ZIIHERA® *(zanidatamab-hrii)* injection, for IV use

<table>
<tr><th>PA Criteria</th><th>Criteria Details</th></tr>
<tr><td>Description</td><td>ZIIHERA® is a bispecific HER2-directed antibody.</td></tr>
<tr><td>Covered Uses
(FDA approved indication)</td><td>ZIIHERA is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC) including intra-hepatic cholangiocarcinoma, extra-hepatic cholangiocarcinoma, and gallbladder cancer, as detected by an FDA-approved test*.

Information on FDA-approved tests for HER2 protein expression in biliary tract cancers is available at: http://www.fda.gov/CompanionDiagnostics.

*This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.</td></tr>
<tr><td>Dosing and Administration</td><td>
<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>Biliary Tract Cancer (BTC)</td><td>20 mg/kg IV infusion every two weeks

Continue until disease progression or unacceptable toxicity.

<table>
<tr><th>Dose</th><th>Infusion Time</th></tr>
<tr><td>1st and 2nd</td><td>120-150 min</td></tr>
<tr><td>3rd and 4th</td><td>90 min
(if previous infusions well tolerated)</td></tr>
<tr><td>Subsequent</td><td>60 min
(if previous infusions well tolerated)</td></tr>
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</td><td>20 mg/kg/dose</td></tr>
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</td></tr>
<tr><td>Billing and Coding Information</td><td>
<table>
<tr><th>10-digit NDC</th><th>11-digit NDC</th></tr>
<tr><td>Vial: 68727-950-01
Carton: 68727-950-02</td><td>Vial: 68727-0950-01
Carton: 68727-0950-02</td></tr>
</table>
<table>
<tr><th>HCPCS Code</th><th>Description</th></tr>
<tr><td>J9276</td><td>Injection, zanidatamab-hrii, 2 mg</td></tr>
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<table>
<tr><th>CPT Procedural Codes</th><th>Description</th></tr>
<tr><td>96413</td><td>Chemotherapy IV infusion, up to one hour</td></tr>
<tr><td>96415</td><td>Chemotherapy IV infusion, additional hour*</td></tr>
</table>
* Used as an add-on code for every hour of infusion that is more than 30 min past the initial one hour.
</td></tr>
<tr><td>Product Availability</td><td>Single-dose vial: 300 mg lyophilized powder

Each carton contains two 300 mg single-dose vials.</td></tr>
<tr><td>Contraindications</td><td>None.</td></tr>
</table>

Recommended Medical Monitoring	**BLACK BOX WARNING: Embryo-Fetal Toxicity** – Based on the mechanism of action, ZIIHERA can cause fetal harm when administered to pregnant women; there are no human or animal data on the use of ZIIHERA in pregnancy. In literature reports, HER2-directed antibody use during pregnancy resulted in cases of pediatric pulmonary hypoplasia, skeletal abnormalities, and neonatal death. a. Advise patients of potential risk to fetus; verify pregnancy status of females of reproductive potential prior to initiation of therapy b. Recommend effective contraception during treatment and for four months after last dose. ZIIHERA has been associated with: • Left Ventricular Dysfunction • Infusion Related Reactions (IRR) • Diarrhea Patients should be monitored for any of these reactions. ZIIHERA dose may be delayed, reduced or permanently discontinued based on the severity of adverse reactions.
Approval Criteria	A. Physician administered IV infusion; in-office or HOPD i. Cannot be self-administered B. Biliary Tract Cancer **(must meet all)**: i. Diagnosis of Biliary Tract Cancer ii. Prescribed by or in consultation with an oncologist iii. Patient age ≥ 18 years iv. Disease is HER2-positive (IHC 3+) determined by FDA-approved test v. Disease is unresectable, resected gross residual (R2) or metastatic vi. Patient does NOT have untreated or symptomatic CNS metastases vii. Failure of at least one prior systemic treatment (see Appendix) viii. LVEF ≥ 50% prior to start of therapy ix. Prescribed as a single agent x. Request meets one of the following: 1. Dose does not exceed 20 mg/kg every two weeks 2. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence)
Age Restriction	Adults ≥ 18 years old.
Coverage Duration	Initial: six months. Reauthorization: 12 months. Dose will be approved according to the FDA approved labeling or within accepted standards of medical practice.

Appendix	Examples of Prior Systemic Therapies for BTC: • 5-FU • Capecitabine • Capecitabine + Oxaliplatin • FOLFOX (5-FU + leucovorin + Oxaliplatin) • Gemcitabine • Gemcitabine + Abraxane • Gemcitabine + Capecitabine • Gemcitabine + Cisplatin • Gemcitabine + Imfinzi + cisplatin • Gemcitabine + Keytruda + Cisplatin • Gemcitabine + Oxaliplatin

STATUS	DATE REVISED	REVIEW DATE	APPROVED/REVIEWED BY	EFFECTIVE DATE
Created	9/22/2025	9/22/2025	Tamara Chinarian, PharmD, Clinical Pharmacist	N/A
Approved	N/A	11/13/2025	Pharmacy & Therapeutics (P&T) Committee	11/13/2025