5-fluorouracil, leucovorin, oxaliplatin) • gemcitabine + Abraxane® (paclitaxel, protein-bound) • gemcitabine + capecitabine (Xeloda) • Single agents: 5-fluorouracil, capecitabine (Xeloda), gemcitabine	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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. 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. 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.

HCPCS 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.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.