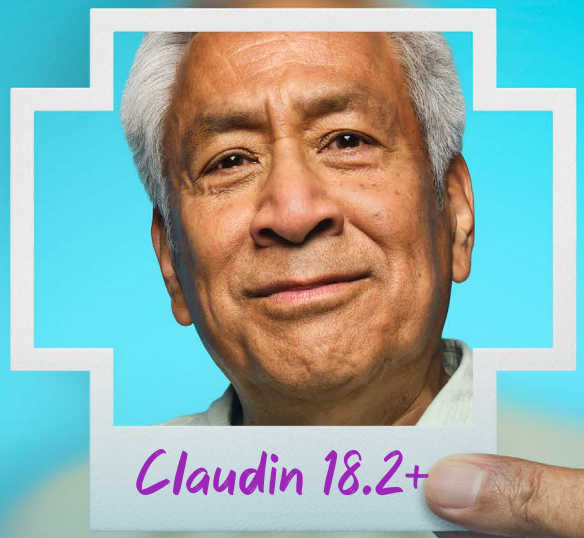
NOW APPROVED

Detect a new target for a new therapy.

A new predictive biomarker in advanced* gastric/GEJ cancer has come into focus.[1,2]



*Locally advanced unresectable or metastatic.[1]
GEJ=gastroesophageal junction.

INDICATION

VYLOY® (zolbetuximab-clzb), 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 anaphylaxis, and infusion-related reactions (IRR) have been reported in clinical studies when VYLOY has been administered with mFOLFOX6 or CAPOX. **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.

Please see Important Safety Information continued throughout and on page 4, and full Prescribing Information.

VYLOY®
zolbetuximab-clzb
for injection 100mg vial

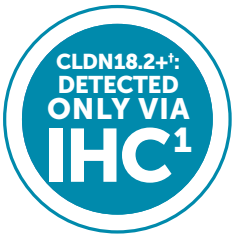
VYLOY (zolbetuximab-clzb) is a first-in-class FDA-approved monoclonal antibody that targets a predictive biomarker: **claudin 18.2 (CLDN18.2)**[1-4]

According to estimates from two global Phase 3 studies:

38% **OF PATIENTS** with advanced* G/GEJ adenocarcinoma are CLDN18.2+† and may be candidates for VYLOY + chemo[1,3,4‡]

Data from 2 global randomized Phase 3 studies: SPOTLIGHT, which included 2,403 assessable patients, of which 922 were CLDN18.2 positive; and GLOW, which included 2,104 assessable patients, of which 808 were CLDN18.2 positive as determined by immunohistochemistry in a central laboratory using the investigational VENTANA CLDN18 (43-14A) RxDx Assay.[3,4]

Test for CLDN18.2 status alongside HER2 and other biomarkers[3-6]



The VENTANA CLDN18 (43-14A) RxDx Assay is now available on the BenchMark ULTRA IHC/ISH platform[7]

- FDA approved as a companion diagnostic to identify patients who may be candidates for treatment with VYLOY + chemo[1,7]
- This assay is used with OptiView DAB IHC Detection Kit for staining on a BenchMark ULTRA instrument[7]

VENTANA CLDN18 (43-14A) RxDx Assay and BenchMark ULTRA are registered trademarks of Roche Diagnostics.

*Locally advanced unresectable or metastatic.[1]
†CLDN18.2+ (claudin 18.2 positive) is defined as ≥75% of tumor cells demonstrating moderate to strong membranous CLDN18 staining by IHC.[1,3,4]
‡Fluoropyrimidine- and platinum-containing chemotherapy.[1]
CLDN18.2=claudin 18.2; **G/GEJ=**gastric/gastroesophageal junction; **IHC=**immunohistochemistry; **ISH=**in situ hybridization.

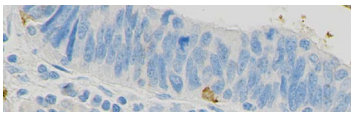
SELECT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

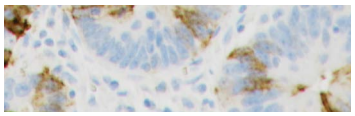
Severe Nausea and Vomiting. VYLOY is emetogenic. Nausea and vomiting occurred more often during the first cycle of treatment. **All grade nausea and vomiting** occurred in 82% and 67% respectively of patients treated with VYLOY in combination with mFOLFOX6 and 69% and 66% in combination with CAPOX, respectively. **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.

Help oncologists identify the right patients for a first-line treatment strategy with **VYLOY + chemo**[1]

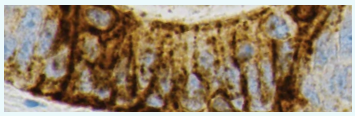
CLDN18.2 status is evaluated using both membranous staining intensity and percentage of viable tumor cells stained.[7,8]



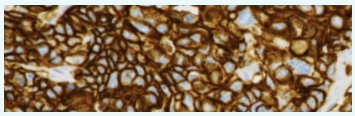
NO STAINING



WEAK STAINING



MODERATE STAINING



STRONG STAINING

The clinical cutoff is ≥75% viable tumor cells demonstrating moderate-to-strong membranous CLDN18 staining above background.[7]*

*Test results of the VENTANA CLDN18 (43-14A) RxDx assay should be interpreted by a qualified pathologist in conjunction with histological examination, relevant clinical information, and proper controls.[7]

Testing is available at various labs throughout the United States.

The following locations are testing sites that offer the VENTANA CLDN18 (43-14A) RxDx Assay†:

CARIS LIFE SCIENCES
Phoenix, AZ
https://www.carislifesciences.com

labcorp | Oncology
Shelton, CT
https://oncology.labcorp.com

PathAI Diagnostics
Memphis, TN
https://www.pathai.com/diagnostics

CSI Laboratories
A FULGENT GENETICS COMPANY
Alpharetta, GA
https://www.csilaboratories.com

MAYO CLINIC
Rochester, MN
https://mayoclinic.org

PhenoPath
A Quest Diagnostics Company
Seattle, WA
https://www.phenopath.com

INFORM DIAGNOSTICS
A FULGENT GENETICS COMPANY
Irving, TX
https://www.informdx.com

NEO GENOMICS
Aliso Viejo, CA
Fort Myers, FL
https://neogenomics.com

†These listings may not be inclusive of all locations. All trademarks are the properties of their respective owners. Astellas is not affiliated with and does not endorse any of the listed laboratories. The information provided by Astellas is for informational purposes only.

Visit VYLOYhcp.com to learn more and explore resources including links to eLearning through Roche Diagnostics.

SELECT SAFETY INFORMATION

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, decreased glucose, increased alanine aminotransferase, decreased sodium, increased phosphate, decreased potassium, and decreased magnesium.

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IMPORTANT SAFETY INFORMATION

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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, decreased glucose, increased alanine aminotransferase, 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%). 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%), platelet count decreased (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.

References:

1. VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** US Department of Health and Human Services. Understand translational research tools: biomarkers. https://toolkit.ncats.nih.gov/module/discovery/developing-translational-research-tools/biomarkers/. Accessed 08-30-2023. **3.** 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;401(10389):1655-68. Errata in: Lancet 2023;402(10398):290.; Lancet 2024;403(10421):30. **4.** 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;29(8):2133-41. **5.** Abrahao-Machado LF, Scapulatempo-Neto C. HER2 testing in gastric cancer: an update. World J Gastroenterol 2016;22(19):4619-25. **6.** Fuchs CS, Özgüroğlu M, Bang YJ, et al. Pembrolizumab versus paclitaxel for previously treated PD-L1-positive advanced gastric or gastroesophageal junction cancer: 2-year update of the randomized Phase 3 KEYNOTE-061 trial. Gastric Cancer. 2022;25(1):197-206. **7.** VENTANA CLDN18 (43-14A) RxDx assay [package insert]. Tucson, AZ: Ventana Medical Systems, Inc. **8.** VENTANA CLDN18 (43-14A) RxDx Assay Interpretation Guide for Gastric Adenocarcinoma including Gastroesophageal Junction (GEJ). Tucson, AZ; 2023.

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