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Section:	Prescription Drugs	**Effective Date:**	July 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	January 10, 2025
Subject:	Bizengri	**Page:**	1 of 4

Last Review Date: June 12, 2025

Bizengri

Description

Bizengri (zenocutuzumab-zbco)

Background
Bizengri (zenocutuzumab-zbco) is a bispecific antibody that binds to the extracellular domains of human epidermal growth factor receptors 2 and 3 (HER2 and HER3) expressed on the surface of cells, including tumor cells, inhibiting HER2:HER3 dimerization and preventing neuregulin 1 (NRG1) binding to HER3. Bizengri decreased cell proliferation and signaling through the phosphoinositide 3-kinase (PI3K)-AKT-mammalian target of rapamycin (mTOR) pathway. In addition, Bizengri mediates antibody-dependent cellular cytotoxicity (ADCC). Bizengri showed antitumor activity in mouse models of NRG1 fusion-positive lung and pancreatic cancers (1).

Regulatory Status
FDA-approved indications: Bizengri is a bispecific HER2- and HER3-directed antibody indicated for the treatment of: (1)

- 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.
- Adults with advanced, unresectable or metastatic pancreatic adenocarcinoma harboring a neuregulin 1 (NRG1) gene fusion with disease progression on or after prior systemic therapy.

Bizengri has a boxed warning for embryo-fetal toxicity. Bizengri can cause harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive

potential prior to Bizengri treatment. Advise females of reproductive potential to use effective contraception while receiving Bizengri and for 2 months following the last dose (1).

Infusion-related reactions (IRR)/hypersensitivity/anaphylaxis, interstitial lung disease (ILD)/pneumonitis, and left ventricular dysfunction can occur in patients treated with Bizengri. Patient should be monitored for signs and symptoms of IRRs and ILD/pneumonitis. Left ventricular ejection fraction (LVEF) should be assessed prior to Bizengri treatment and at regular intervals during treatment as clinically indicated. Treatment should be permanently discontinued if the patient experiences Grade 4 or life-threatening IRR or hypersensitivity/anaphylaxis, ≥ Grade 2 ILD/pneumonitis, LVEF of less than 45% or less than 50% with absolute decrease from baseline of 10% or greater, or systematic congestive heart failure (CHF) (1).

The safety and effectiveness of Bizengri in pediatric patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Bizengri may be considered **medically necessary** if the conditions indicated below are met.

Bizengri may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Advanced, unresectable or metastatic non-small cell lung cancer (NSCLC)
2. Advanced, unresectable or metastatic pancreatic adenocarcinoma

AND ALL of the following:

1. Presence of neuregulin 1 (NRG1) gene fusion

2. Patient has had disease progression on or after prior systemic therapy
3. Prescriber agrees to monitor for signs and symptoms of interstitial lung disease (ILD)
4. Prescriber agrees to assess left ventricular ejection fraction (LVEF) prior to initiation and at regular intervals during treatment as clinically indicated
5. Females of reproductive potential **only**: patient has had a negative pregnancy test
6. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Bizengri and for 2 months after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Advanced, unresectable or metastatic non-small cell lung cancer (NSCLC)
2. Advanced, unresectable or metastatic pancreatic adenocarcinoma

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor for signs and symptoms of interstitial lung disease (ILD)
3. Prescriber agrees to assess left ventricular ejection fraction (LVEF) at regular intervals during treatment as clinically indicated
4. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Bizengri and for 2 months after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Bizengri (zenocutuzumab-zbco) is a bispecific HER2- and HER3-directed antibody indicated for the treatment of adult patients with advanced, unresectable or metastatic NSCLC and pancreatic adenocarcinoma. Bizengri has a boxed warning regarding embryo-fetal toxicity. Bizengri also has warnings for infusion-related reactions, interstitial lung disease, and left ventricular dysfunction. The safety and effectiveness of Bizengri in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Bizengri while maintaining optimal therapeutic outcomes.

References

1. Bizengri [package Insert]. Lexington, MA: Partner Therapeutics, Inc.; March 2025.
2. NCCN Drugs & Biologics Compendium® Zenocutuzumab-zbco 2025. National Comprehensive Cancer Network, Inc. Accessed on April 11, 2025.

Policy History

Date	Action
January 2025	Addition to PA
March 2025	Annual review and reference update
June 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 12, 2025 and is effective on July 1, 2025.