VYLOY Product Information for Order Sets

VYLOY®
zolbetuximab-clzb
for injection 100mg vial

INDICATION

VYLOY, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated 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.

SELECT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity reactions, including serious anaphylaxis reactions, and serious and fatal infusion-related reactions (IRR) have been reported in clinical studies when VYLOY has been administered. **Any grade hypersensitivity reactions**, including anaphylactic reactions, occurring with VYLOY in combination with mFOLFOX6 or CAPOX was 18%. **Severe (Grade 3 or 4) hypersensitivity reactions**, including anaphylactic reactions, occurred in 2% of patients. Seven patients (1.3%) permanently discontinued VYLOY for hypersensitivity reactions, including two patients (0.4%) who permanently discontinued VYLOY due to anaphylactic reactions. Seventeen (3.2%) patients required dose interruption, and three patients (0.6%) required infusion rate reduction due to hypersensitivity reactions. **All grade IRRs** occurred in 3.2% in patients administered VYLOY in combination with mFOLFOX6 or CAPOX. Severe (Grade 3) IRRs occurred in 2 (0.4%) patients who received VYLOY. An IRR led to permanent discontinuation of VYLOY in 2 (0.4%) patients and dose interruption in 7 (1.3%) patients. The infusion rate was reduced for VYLOY for 2 (0.4%) patients due to an IRR. Monitor patients during infusion with VYLOY and for 2 hours after completion of infusion or longer if clinically indicated, for hypersensitivity reactions with symptoms and signs that are highly suggestive of anaphylaxis (urticaria, repetitive cough, wheeze and throat tightness/change in voice). Monitor patients for signs and symptoms of IRRs including nausea, vomiting, abdominal pain, salivary hypersecretion, pyrexia, chest discomfort, chills, back pain, cough and hypertension. If a severe or life-threatening hypersensitivity or IRR reaction occurs, discontinue VYLOY permanently, treat symptoms according to standard medical care, and monitor until symptoms resolve. For any Grade 2 hypersensitivity or IRR, interrupt the VYLOY infusion until Grade ≤1, then resume at a reduced infusion rate for the remaining infusion. Follow Grade 2 management for Grade 3 infusion-related nausea and vomiting. Premedicate the patient with antihistamines for the subsequent infusions, and closely monitor the patient for symptoms and signs of a hypersensitivity reaction. The infusion rate may be gradually increased as tolerated.

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This document details information about VYLOY® (zolbetuximab-clzb), such as the indication, cycle information, treatment calendar, important dosing information, and dosing modifications; however, the information contained in this document is not fully inclusive of all details of the VYLOY Prescribing Information. The clinical data elements are suggestions only. The customer must determine the final elements to include in line with the organization's expectations, goals, and electronic health record (EHR) governing principles. The customers (ie, physicians, medical groups, integrated delivery networks [IDNs]) shall be solely responsible for implementation, testing, and monitoring of the instructions to ensure proper orientation in each customer's EHR system.

While EHRs may assist providers in identifying appropriate patients for consideration of assessment and treatment, the decision and action should ultimately be made by a provider in consultation with the patient after a review of the patient's records to determine eligibility, and Astellas shall have no liability thereto.

Please consult the most recent version of the VYLOY Prescribing Information for full medication details. The most recent version of the VYLOY Prescribing Information may be found at: https://www.astellas.com/us/system/files/vyloy_pi.pdf.

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Indication and Important Safety Information

INDICATION

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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity reactions, including serious anaphylaxis reactions, and serious and fatal infusion-related reactions (IRR) have been reported in clinical studies when VYLOY has been administered. **Any grade hypersensitivity reactions**, including anaphylactic reactions, occurring with VYLOY in combination with mFOLFOX6 or CAPOX was 18%. **Severe (Grade 3 or 4) hypersensitivity reactions**, including anaphylactic reactions, occurred in 2% of patients. Seven patients (1.3%) permanently discontinued VYLOY for hypersensitivity reactions, including two patients (0.4%) who permanently discontinued VYLOY due to anaphylactic reactions. Seventeen (3.2%) patients required dose interruption, and three patients (0.6%) required infusion rate reduction due to hypersensitivity reactions. **All grade IRRs** occurred in 3.2% in patients administered VYLOY in combination with mFOLFOX6 or CAPOX. Severe (Grade 3) IRRs occurred in 2 (0.4%) patients who received VYLOY. An IRR led to permanent discontinuation of VYLOY in 2 (0.4%) patients and dose interruption in 7 (1.3%) patients. The infusion rate was reduced for VYLOY for 2 (0.4%) patients due to an IRR. Monitor patients during infusion with VYLOY and for 2 hours after completion of infusion or longer if clinically indicated, for hypersensitivity reactions with symptoms and signs that are highly suggestive of anaphylaxis (urticaria, repetitive cough, wheeze and throat tightness/change in voice). Monitor patients for signs and symptoms of IRRs including nausea, vomiting, abdominal pain, salivary hypersecretion, pyrexia, chest discomfort, chills, back pain, cough and hypertension. If a severe or life-threatening hypersensitivity or IRR reaction occurs, discontinue VYLOY permanently, treat symptoms according to standard medical care, and monitor until symptoms resolve. For any Grade 2 hypersensitivity or IRR, interrupt the VYLOY infusion until Grade ≤1, then resume at a reduced infusion rate for the remaining infusion. Follow Grade 2 management for Grade 3 infusion-related nausea and vomiting. Premedicate the patient with antihistamines for the subsequent infusions, and closely monitor the patient for symptoms and signs of a hypersensitivity reaction. The infusion rate may be gradually increased as tolerated.

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Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Severe Nausea and Vomiting. VYLOY is emetogenic. Nausea and vomiting occurred more often during the first cycle of treatment. **All grade nausea and vomiting** occurred in 82% and 67% respectively of patients treated with VYLOY in combination with mFOLFOX6 and 69% and 66% in combination with CAPOX, respectively. **Severe (Grade 3) nausea** occurred in 16% and 9% of patients treated with VYLOY in combination with mFOLFOX6 or CAPOX respectively. **Severe (Grade 3) vomiting** occurred in 16% and 12% of patients treated with VYLOY in combination with mFOLFOX6 or CAPOX. Nausea led to permanent discontinuation of VYLOY in combination with mFOLFOX6 or CAPOX in 18 (3.4%) patients and dose interruption in 147 (28%) patients. Vomiting led to permanent discontinuation of VYLOY in combination with mFOLFOX6 or CAPOX in 20 (3.8%) patients and dose interruption in 150 (28%) patients. Pretreat with antiemetics prior to each infusion of VYLOY. Manage patients during and after infusion with antiemetics or fluid replacement. Interrupt the infusion, or permanently discontinue VYLOY based on severity.

ADVERSE REACTIONS

Most common adverse reactions (≥15%): Nausea, vomiting, fatigue, decreased appetite, diarrhea, peripheral sensory neuropathy, abdominal pain, constipation, decreased weight, hypersensitivity reactions, and pyrexia.

Most common laboratory abnormalities (≥15%): Decreased neutrophil count, decreased leucocyte count, decreased albumin, increased creatinine, decreased hemoglobin, increased glucose, decreased lymphocyte count, increased aspartate aminotransferase, decreased platelets, increased alkaline phosphatase, increased alanine aminotransferase, decreased glucose, decreased sodium, increased phosphate, decreased potassium, and decreased magnesium.

SPOTLIGHT Study: 279 patients with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors were CLDN18.2 positive who received at least one dose of VYLOY in combination with mFOLFOX6

Serious adverse reactions occurred in 45% of patients treated with VYLOY in combination with mFOLFOX6; the **most common serious adverse reactions** (≥2%) were vomiting (8%), nausea (7%), neutropenia (2.9%), febrile neutropenia (2.9%), diarrhea (2.9%), intestinal obstruction (3.2%), pyrexia (2.5%), pneumonia (2.5%), respiratory failure (2.2%), pulmonary embolism (2.2%), decreased appetite (2.1%) and sepsis (2.0%). **Fatal adverse reactions** occurred in 5% of patients who received VYLOY in combination with mFOLFOX6 including sepsis (1.4%), pneumonia (1.1%), respiratory failure (1.1%), intestinal obstruction (0.7%), acute hepatic failure (0.4%), acute myocardial infarction (0.4%), death (0.4%), disseminated intravascular coagulation (0.4%), encephalopathy (0.4%), and upper gastrointestinal hemorrhage (0.4%).

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Important Safety Information (cont'd)

ADVERSE REACTIONS (cont'd)

Permanent discontinuation of VYLOY due to an adverse reaction occurred in 20% of patients; the **most common adverse reactions leading to discontinuation** (≥2%) were nausea and vomiting. Dosage interruptions of VYLOY due to an adverse reaction occurred in 75% of patients; **the most common adverse reactions leading to dose interruption** (≥5%) were nausea, vomiting, neutropenia, abdominal pain, fatigue, and hypertension.

GLOW Study: 254 patients with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors were CLDN18.2 positive who received at least one dose of VYLOY in combination with CAPOX

Serious adverse reactions occurred in 47% of patients treated with VYLOY in combination with CAPOX; the **most common serious adverse reactions** (≥2%) were vomiting (6%), nausea (4.3%), decreased appetite (3.9%), decreased platelet count (3.1%), upper gastrointestinal hemorrhage (2.8%), diarrhea (2.8%), pneumonia (2.4%), pulmonary embolism (2.3%), and pyrexia (2.0%). **Fatal adverse reactions** occurred in 8% of patients who received VYLOY in combination with CAPOX including sepsis (1.2%), pneumonia (0.4%), death (0.8%), upper gastrointestinal hemorrhage (0.8%), cerebral hemorrhage (0.8%), abdominal infection (0.4%), acute respiratory distress syndrome (0.4%), cardio-respiratory arrest (0.4%), decreased platelet count (0.4%), disseminated intravascular coagulation (0.4%), dyspnea (0.4%), gastric perforation (0.4%), hemorrhagic ascites (0.4%), procedural complication (0.4%), sudden death (0.4%), and syncope (0.4%). Permanent discontinuation of VYLOY due to an adverse reaction occurred in 19% of patients; the **most common adverse reaction leading to discontinuation** (≥2%) was vomiting. Dosage interruption of VYLOY due to an adverse reaction occurred in 55% of patients; the **most common adverse reactions leading to dose interruption** (≥2%) were nausea, vomiting, neutropenia, thrombocytopenia, anemia, fatigue, infusion-related reaction, and abdominal pain.

SPECIFIC POPULATIONS

Lactation Advise lactating women not to breastfeed during treatment with VYLOY and for 8 months after the last dose.

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Patient counseling information[1]

Consider discussing the following patient counseling information with patients and advise the patient to read the FDA-approved patient labeling.

Hypersensitivity reactions, including anaphylaxis and infusion-related reactions

Advise patients of the risk of hypersensitivity reactions, including anaphylaxis and infusion-related reactions, and to contact their HCP right away if they experience symptoms of a hypersensitivity or infusion-related reaction during or after the administration of VYLOY.

Severe nausea and vomiting

Advise patients of the risk of severe nausea and vomiting and to immediately contact their HCP if they experience persistent or worsening nausea or vomiting.

Lactation

Advise women not to breastfeed during treatment with VYLOY and for 8 months after the last dose of VYLOY.

FDA, United States Food and Drug Administration; **HCP,** healthcare provider.

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Use in specific populations

Pregnancy

There are no data with VYLOY use in pregnant women to inform any drug-associated risks. VYLOY should only be given to a pregnant woman if the benefit outweighs the potential risk. Advise patients to inform their HCP if they become pregnant or plan to become pregnant during treatment with VYLOY.

- The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively

Lactation

There are no data on the presence of zolbetuximab-clzb in human milk, the effects on the breastfed child, or the effects on milk production. Because antibodies may be excreted in human milk and because of the potential for adverse reactions in a breastfed child, advise a lactating woman not to breastfeed during treatment with VYLOY and for 8 months after the last dose.

Females and males of reproductive potential

VYLOY is used in combination with fluoropyrimidine- or platinum-containing chemotherapy. Refer to the Full Prescribing Information of fluoropyrimidine- and platinum-containing chemotherapy products for pregnancy testing, contraception, and infertility information.

Pediatric use

The safety and effectiveness of VYLOY in pediatric patients have not been established.

Geriatric use

Of the 533 patients in clinical studies of VYLOY in combination with mFOLFOX6 or CAPOX, 34% (n = 179) were older than 65 years, and 5% were older than 75 years (n = 28). No overall differences in safety or effectiveness were observed between patients aged 65 years or older and younger patients.

CAPOX, capecitabine, oxaliplatin; **mFOLFOX6,** oxaliplatin, leucovorin, fluorouracil.

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Prescriber considerations[1]

Prior to VYLOY administration

- Prior to each infusion of VYLOY, premedicate patients with a combination of antiemetics (eg, NK-1 receptor blockers and/or 5-HT_3 receptor blockers, as well as other drugs as indicated) for the prevention of nausea and vomiting
- Gather information on all patient's medical conditions, including
  - If they are currently experiencing symptoms of nausea or vomiting
  - If they are pregnant or plan to become pregnant
  - If they are breastfeeding or plan to breastfeed
- Gather information on all patient's medications, including prescription and over-the-counter medicines, vitamins, and herbal supplements
- Provide patient counseling information to patients (see *Patient Counseling* on page 6)

NK-1, neurokinin-1.

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Possible side effects of VYLOY[1]

VYLOY may cause serious side effects, including

- **Allergic reactions, including anaphylaxis and infusion-related reactions.** Allergic reactions are common during treatment with VYLOY and can sometimes be serious. Serious allergic reactions can happen during or after VYLOY infusion, including life-threatening allergic reactions and serious infusion-related reactions that may lead to death. The patient's HCP will monitor them during the infusion and for 2 hours after or longer if needed. Encourage patients to tell their HCP or nurse or get emergency medical help right away if they get any of the following symptoms of a serious allergic reaction during or after the infusion of VYLOY:
  - Itchy, raised bumps on the skin (hives)
  - Coughing that does not go away
  - Breathing problems such as wheezing
  - Throat tightness or change in voice
  - Nausea or vomiting
  - Stomach (abdominal) pain
  - Increased saliva
  - Fever
  - Chest discomfort
  - Chills or shaking
  - Back pain
- **Severe nausea and vomiting.** Nausea and vomiting are common during treatment with VYLOY and can sometimes be severe. Nausea and vomiting happened more often during the first treatment cycle. Before patients receive each VYLOY infusion, their HCP will give them medicines to help prevent nausea and vomiting. Encourage patients to tell their HCP right away if nausea or vomiting does not go away or gets worse.

The most common side effects of VYLOY include:

- Tiredness
- Decreased appetite
- Diarrhea
- Tingling or numbness of the arms or legs
- Stomach (abdominal) pain
- Constipation
- Decreased weight
- Fever
- Decreased white blood cells, red blood cells, and platelets
- Decreased protein (albumin) in the blood
- Changes in kidney function tests
- Changes in blood sugar (glucose)
- Changes in liver function tests
- Changes in body salts (electrolytes) in blood

If patients experience certain side effects, their HCP may slow the rate of infusion, temporarily stop or completely stop treatment with VYLOY.

These are not all of the possible side effects of VYLOY.

Patients should call their doctor for medical advice about side effects. Side effects may be reported to the FDA at 1-800-FDA-1088.

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Patient selection

Select patients with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors are CLDN18.2 positive (defined as ≥75% of tumor cells demonstrating moderate to strong membranous CLDN18 immunohistochemical staining) for treatment with VYLOY in combination with fluoropyrimidine- and platinum-containing chemotherapy using an FDA-approved test.

Nurse verification

Assess patients for all adverse events during the course of treatment. If a patient is experiencing nausea and/or vomiting prior to administration of VYLOY, the symptoms should be resolved to Grade ≤1 before administering the first infusion.

Pharmacist verification

Verify VYLOY indication, dosing, and administration

- VYLOY, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors are claudin (CLDN) 18.2 positive as determined by an FDA-approved test
- Administer VYLOY in combination with fluoropyrimidine- and platinum-containing chemotherapy as follows:
  - First dose: 800 mg/m^2 intravenously
  - Subsequent doses:
    - 600 mg/m^2 intravenously every 3 weeks, or
    - 400 mg/m^2 intravenously every 2 weeks
  - Continue treatment until disease progression or unacceptable toxicity
- Ensure the dosing and administration aligns with the indicated use of VYLOY (see Recommended dosing on page 11 and Dose modifications on page 12)

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Dosing and administration[1]

Recommended dosing

Infusion rates recommended for each VYLOY infusion

VYLOY dose		Initial infusion rate (first 30-60 minutes)*	Subsequent infusion rate
First dose	800 mg/m^2	100 mg/m^2/hr	200-265 mg/m^2/hr
Subsequent doses	600 mg/m^2 every 3 weeks or 400 mg/m^2 every 2 weeks	75 mg/m^2/hr or 50 mg/m^2/hr	150-265 mg/m^2/hr or 100-200 mg/m^2/hr

*In the absence of adverse reactions after 30 to 60 minutes, the infusion rate can be increased to the subsequent infusion rate as tolerated.

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Dosing and administration (cont'd)[1]

Dose modifications for certain adverse events

No dose reduction for VYLOY is recommended. Adverse reactions for VYLOY are managed by reducing the infusion rate, interruption of the infusion, withholding the dose, and/or permanently discontinuing VYLOY as described in the table.

Dose modifications for VYLOY

Adverse reaction	Severity*	Dose modification
Hypersensitivity reactions or infusion-related reactions	Grade 2	• Interrupt the infusion until Grade ≤1, then resume at a reduced infusion rate for the remaining infusion • Premedicate and administer the next infusion per the infusion rates in the full Prescribing Information
	Grade 3† or 4 or anaphylaxis	Immediately stop the infusion and permanently discontinue.

*Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0).[1]
†Follow Grade 2 management for Grade 3 infusion-related nausea and vomiting.[1]

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Dosage forms and strengths[1,2]

VYLOY (zolbetuximab-clzb) for injection is supplied as a sterile, preservative-free, white to off-white lyophilized powder in single-dose vials. Each vial contains 100 mg of VYLOY and is available in the following package:

Carton of one 100 mg single-dose vial (NDC 0469-3425-10)

Administration[1]

- See full Prescribing Information for details
- Administer VYLOY as an intravenous infusion only. Do NOT administer as an IV push or bolus
- If VYLOY and fluoropyrimidine- and platinum-containing chemotherapy are administered on the same day, VYLOY must be administered first
- Prior to administration, the VYLOY vial is reconstituted with SWFI. The reconstituted solution is subsequently diluted in an intravenous infusion bag containing 0.9% Sodium Chloride Injection, USP

NDC, National Drug Code; **SWFI,** Sterile Water for Injection; **USP,** The United States Pharmacopeia.

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VYLOY Support Solutions™ Website	https://vyloysupportsolutions.com
VYLOY HCP Website	https://www.vyloyhcp.com
GLOW Study Protocol	https://www.nature.com/articles/s41591-023-02465-7
SPOTLIGHT Study Protocol	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00620-7/fulltext
VYLOY Patient Website	https://vyloy.com

References: 1. VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Astellas. VYLOY. Data on File.

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