Clinical Policy: Zanidatamab-hrii (Ziihera)

Reference Number: PA.CP.PHAR.709
Effective Date: 01/2025
Last Review Date: 12/2024

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 PA Health & Wellness® 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*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
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*).

Approval duration: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.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 policies – PA.CP.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)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• Single agents: 5-fluorouracil, capecitabine (Xeloda), gemcitabine		

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
J9999	Not otherwise classified, antineoplastic drugs
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date
Policy created	12/2024