VYLOY® Infusion and Treatment Management Guide

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 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.

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

VYLOY®
zolbetuximab-clzb
for injection 100mg and 300mg vials

Focusing on helping you support patients

Use this guide to learn about administering VYLOY (zolbetuximab-clzb) to your patients and how to support them throughout treatment.

In the following pages, you'll find out about:

Dosing and administration of VYLOY

Understanding possible adverse reactions

Helping patients understand their infusion treatment

Managing nausea and vomiting

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

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VYLOY®
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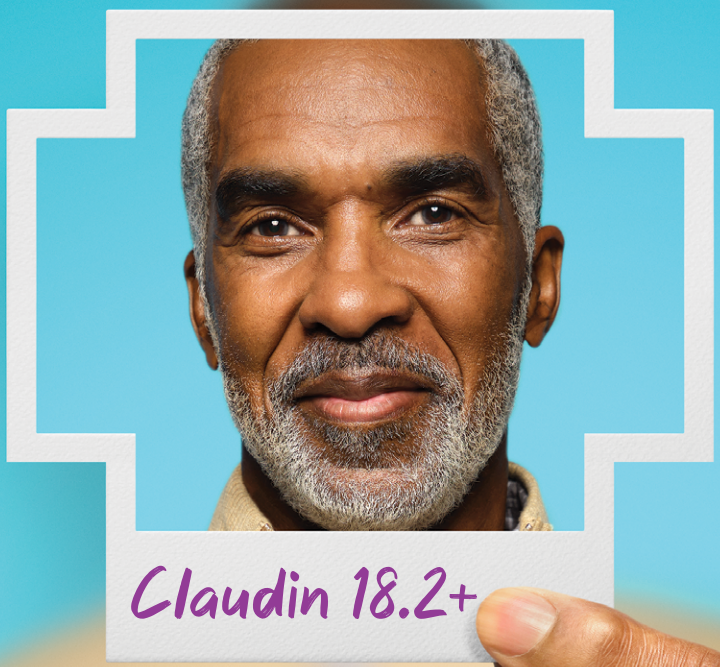

SELECT SAFETY INFORMATION

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.

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VYLOY is a first-line monoclonal antibody that targets an actionable biomarker in advanced* G/GEJ cancer: claudin 18.2[1-3]

38%

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†‡]

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.[2,3]

PFS + OS

VYLOY (zolbetuximab-clzb) was studied in combination with mFOLFOX6 or CAPOX in two Phase 3 clinical trials

Both trials (SPOTLIGHT and GLOW) included progression-free survival (major endpoint) and overall survival (additional endpoint) in evaluating VYLOY + chemotherapy‡ vs chemotherapy alone.[1]

*Locally advanced unresectable or metastatic.[1]

†Claudin 18.2 positive (CLDN18.2+) is defined as ≥75% of tumor cells demonstrating moderate to strong membranous CLDN18 staining by immunohistochemistry.[2,3]

‡Fluoropyrimidine- and platinum-containing chemotherapy.[1]

CLDN18.2=claudin 18.2; **G/GEJ**=gastric/gastroesophageal junction.

LEARN MORE ABOUT VYLOY AND EXPLORE RESULTS FROM TWO PHASE 3 CLINICAL TRIALS (SPOTLIGHT AND GLOW) AT VYLOYHCP.COM

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

VYLOY®
zolbetuximab-clzb
for injection 100mg and 300mg vials

02 Dosing and Administration

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

Preparing VYLOY (zolbetuximab-clzb)

Reconstitution and dilution steps for single-dose vials of VYLOY

1. Calculate the recommended dose based on the patient's body surface area as described in the table on page 9 to determine the total volume and number of vials needed
2. Reconstitute each vial by slowly adding 5 mL (for 100 mg vial) or 15 mL (for 300 mg vial) of Sterile Water for Injection (SWFI). While adding SWFI, direct the stream along the walls of the vial and not directly onto the lyophilized powder. The reconstituted solution contains 20 mg/mL of VYLOY.
3. Slowly swirl each vial until the contents are completely dissolved. Allow the reconstituted vial(s) to settle until the bubbles are gone. **Do not shake the vial**
4. Visually inspect the reconstituted solution for particulate matter and discoloration. The reconstituted solution should be clear to slightly opalescent, colorless to slight yellow, and free of visible particles. Discard any vial with visible particles or discoloration

NOTE: Store reconstituted vial(s) at room temperature 15°C to 30°C (59°F to 86°F) for up to 5 hours if not used immediately. This product does not contain a preservative.

5. Withdraw the required volume of reconstituted VYLOY vial(s) and transfer into an infusion bag containing 0.9% sodium chloride injection, to a final concentration of 5 mg/mL.
   - The diluted solution of VYLOY is compatible with intravenous infusion bags composed of polyethylene (PE), polypropylene (PP), polyvinyl chloride (PVC) (with either Di[2-ethylhexyl] phthalate [DEHP] or trioctyl trimellitate [TOTM] plasticizers), ethylene propylene copolymer, ethylene-vinyl acetate (EVA) copolymer, PP and styrene-ethylene-butylene-styrene copolymer
   - The diluted solution of VYLOY is compatible with infusion tubing composed of PE, PVC (with DEHP, TOTM or Di[2-ethylhexyl] terephthalate plasticizers), polybutadiene (PB), or elastomer modified polypropylene with in-line filter membranes composed of polyethersulfone (PES) or polysulfone
6. Mix diluted solution by gentle inversion. **Do not shake the bag**.
7. Visually inspect the infusion bag for any particulate matter prior to use. The diluted solution should be free of visible particles. Do not use the infusion bag if particulate matter is observed.
8. Discard any unused portion left in the single-dose vials.

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

VYLOY (zolbetuximab-clzb) infusion

VYLOY can be administered every 2 or 3 weeks aligning with selected chemo dosing schedule[1]

PRIOR TO ADMINISTRATION[1]

If a patient is experiencing nausea and/or vomiting, symptoms should be resolved to Grade ≤1 before the first infusion.

PREMEDICATION[1]

Prior to each VYLOY infusion, 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.

VYLOY Dosing[1]*

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

BSA

Recommended VYLOY dosage for each patient is based on body surface area.

VYLOY Administration[1]

If VYLOY + chemotherapy† are administered on the same day, **VYLOY must be administered first.**

Recommended duration of treatment is until disease progression or unacceptable toxicity.

VYLOY is available in 100 mg and 300 mg vials.

Vials shown are not actual size.

*Administer VYLOY in combination with fluoropyrimidine- and platinum-containing chemotherapy.[1]
† Fluoropyrimidine- and platinum-containing chemotherapy.[1]
5-HT3=5-hydroxytryptamine 3; **NK-1**=neurokinin-1.

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zolbetuximab-clzb
for injection 100mg and 300mg vials

Recommended VYLOY dosage and infusion rates[1]

VYLOY Dose		Initial Infusion Rate (first 30-60 minutes)*	Subsequent Infusion Rate
First Dose	800 mg/m²	100 mg/m²/hr	200-265 mg/m²/hr
Subsequent Doses	600 mg/m² every 3 weeks	75 mg/m²/hr	150-265 mg/m²/hr
	or	or	or
	400 mg/m² every 2 weeks	50 mg/m²/hr	100-200 mg/m²/hr

*In the absence of adverse reactions after 30-60 minutes, the infusion rate can be increased to the subsequent infusion rate as tolerated.[1]

first dose

For the first VYLOY (zolbetuximab-clzb) dose, the estimated minimum infusion time is approximately 3.5 hours. Total infusion time will depend on dose interruptions or infusion rate reductions.[1]

subsequent doses

For subsequent VYLOY doses, the estimated minimum infusion time is approximately 2.5 hours. Total infusion time will depend on dose interruptions or infusion rate reductions.[1]

As shown above: The infusions are started at a slower rate for the first 30-60 minutes to help mitigate potential adverse reactions. The rate can be gradually increased for the remainder of the infusion as tolerated.

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

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

VYLOY Dosing and Infusion Rate Calculator

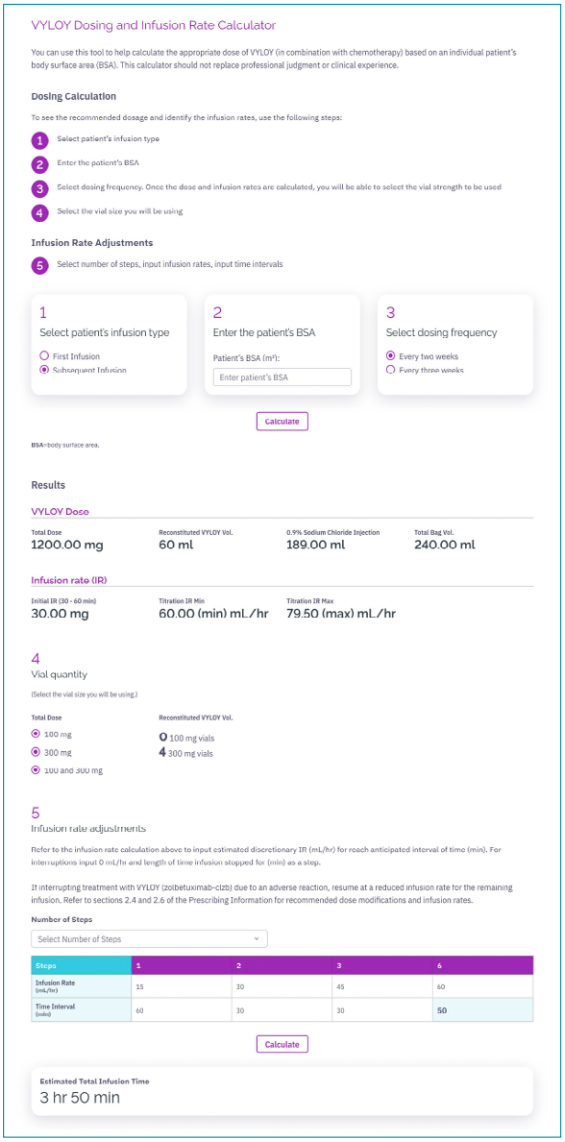
This dosing calculator helps determine the appropriate amount of VYLOY and how long infusions may take, by inputting important patient information and infusion parameters. **The below image is for illustrative purposes only, and the actual dosing calculator can be found on VYLOYhcp.com.**

Enter your patients' information. →

The dose will populate based on the patient input above. →

The infusion rate, according to Prescribing Information, will populate. →

Enter infusion rate adjustments you might need to make based on patients' tolerability. →



SCAN THE QR CODE TO USE THE CALCULATOR OR VISIT VYLOYHCP.COM/DOSING-AND-ADMINISTRATION

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VYLOY administration

Infusion timing

Prior to each infusion of VYLOY (zolbetuximab-clzb), premedicate patients with a combination of antiemetics.[1]

Immediately administer the infusion through an intravenous line. Do not administer as an IV push or bolus.[1]

If the infusion time exceeds the recommended storage time (6 hours from end of preparation of infusion solution at room temperature or 16 hours from end of preparation of infusion solution under refrigeration), the infusion bag must be discarded and a new infusion bag prepared to continue the infusion.

Infusion line considerations[1]

- In-line filters (pore size of 0.2 micron with materials listed in the Prescribing Information) are recommended to be used during administration
- Do not co-administer other drugs through the same infusion line
- **No incompatibilities** have been observed with closed system transfer devices or central ports composed of certain materials (see Prescribing Information for more details)

SELECT SAFETY INFORMATION

ADVERSE REACTIONS

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.

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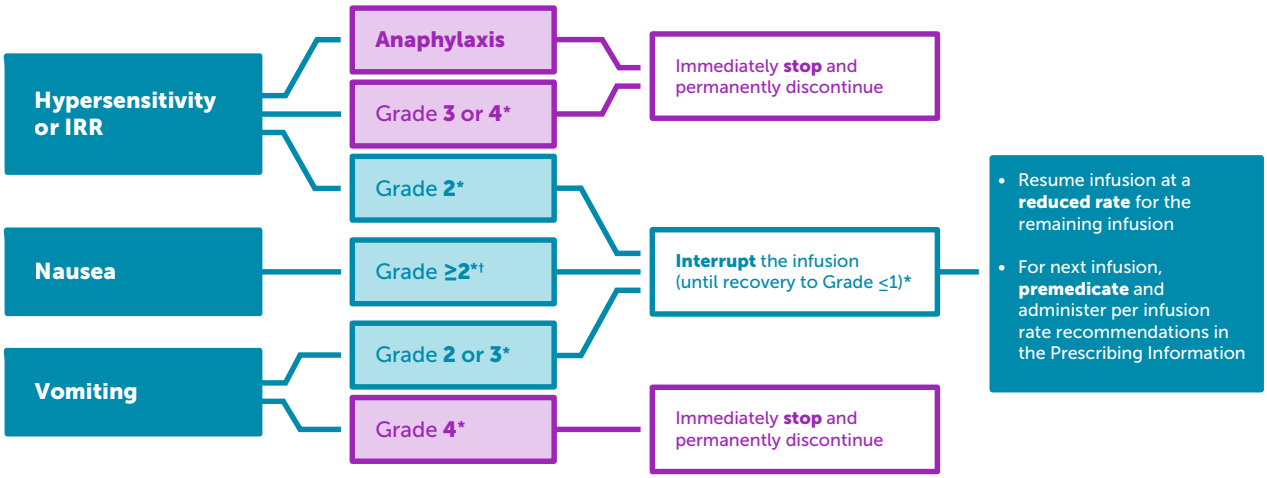
VYLOY adverse reaction management[1]

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 below.

INFUSION MODIFICATIONS FOR VYLOY-RELATED ADVERSE REACTIONS MANAGEMENT, INCLUDING NAUSEA AND VOMITING



Grade 1: mild;
Grade 2: moderate;
Grade 3: severe or medically significant but not immediately life-threatening;
Grade 4: life-threatening consequences.[4]*

*Toxicity was graded per NCI CTCAE v5.0. Per NCI CTCAE v5.0, grade refers to the severity of the adverse reactions.
†NCI CTCAE v5.0 does not list Grade 4 nausea.

IRR=infusion-related reactions; **NCI CTCAE=**National Cancer Institute Common Terminology Criteria for Adverse Events.

SELECT SAFETY INFORMATION

ADVERSE REACTIONS

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.

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03 Adverse Reactions (ARs) in SPOTLIGHT

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

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Adverse reactions in clinical trials

Recognizing the possible adverse reactions[1]

SPOTLIGHT Trial: Adverse reactions reported in ≥15% of patients treated with VYLOY (zolbetuximab-clzb) with a difference between arms of ≥5% compared to placebo[1]

ADVERSE REACTION		VYLOY with mFOLFOX6 (n=279)		PLACEBO with mFOLFOX6 (n=278)	
		All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Gastrointestinal disorders	Nausea	82	16	61	7
	Vomiting	67	16	36	6
Metabolism and nutrition disorders	Decreased appetite	47	6	34	3.2
General disorders and administration site conditions	Peripheral edema	18	0.7	9	0

Median duration of exposure to VYLOY in combination with mFOLFOX6 was 6.2 months (range: 1 day to 40.9 months).

In clinical trials, the median time to onset of nausea and/or vomiting was within the first hour after starting the VYLOY infusion.[5]

See page 12 for details on infusion rate adjustments for adverse reaction management.

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.

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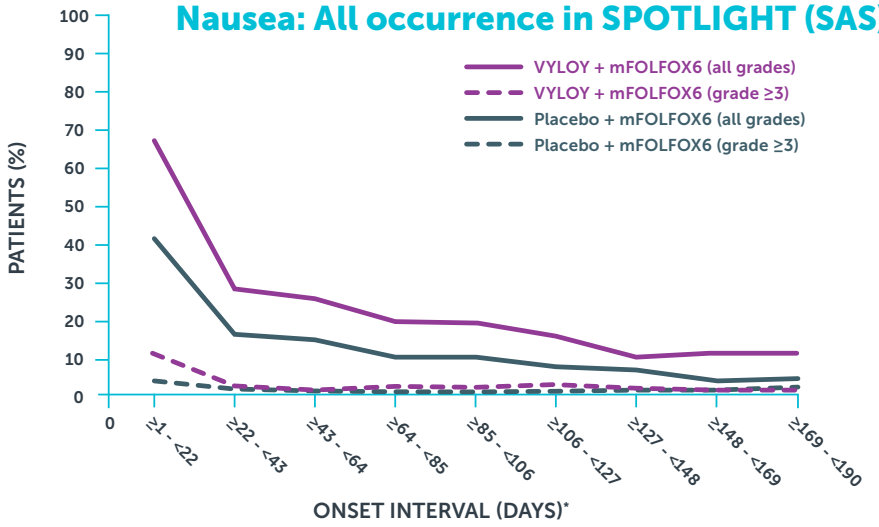
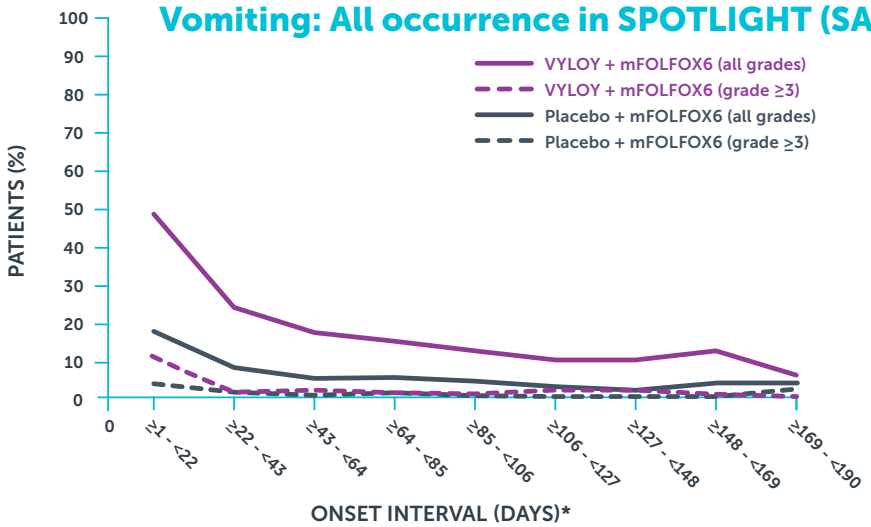
In the SPOTLIGHT clinical study, nausea and vomiting:

- Were the most common AEs when VYLOY (zolbetuximab-clzb) was given with mFOLFOX6 (majority were Grades 1 & 2)[1]
- Nausea and vomiting were managed by infusion rate guidelines, infusion interruptions, and the use of antiemetics[2]
- Occurred more often in the first cycle[1]
- Nausea and vomiting have been confirmed as important identified risks. Adverse events, graded according to NCI CTCAE v4.03, were monitored throughout the trial and for 90 days after treatment discontinuation. Adverse event preferred terms were defined according to the Medical Dictionary for Regulatory Activities terminology version 25.0. Grade 4 nausea is not defined in Common Terminology Criteria for Adverse Events v4.03 and was determined and managed at investigator discretion. These data are not generalizable and cannot be used to predict adverse event outcomes. These data are from the safety analysis set (SAS) in a Phase 3, global, randomized, multicenter trial (VYLOY + mFOLFOX6: n=279; Placebo + mFOLFOX6: n=278). The results presented are provided only as descriptive clinical information.

Nausea: All occurrence in SPOTLIGHT (SAS)[6]



Vomiting: All occurrence in SPOTLIGHT (SAS)[6]



*The onset day in the onset interval was defined as the date of onset minus the date of first dose plus 1.

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VYLOY®
zolbetuximab-clzb
for injection 100mg and 300mg vials

Managing nausea and vomiting

According to NCCN Clinical Practice Guidelines (NCCN Guidelines®) for Antiemesis,* when treating patients who have cancer[7]:

- Prevention of nausea/vomiting is the goal
- Choice of antiemetic(s) used should be based on the emetic risk of the therapy, prior experience with antiemetics, and patient factors

**This is a summary of relevant portions of the NCCN Guidelines®. Please see the full NCCN Guidelines for Antiemesis at NCCN.org.*

During/after infusion

Manage patients during and after infusion with antiemetics or fluid replacement. Interrupt the infusion, or permanently discontinue VYLOY based on severity (see Prescribing Information for more details).[1]

Other advice on antiemetics[1]

GET PRESCRIPTION APPROVAL
so that antiemetics are readily available (during infusion and at home).

REMIND PATIENTS TO TAKE
antiemetics on time as prescribed.

REMIND PATIENTS TO REFILL
their antiemetic prescriptions.

TIP: Remind patients to tell their healthcare provider about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

This information is for informational purposes only and is not meant to replace the advice of a healthcare professional.

NCCN®=National Comprehensive Cancer Network®.

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

04 Storage and Handling

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

VYLOY®
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Storage times for a prepared infusion bag[1]

The following times include the administration period

Stored under refrigeration at 2°C to 8°C (36°F to 46°F) for no longer than 16 hours from the end of the preparation of the infusion bag to the completion of the infusion. Do not freeze.

Stored at room temperature at 15°C to 30°C (59°F to 86°F) for no longer than 6 hours from the end of the infusion bag preparation to the completion of the infusion.

Discard prepared infusion bags beyond the recommended storage time.

Storage of supplied vials[1]

Store VYLOY vials refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton. Do not freeze. Do not shake.

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05 Important Safety Information

Please see Important Safety Information on pages 21-22, and accompanying full Prescribing Information.

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.

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%),

Please see Important Safety Information continued on page 22, and accompanying full Prescribing Information.

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zolbetuximab-clzb
for injection 100mg and 300mg vials

IMPORTANT SAFETY INFORMATION (CONT.)

ADVERSE REACTIONS (CONT.)

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%), 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.

References:

1. VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **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;401(10389):1655-1668. Errata in: Lancet 2023;402(10398):290; Lancet 2024;403(10421):30. **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;29(8):2133-2141. **4**. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf. Accessed May 22, 2024. **5.** Shitara K, Pophale R, Matney C, et al. Management of nausea and vomiting following first-line zolbetuximab + chemotherapy treatment in CLDN18.2+, HER2-, locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma: analysis from the phase 3 SPOTLIGHT and GLOW studies. Poster presented at: ASCO Gastrointestinal Cancers Symposium; January 22, 2024; San Francisco, CA. **6**. Supplement to: 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 (Epub ahead of print) 04-14-2023. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.2.2024. ©National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed October 28, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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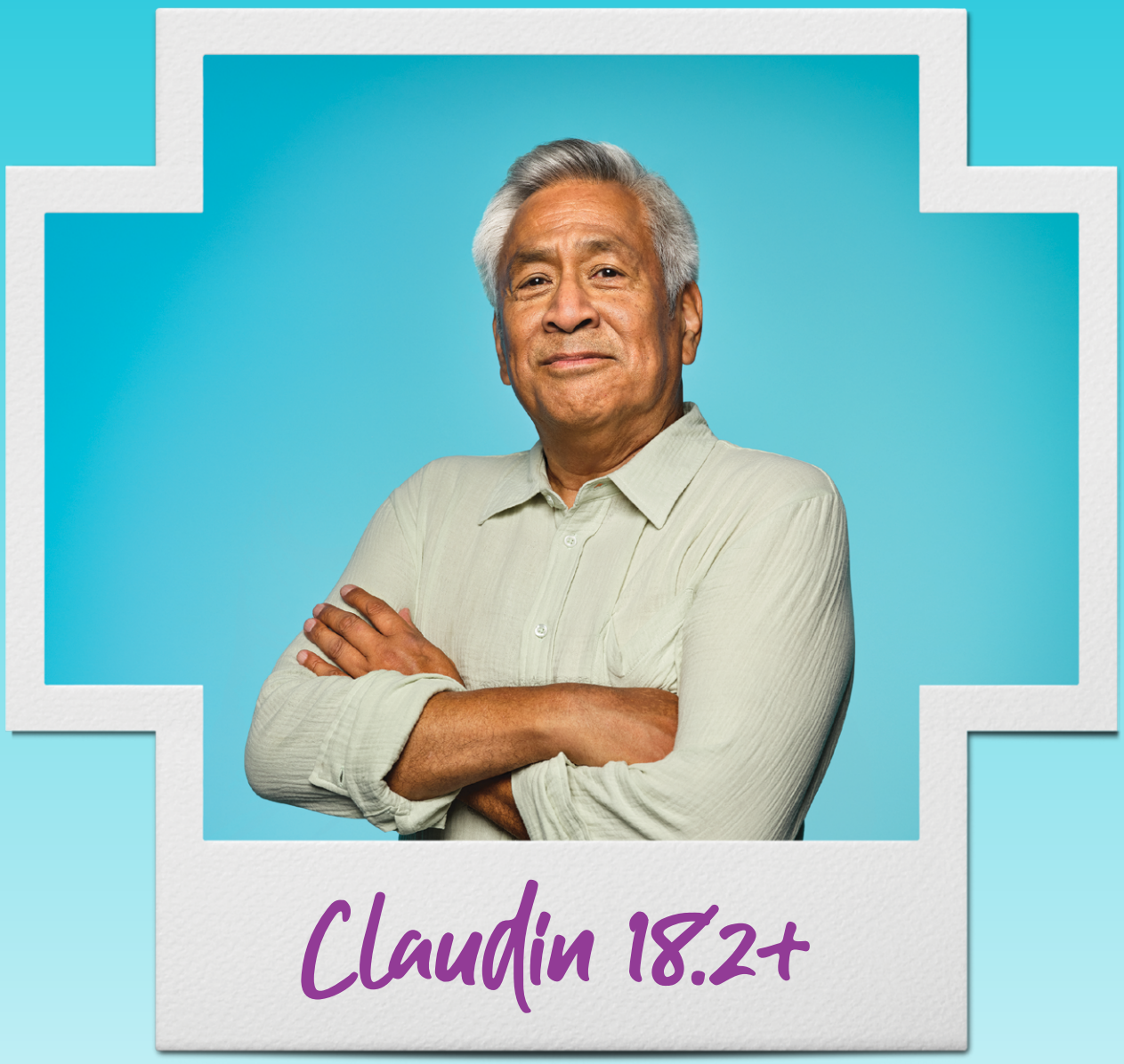

Claudin 18.2+

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