Medical Drug Clinical Criteria

Subject:	Vyloy (zolbetuximab-clzb)		
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Overview

This document addresses the use of Vyloy (zolbetuximab-clzb). Vyloy is a claudin 18.2-directed cytolytic antibody FDA indicated for 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 claudin 18.2 positive. Vyloy is given as an intravenous infusion given every 3 or 2 weeks after first dose. Due to infusion-related reactions, monitoring after infusion with Vyloy is necessary.

Claudin18.2 (CLDN18.2) is a highly selective marker protein that is expressed in differentiated gastric mucosal membrane epithelial cells in approximately 38% of advanced gastric cancer cases. Vyloy is approved specifically for tumors that are CLDN18.2 positive. It is the first CLDN18.2-targeted therapy to be approved by the FDA. The FDA also approved the VENTANA CLDN18 (43-14A) RxDx Assay (Ventana Medical Systems, Inc./Roche Diagnostics) as a companion diagnostic device to identify individuals with gastric or GEJ adenocarcinoma who may be eligible for treatment with Vyloy.

Severe nausea and vomiting may occur with Vyloy. Premedicate with antiemetics prior to each infusion. Interrupt or permanently discontinue Vyloy based on the severity of nausea and vomiting. Manage symptoms during and after infusion with antiemetics or fluid replacement. Approval of Vyloy was based on positive progression-free-survival (PFS) results from the phase 3 SPOTLIGHT and GLOW trials. PFS in SPOTLIGHT was 10.6 months in the Vyloy group compared with 8.7 months in the placebo group. In the GLOW trial, PFS was 8.2 months in the Vyloy group compared with 6.8 months in the placebo group.

Definitions and Measures

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

Chemotherapy: Medical treatment of a disease, particularly cancer, with drugs or other chemicals.

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 house work, 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

Hormonal therapy: Treatment that adds, blocks, or removes hormones. Agents that slow or stop the growth of certain cancers, synthetic hormones or other drugs may be given to block the body's natural hormones.

Immune checkpoint inhibitor: A type of drug that blocks certain proteins made by some types of immune system cells, such as T cells, and some cancer cells. When these proteins are blocked, the "brakes" on the immune system are released and T cells are able to kill cancer cells better. Examples of checkpoint proteins found on T cells or cancer cells include programmed death (PD)-1, PD-ligand 1 (PD-L1), and cytotoxic T-lymphocyte–associated antigen (CTLA)-4/B7-1/B7-2 (NCI, 2018).

Immune thrombocytopenia: A bleeding disorder where the blood is unable to clot, as a result of a low number of platelets or thrombocytes.

Kinase inhibitor: Type of drug which works by blocking several enzymes that promote cell growth, which has been found to be an effective approach to treat a variety of cancers.

KRAS wild-type: The normal or typical form of the KRAS gene, as distinguished from any mutant forms of KRAS; KRAS lacking mutation.

Line of Therapy:

- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Locally advanced cancer: Cancer that has spread only to nearby tissues or lymph nodes.

Maintenance therapy: Designed to maintain a condition to prevent a relapse.

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.

Mutation: A permanent, transmissible change in genetic material.

Primary treatment: The first treatment given for a disease. It is often part of a standard set of treatments, such as surgery followed by chemotherapy and radiation. Also called first-line therapy, induction therapy, and primary therapy.

Progressive Disease (PD): Cancer that is growing, spreading, or getting worse.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Stable disease: Cancer that is not decreasing or increasing in extent or severity.

Targeted biologic agent: A newer type of drug developed specifically to target genetic changes in cells that cause cancer. It works differently than standard chemotherapy drugs, often with different side effects.

Unresectable: Unable to be removed with surgery.

Clinical Criteria

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.

Vyloy (zolbetuximab-clzb)

Requests for Vyloy (zolbetuximab-clzb) may be approved if the following criteria are met:

I. Individual has a diagnosis of gastric or gastroesophageal junction (GEJ) adenocarcinoma; **AND**
II. Individual has locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative disease; **AND**
III. Individual is using as first-line treatment; **AND**
IV. Individual is using in combination with fluoropyrimidine- and platinum-containing chemotherapy; **AND**
V. Individual has a tumor which is claudin (CLDN) 18.2 positive; **AND**
VI. Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1.

Requests for Vyloy (zolbetuximab-clzb) may not be approved for the following:

I. Individual with complete or partial gastric outlet syndrome with persistent/recurrent vomiting; **OR**
II. History of central nervous system metastases; **OR**
III. History of carcinomatous meningitis from gastric/GEJ cancer.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS	
C9399	Unclassified drugs or biologicals [Vyloy (zolbetuximab-clzb)]
J9999	Not otherwise classified, antineoplastic drugs [Vyloy (zolbetuximab-clzb)]
ICD-10 Diagnosis	
	All diagnosis pend

Document History

New: 11/22/2024
Document History:

- 11/22/2024 – Select Review: New PA for Vyloy (zolbetuximab-clzb). Coding Reviewed: Added HCPCS NOC C9399 and J9999. Added all diagnosis pend.

References

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2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
4. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on November 18, 2024.
    a. Gastric Cancer. V4.2024. Revised August 12, 2024.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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