POLICY: Oncology (Injectable) – Bizengri Utilization Management Medical Policy
- Bizengri® (zenocutuzumab-zbco intravenous infusion –Merus/Partner)

EFFECTIVE DATE: 5/1/2025
LAST REVISION DATE: 12/18/2024

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

Bizengri, a bispecific human epidermal growth factor receptor 2 and 3 (HER2)- and (HER3)-directed antibody, is indicated for the treatment of: [1]

- Non-small cell lung cancer (NSCLC), advanced, unresectable or metastatic, harboring a neuregulin 1 (*NRG1*) gene fusion with disease progression on or after prior systemic therapy in adults.
- Pancreatic adenocarcinoma, advanced, unresectable or metastatic, harboring a *NRG1* gene fusion with disease progression on or after prior systemic therapy in adults.

Dosing Information

The recommended dose of Bizengri is 750 mg as an intravenous infusion every two weeks until disease progression or unacceptable toxicity.[1]

Guidelines

Bizengri is not discussed in guidelines from the National Comprehensive Cancer Network (NCCN):

- **NSCLC:** NCCN guidelines (version 1.2025 – December 20, 2024) recommend molecular testing for patients with advanced or metastatic disease.[2] Recommendations are given based on the type of mutation or gene fusion. Generally, platinum based therapy such as carboplatin and cisplatin are used and programmed cell death protein 1 (PD)-1 or PD-ligand 1 (PD-L1) blockers are used as systemic therapy. Bizengri is recommended as a subsequent therapy for patients with the *NRG1* gene fusion for patients with recurrent, advanced, or metastatic disease (category 2A).
- **Pancreatic Adenocarcinoma:** NCCN guidelines (version 1.2025 – December 20, 2024) recommend tumor/somatic molecular profiling for patients with locally advanced/metastatic disease who are candidates for anti-cancer therapy to identify uncommon mutations, such as *NRG1* fusions.[3] Bizengri is not included in these guidelines. For patient with advanced or metastatic disease, clinical trial is preferred. For patients with metastatic or advanced disease, some of the "Preferred" regimens include FOLFIRINOX (fluorouracil + leucovorin + irinotecan + oxaliplatin) or a modified FOLFIRINOX with or without subsequent chemoradiation; and gemcitabine + albumin-bound paclitaxel with or without subsequent chemoradiation. There are other recommendations based on performance status and mutation type. There are no recommendations for patients with *NRG1* fusions.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Bizengri. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Bizengri as well as the monitoring required

for adverse events and long-term efficacy, approval requires Bizengri to be prescribed by or in consultation with a physician who specializes in the condition being treated.
Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Bizengri is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has advanced, unresectable, or metastatic disease; AND
   - **C)** The disease is neuregulin 1 (*NRG1*) gene fusion positive; AND
   - **D)** Patient has tried at least one systemic regimen; AND
     Note: Examples of a systemic regimen include one or more of the following drugs: carboplatin, cisplatin, or programmed cell death protein 1 (PD)-1 or PD-ligand 1 (PD-L1) blockers.
   - **E)** The medication will be prescribed by or in consultation with an oncologist.

   Dosing. Approve 750 mg as an intravenous infusion administered not more frequently than once every 2 weeks.

2. **Pancreatic Adenocarcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has advanced, unresectable, or metastatic disease; AND
   - **C)** The disease is neuregulin 1 (*NRG1*) gene fusion positive; AND
   - **D)** Patient has tried at least one systemic regimen; AND
     Note: Examples of systemic regimen include one or more of the following drugs: fluorouracil, leucovorin, irinotecan, oxaliplatin, gemcitabine, paclitaxel, capecitabine
   - **E)** The medication will be prescribed by or in consultation with an oncologist.

   Dosing. Approve 750 mg as an intravenous infusion administered not more frequently than once every 2 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Bizengri is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Bizengri® intravenous infusion [prescribing information]. Cambridge, MA: Merus; December 2024.
2. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 1.2025 – December 20, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 30, 2024.

3. The NCCN Pancreatic Adenocarcinoma Cancer Clinical Practice Guidelines in Oncology (version 1.2025 – December 20, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 30, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	12/18/2024
Update	Updated the overview section to include updated NCCN guidelines.	12/30/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	03/10/2025