

## Utilization Management and Clinical Medical Policy

<b>Policy Name:</b> Bizengri® (zenocutuzumab-zbco)	<b>Policy Number:</b> MP-RX-FP-165-25	<b>Scope:</b> <input checked="" type="checkbox"/> MMM MA <input checked="" type="checkbox"/> MMM MultiHealth	<b>Origination Date:</b> 4/2/2025 <b>Last Review Date:</b> 2/22/2026	<b>Effective Date:</b> 2/22/2026 <b>Frequently Revision:</b> 2/22/2027
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### Service Category

- |  |   |
|--|---|
| <input type="checkbox"/> Anesthesia                          | <input type="checkbox"/> Medicine Services and Procedures   |
| <input type="checkbox"/> Surgery                             | <input type="checkbox"/> Evaluation and Management Services |
| <input type="checkbox"/> Radiology Procedures                | <input type="checkbox"/> DME/Prosthetics or Supplies        |
| <input type="checkbox"/> Pathology and Laboratory Procedures | <input checked="" type="checkbox"/> Part B Drugs            |

### Service Description:

This document addresses the use of Bizengri (zenocutuzumab-zbco), a injection bispecific HER2- and HER3-directed antibody drug approved by the Food and Drug Administration (FDA) for the treatment of non-small cell lung cancer (NSCLC) and pancreatic adenocarcinoma.

### Background Information:

The FDA approved indications for Bizengri include adults with advanced, unresectable or metastatic non-small cell lung cancer (NSCLC) harboring a neuregulin 1 (NRG1) gene fusion with disease progression on or after prior systemic therapy. Bizengri is also indicated for adults with advanced, unresectable or metastatic pancreatic adenocarcinoma harboring a neuregulin 1 (NRG1) gene fusion with disease progression on or after prior systemic therapy. These indications are 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).

The NCCN Compendium and Clinical Practice Guidelines in Oncology in 2025 provided a 2A recommendation for the use of Bizengri as subsequent therapy as a single agent for pancreatic adenocarcinoma if NRG1 gene fusion-positive for locally advanced or metastatic disease and disease progression on or after prior systemic therapy if good performance status (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake) or intermediate PS (ECOG 2). Also, for local recurrence in the pancreatic operative bed after resection or recurrent metastatic disease with or without local recurrence after resection.

NCNN also provides a 2A recommendation for the use of Bizengri as subsequent therapy as a single agent for NRG1 gene fusion positive recurrent, advanced, or metastatic non-small cell lung cancer.

Bizengri has a black box warning regarding embryo-fetal toxicity. It is recommended to advise patients of this risk and the need for effective contraception.

### Definitions and Measures

**Adenocarcinoma:** Cancer originating in cells that line specific internal organs and that have gland-like (secretory) properties.

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**Disease Progression:** Cancer that continues to grow or spread.

**ECOG or Eastern Cooperative Oncology Group Performance Status:** A scale and criteria used by doctors and researchers to assess how an individual’s disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 0 = Fully active, able to carry on all pre-disease performance without restriction.
- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light housework, office work.
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.
- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.
- 5 = Dead

**Metastasis:** The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.

**Non-small cell lung cancer:** A group of lung cancers that are named for the kinds of cells found in the cancer and how the cells look under a microscope. The three main types of non-small cell lung cancer are squamous cell carcinoma, large cell carcinoma, and adenocarcinoma.

**Subsequent Therapy:** Includes second-line and later-line systemic treatments used after failure, intolerance, or disease progression on prior therapy.

**Unresectable:** Unable to be removed with surgery.

### Approved Indications

- A. Adults with advanced, unresectable or metastatic non-small cell lung cancer (NSCLC) harboring a neuregulin 1 (NRG1) gene fusion with disease progression on or after prior systemic therapy
- B. Adults with advanced, unresectable or metastatic pancreatic adenocarcinoma harboring a neuregulin 1 (NRG1) gene fusion with disease progression on or after prior systemic therapy.

### Other Uses

- A. N/A

# Medical Policy



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### Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9382	Injection, zenocutuzumab-zbco, 1 mg

ICD-10	Description
C25.0-C25.3	Malignant neoplasm of pancreas, 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-C34.92	Malignant neoplasm of bronchus and lung
Z85.07	Personal history of malignant neoplasm of pancreas
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

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### Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

### Bizengri® (zenocutuzumab-zbco)

#### A. Criteria For Initial Approval

- i. Individual has a diagnosis of advanced, recurrent, unresectable or metastatic non-small cell lung cancer (NSCLC); **AND**
  - A. Individual has neuregulin 1 (NRG1) gene fusion; **AND**
  - B. Individual has disease progression on or after prior systemic therapy;

**OR**

- ii. Individual has a diagnosis of recurrent, advanced, or metastatic disease non-small cell lung cancer (NSCLC), including adenocarcinoma, large cell carcinoma, or squamous cell carcinoma (NCCN 2A); **AND**
  - A. Individual has neuregulin 1 (NRG1) gene fusion; **AND**
  - B. Individual is using as subsequent-line therapy as a single agent;

**OR**

- iii. Individual has a diagnosis of advanced, recurrent, unresectable or metastatic pancreatic adenocarcinoma; **AND**
  - A. Individual has neuregulin 1 (NRG1) gene fusion; **AND**
  - B. Individual has disease progression on or after prior systemic therapy.

**OR**

- iv. Individual has a diagnosis of pancreatic adenocarcinoma, adenosquamous carcinoma or squamous carcinoma (NCCN 2A); **AND**
  - A. Individual has advanced or metastatic pancreatic disease; **AND**
  - B. Individual is using as a single agent; **AND**
  - C. Individual has neuregulin 1 (NRG1) gene fusion; **AND**

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- D. Individual has disease progression on or after prior systemic therapy; **AND**
  - E. Individual has good performance status (ECOG PS 0-1) or intermediate PS (ECOG 2);
- OR**
- B. Individual is using as a single agent; **AND**
  - C. Individual has neuregulin 1 (NRG1) gene fusion; **AND**
  - D. Individual has disease progression on or after prior systemic therapy; **AND**
  - E. Individual has good performance status (ECOG PS 0-1) or intermediate PS (ECOG 2); **AND**
  - F. Individual has local recurrence in the pancreatic operative bed after resection.
- OR**
- G. Individual has recurrent metastatic disease with or without local recurrence after resection

### B. Criteria For Continuation of Therapy

- a. MMM considers continuation of Bizengri (zenocutuzumab-zbco) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of unacceptable toxicity or disease progression, or the maximum duration of therapy has not been exceeded. The following information should be supplied for reauthorization:
  - i. A current oncology note documenting the patient’s response to treatment showing no progression of disease.
  - ii. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

### C. Authorization Duration

- a. Initial Approval Duration: 6 months
- b. Reauthorization Approval Duration: Up to 6 months

### D. Conditions Not Covered

*Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):*

- a. Bizengri (zenocutuzumab-zbco) may not be approved when the above criteria are not met and for all other indications.

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### Limits or Restrictions:

#### A. Therapeutic Alternatives

*The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.*

- i. N/A

#### B. Quantity Limitations

*Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.*

Drug	Limit
Bizengri ((zenocutuzumab-zbco) 375 mg/18.75 mL	4 vials per 28 days
Exceptions	
N/A	

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### Reference Information:

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. <http://dailymed.nlm.nih.gov/dailymed/about.cfm>. Updated periodically.
2. 2025 ICD-10-CM codes C25\*: Malignant neoplasm of pancreas (no date) ICD10data.com. Available at: <https://www.icd10data.com/ICD10CM/Codes/C00-D49/C15-C26/C25-> (Accessed: 04 March 2025).
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. ICD10DATA.COM. ICD-10 Code Search. Accessed January 14, 2026. <https://www.icd10data.com/search>
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
6. National Comprehensive Cancer Network (NCCN). *NCCN Drug Compendium*. Accessed January 14, 2026. [https://www.nccn.org/professionals/drug\\_compendium/content/](https://www.nccn.org/professionals/drug_compendium/content/)
7. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. Accessed January 14, 2026. <http://www.nccn.org/index.asp>.
  - a. Non-Small Cell Lung Cancer. V3.202. Revised December 24, 2025.
  - b. Pancreatic Adenocarcinoma. V2.2025. Revised February 3, 2025.

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### Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Add pharmacologic class to service description and NCCN 2A recommendations to Background information. Add ECOG and subsequent therapy definitions. Add recurrent disease to lung and pancreatic cancer criteria. Add NCCN 2A recommendation for pancreatic adenocarcinoma as single agent if good ECOG local recurrence in the pancreatic operative bed after resection recurrent metastatic disease with or without local recurrence after resection. Add NCCN 2A recommendation for NSCLC for therapy as subsequent therapy as a single agent for NRG1 gene fusion positive recurrent, advanced, or metastatic disease to the criteria for initial approval. Coding reviewed: Added ICD-10-CM C25.0-C25.3, C25.7-C25.9, C33, C34.00-C34.92, Z85.07, Z85.118. Update reference list. Minor formatting changes.	2/13/2026	2/22/2026
Focus Review	Coding reviewed: J9382 added for Bizengri.	N/A	N/A
Policy Inception	Elevance Health's Medical Policy adoption	N/A	4/2/2025