Reference number(s)
6736-A

Standard Medicare Part B Management Ziihera

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Ziihera	zanidatamab-hrii

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication[1]

HER2-positive Biliary Tract Cancer

Ziihera is indicated for the treatment of adults with previously treated, unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive immunohistochemistry (IHC 3+) biliary tract cancer (BTC), as detected by an FDA-approved test.

Compendial Use[2]

- HER2-positive biliary tract cancer

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

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Documentation

The following documentation must be available, upon request, for all submissions: human epidermal growth factor receptor 2 (HER2) status (e.g., immunohistochemistry [IHC] score).

Coverage Criteria

Biliary Tract Cancer[1,2]

Authorization of 12 months may be granted for subsequent treatment of unresectable or resected gross residual (R2) disease or metastatic HER2-positive (IHC 3+) biliary tract cancer (intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, or gallbladder cancer) when used as a single agent.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested medication.

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication
- The requested medication is being used to treat an indication listed in the coverage criteria section
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease progression while on the current regimen

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Ziihera.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology

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- NCCN Guideline: Biliary Tract Cancers

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Ziihera are covered in addition to the following:

- Resected gross residual (R2) biliary tract cancer

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Ziihera to treat resected gross residual (R2) biliary tract cancer can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

References

1. Ziihera [package insert]. Palo Alto, CA: Jazz Pharmaceuticals Inc.; July 2025.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 15, 2025.

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