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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	November 8, 2024
Subject:	Vyloy	**Page:**	1 of 4

Last Review Date: March 7, 2025

Vyloy

Description

Vyloy (zolbetuximab-clzb)

Background
Vyloy (zolbetuximab-clzb) is a claudin 18.2 (CLDN18.2)-directed cytolytic antibody that depletes CLDN18.2-positive cells via antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). Vyloy in combination with chemotherapy had increased antitumor activity in CLDN18.2-expressing mouse tumor models compared to Vyloy or chemotherapy alone (1).

Regulatory Status
FDA-approved indications: Vyloy is a claudin 18.2-directed cytolytic antibody and is indicated in combination with fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of adults with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors are claudin (CLDN) 18.2 positive as determined by an FDA-approved test (1).

Prior to each infusion of Vyloy, premedicate patients with a combination of antiemetics (e.g., NK-1 receptor blockers and/or 5-HT3 receptor blockers, as well as other drugs as indicated) for the prevention of nausea and vomiting (1).

Vyloy contains warnings regarding hypersensitivity reactions (including anaphylaxis reactions and infusion related reactions) and severe nausea and vomiting (1).

Vyloy is administered as an intravenous infusion only (1).

The safety and effectiveness of Vyloy 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.

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

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

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma
    a. Used as first-line treatment in combination with fluoropyrimidine- and platinum-containing chemotherapy
    b. Tumors are claudin (CLDN) 18.2 positive as determined by an FDA-approved test

AND ALL of the following:

1. Prescriber agrees to monitor patients for hypersensitivity reactions during infusion with Vyloy and for at least 2 hours after completion of infusion
2. Prescriber agrees to premedicate with antiemetics prior to each infusion of Vyloy as clinically indicated

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma
    a. Used in combination with fluoropyrimidine- and platinum-containing chemotherapy

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor patients for hypersensitivity reactions during infusion with Vyloy and for at least 2 hours after completion of infusion
3. Prescriber agrees to premedicate with antiemetics prior to each infusion of Vyloy as clinically indicated

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Vyloy is indicated in combination with fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of adults with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors are claudin (CLDN) 18.2-positive as determined by an FDA-approved test. The safety and effectiveness of Vyloy 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 Vyloy while maintaining optimal therapeutic outcomes.

References

1. Vyloy [package Insert]. Northbrook, IL: Astellas Pharma US, Inc.; October 2024.
2. NCCN Drugs & Biologics Compendium® Zolbetuximab-clzb 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.

Policy History

Date	Action
November 2024	Addition to PA
December 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.