

Bizen gri® (zenocutuzumab-zbco) (Intravenous)

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Dates Reviewed: 01/2025

I. Length of Authorization

Coverage is provided for 6 months and may be renewed.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- 750 mg every 14 days

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Females of reproductive potential have a negative pregnancy test prior to initiating treatment and will use effective contraception during treatment and for 2 months after the last dose; **AND**

Universal Criteria ¹

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient tumor has the presence of a neuregulin-1 (*NRG1*) gene fusion partners* (*Lung: CD74, SLC3A2, SDC4, CDH1 or VAMP2*) or (*Pancreatic: ATP1B1, NOTCH2, SLC4A4, AGRN, APP, CDH1, SDC4, or VTCN1*) as determined by an FDA-approved or CLIA-compliant test❖; **AND**

**Note: Requests for NRG1 gene fusion partners not listed above will be reviewed on a case-by-case basis.*

Non-Small Cell Lung Cancer (NSCLC) † Φ ^{1,2,3,8}

- Patient has a diagnosis of advanced unresectable or metastatic disease; **AND**
- Used as subsequent therapy after disease progression

Pancreatic Adenocarcinoma † Φ ^{1,2,4,8}

- Patient has advanced unresectable or metastatic disease; **AND**
- Used as subsequent therapy after disease progression

❖ If confirmed using an immunotherapy assay-<http://www.fda.gov/companiondiagnostics>

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria ¹

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion-related reactions, congestive heart failure/left ventricular cardiac dysfunction, interstitial pneumonitis or lung disease, etc.; **AND**
- Left ventricular ejection fraction (LVEF) obtained within the previous 3 months as follows:
 - LVEF is $\geq 50\%$; **OR**
 - LVEF is between 45-49%, and has NOT had an absolute decrease of $\geq 10\%$ from pre-treatment baseline

V. Dosage/Administration ¹

Indication	Dose
All indications	Administer 750 mg as an intravenous (IV) infusion every 2 weeks until disease progression or unacceptable toxicity <i>Note: Administer pre-medications (corticosteroid [optional], antipyretic, H1-antihistamine) before each infusion as recommended to reduce the risk of infusion-related reactions.</i>

VI. Billing Code/Availability Information

HCPCS Code:

- J9999 – Not otherwise classified, antineoplastic drugs

NDC:

- Bizengri 375 mg/18.75 mL (20 mg/mL) p/f solution in a single-dose vial: 83077-0100-xx

VII. References

1. Bizengri [package insert]. Cambridge, MA; Merus US, Inc.; December 2024. Accessed December 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium[®]) for zenocutuzumab. National Comprehensive Cancer Network, 2024. The NCCN Compendium[®] is a derivative work of the NCCN Guidelines[®]. NATIONAL COMPREHENSIVE CANCER NETWORK[®], NCCN[®], and NCCN GUIDELINES[®] are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed December 2024.

3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Lung Cancer, Version 11.2024. National Comprehensive Cancer Network, 2024. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed December 2024.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma, Version 3.2024. National Comprehensive Cancer Network, 2024. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed December 2024.
5. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
6. Hematology/Oncology Pharmacy Association (2019). *Intravenous Cancer Drug Waste Issue Brief*. Retrieved from <https://www.hoparx.org/about-us/advocacy-awareness/issue-briefs/>
7. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
8. Gerlach J, Odintsov I, Schackman R, et al. Abstract P201: Zenocutuzumab is an effective HER2/HER3 Bionics® antibody in cancers with NRG1 fusions. Mol Cancer Ther (2021) 20 (12_Supplement): P201..

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of the pancreas
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C25.9	Malignant neoplasm of pancreas, unspecified
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung

ICD-10	ICD-10 Description
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
Z85.07	Personal history of malignant neoplasm of pancreas
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC