Clinical Policy: Zolbetuximab-clzb (Vyloy)

Reference Number: PA.CP.PHAR.705
Effective Date: 01/2025
Last Review Date: 10/2025

Description

Zolbetuximab-clzb (Vyloy®) is a claudin (CLDN) 18.2-directed cytolytic antibody.

FDA Approved Indication(s)

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 adenocarcinoma whose tumors are CLDN 18.2 positive as determined by an FDA-approved test.

Policy/Criteria

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

It is the policy of PA Health & Wellness® that Vyloy is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Gastric or Gastroesophageal Junction Adenocarcinoma (must meet all)**:**

1. Diagnosis of gastric or gastroesophageal junction adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. Disease is locally advanced unresectable, recurrent or metastatic;
   b. Member is not a sugical candidate, and request is for palliative therapy;
5. Disease is HER2-negative;
6. Tumor is CLDN 18.2 positive;
7. Request is for first-line treatment;
8. Vyloy is prescribed in combination with both of the following (a and b):
   a. Fluoropyrimidine (e.g., capecitabine, fluorouracil)-containing chemotherapy;
   b. Platinum (e.g., oxaliplatin)-containing chemotherapy;
9. Request meets one of the following (a or b):
   a. Dose does not exceed an initial 800 mg/m^2 dose followed by either 600 mg/m^2 every 3 weeks or 400 mg/m^2 every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Gastric or Gastroesophageal Junction Adenocarcinoma (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 600 mg/m^2 every 3 weeks or 400 mg/m^2 every 2 weeks;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLDN: claudin
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Gastric or gastroesophageal junction adenocarcinoma	First dose: 800 mg/m^2 IV Subsequent doses: • 600 mg/m^2 IV every 3 weeks, or • 400 mg/m^2 IV every 2 weeks	See dosing regimen

VI. Product Availability

Lyophilized powder in single-dose vials: 100 mg, 300 mg

VII. References

1. Vyloy Prescribing Information. Northbrook, IL: Astellas Pharma US, Inc.; June 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761365s000lbl.pdf. Accessed July 14, 2025.
2. Shitara K, Lordick F, Bang YJ, et al. Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial. Lancet. 2023 May 20; 401(10389): 1655-1668.
3. Shah MA, Shitara K, Ajani JA, et al. Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial. Nat Med. 2023 Aug; 29(8): 2133-2141.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 15, 2025.
5. National Comprehensive Cancer Network. Esophageal and Esophagogastric Junction Cancers Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed July 15, 2025.July 15, 2025.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1326	Injection, zolbetuximab-clzb, 2 mg

Reviews, Revisions, and Approvals	Date
Policy created	12/2024
4Q 2025 annual review: added options for use in recurrent disease and as palliative therapy in members who are not surgical candidates per NCCN; extended initial approval duration from 6 to 12 months; HCPCS code added [J1326], removed codes [J9999, C9399]. RT4: added new dosage strength of 300 mg; references reviewed and updated.	10/2025