Drug Monograph

A - Drug Name

zolbetuximab

COMMON TRADE NAME(S): Vyloy®

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B - Mechanism of Action and Pharmacokinetics

Zolbetuximab is a chimeric monoclonal antibody which targets the tight junction protein Claudin (CLDN)18.2. It binds selectively to CLDN18.2 leading to antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). Chemotherapy increases CLDN18.2 expression on human cancer cells and improves zolbetuximab-induced ADCC and CDC activities.

Absorption	Time to reach steady state	24 weeks (administered at a first dose of 800 mg/m^2 followed by 600 mg/m^2 every 3 weeks) 22 weeks (administered at a first dose of 800 mg/m^2 followed by 400 mg/m^2 every 2 weeks)
Metabolism	Catabolised into small peptides and amino acids	
Elimination	Half-life	17 days

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C - Indications and Status

Health Canada Approvals:

- Gastric or gastroesophageal junction (GEJ) cancer

Refer to the product monograph for a full list and details of approved indications

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D - Adverse Effects

Emetogenic Potential: High

The following table lists adverse effects that occurred in patients with gastric or GEJ adenocarcinoma treated with zolbetuximab or placebo in combination mFOLFOX6, in a phase III study, where the incidence was ≥2% higher in the treatment arm than the placebo arm. It also includes severe, life-threatening and post-marketing adverse effects from other sources. Incidences denoted with "†" were reported from pooled data based on zolbetuximab studies with mFOLFOX6 or XELOX.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Hypertension (11%) (5% severe)	E
	Venous thromboembolism (<10%)	E
Gastrointestinal	Anorexia, weight loss (47%)	E
	Nausea, vomiting (82%) (16% severe)	E
General	Edema - limbs (19%)	E
	Fatigue (27%)	E
Hematological	Hemorrhage (1%) (GI and CNS)	E
	Myelosuppression (37%) (28% severe)	E
Hepatobiliary	↓ albumin (15%) (4% severe)	E
	↑ LFTs (18%)	E
Hypersensitivity	Hypersensitivity (36%) (including anaphylaxis) (5% severe)†	E
	Infusion related reaction (3%) (<1% severe)†	E
Metabolic / Endocrine	Abnormal electrolyte(s) (18%) (↓K, ↓Ca) (6% severe)	E
Nervous System	Dizziness (13%)	E

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for zolbetuximab include nausea/vomiting, anorexia/weight loss, myelosuppression, hypersensitivity, fatigue, peripheral edema , ↑ LFTs, abnormal electrolytes, ↓ albumin and dizziness.

Hypersensitivity reactions, including anaphylaxis, or **infusion related reactions**, have been reported in patients treated with zolbetuximab in combination with mFOLFOX6 or CAPOX. Monitor patients for these reactions during zolbetuximab infusion, for at least 2 hours post-infusion, or longer if clinically indicated. Signs and symptoms include urticaria, repetitive cough, wheeze and throat tightness/change in voice, chest discomfort, nausea, vomiting, abdominal pain, salivary hypersecretion, pyrexia, chills, back pain, and hypertension.

Nausea and vomiting occurred commonly (mostly Grades 1 to 2) when zolbetuximab was given with fluoropyrimidine- and platinum-based chemotherapy. Antiemetics are recommended prior to each infusion of zolbetuximab, and the infusion rate may need to be reduced in some cases (see Dosage with Toxicity section). Nausea and vomiting occurred more frequently during the first cycle of treatment but decreased with subsequent cycles in the clinical trials.

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E - Dosing

Refer to protocol by which the patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

CLDN18.2 status should be confirmed by a validated test prior to starting zolbetuximab.

Nausea and/or vomiting should be resolved to Grade ≤1 prior to administering the first infusion.

Adults:

Combination treatment*

Intravenous: Single loading dose: 800 mg/m^2 on Day 1 of Cycle 1, then

600 mg/m^2 every 3 weeks, or

400 mg/m^2 every 2 weeks

*In combination with fluoropyrimidine- and platinum-containing chemotherapy.
Refer to regimen monographs for details.

Dosage with Toxicity:

Dose reductions are not recommended for zolbetuximab.

Toxicity	Severity/ Grade	Action	Next Infusion
Nausea	Grade 2 or 3	Hold infusion until Grade ≤1, then resume at a reduced rate*.	Administer per infusion rates in Administration Guidelines section.
Vomiting	Grade 2 or 3	Hold infusion until Grade ≤1, then resume at a reduced rate*.	Administer per infusion rates in Administration Guidelines section.
	Grade 4	Discontinue.	Not applicable

*Reduced infusion rate should be determined based on patient tolerability, toxicity severity, and previously tolerated rate.

Management of Infusion-related reactions:

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Grade	Management	Re-challenge
2	• Stop the infusion. Manage the symptoms **Restart** • After symptom resolution (Grade ≤ 1), resume at a reduced infusion rate*.	• Premedicate with antihistamines and administer according to the infusion rates in Administration Guidelines section.
3 or 4	• Stop the infusion. • Aggressively manage symptoms.	• Permanently discontinue (do not re-challenge)

*Reduced infusion rate should be determined based on patient tolerability, toxicity severity, and previously tolerated rate.

Dosage with Hepatic Impairment:

Total bilirubin		AST	Zolbetuximab Dose
≤ ULN	and	> ULN	No dose adjustments recommended.
>1 to 1.5 x ULN	and	Any	
>1.5 to 3 x ULN	and	Any	Limited data available.
>3 to 10 x ULN	and	Any	Not studied.

Dosage with Renal Impairment:

Creatinine Clearance (mL/min)	Zolbetuximab Dose
≥30	No dose adjustment recommended.
<30	Limited data available.

Dosage in the elderly:

No dose adjustment is required in patients ≥65 years old. There were no overall differences in safety or efficacy of zolbetuximab when compared to younger patients

Dosage based on gender:

There were no clinically significant differences in the pharmacokinetics of zolbetuximab based on gender.

Dosage based on ethnicity:

There were no clinically significant differences in the pharmacokinetics of zolbetuximab based on race.

Children:

The safety and efficacy of zolbetuximab in children (<18 years of age) have not been established. No data is available for pediatric use.

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F - Administration Guidelines

- Dilute the reconstituted solution with 0.9% Sodium Chloride Injection to a final concentration of 2 mg/mL.
- Do not shake the solution.
- Compatible with glass, polyvinyl chloride (PVC), polyethylene (PE), and polypropylene (PP) infusion bags, infusion tubing composed of PE, PVC, polyurethane, or polybutadiene, and in-line filter membranes composed of polyethersulfone or polysulfone. Refer to the product monograph for more details on equipment compatibility.
- Zolbetuximab must be administered first if fluoropyrimidine- and platinum-containing chemotherapy are administered on the same day.
- Administer infusion over a minimum of 2 hours.
- **DO NOT** administer as an IV push or bolus
- Do not co-administer with other drugs on the same infusion line.
- Store unopened vials in original package at 2°C to 8°C. Do not freeze. Protect vials, reconstituted or diluted drug from direct sunlight.

Recommended Infusion Rates

Zolbetuximab	**Infusion Rate ($mg/m^2/hr$)**	
	First 30 - 60 minutes	**Remainder of infusion time***
Loading Dose (800 mg/m^2 on Day 1 of Cycle 1)	75	150 - 300
Maintenance Doses (600 mg/m^2 every 3 weeks or 400 mg/m^2 every 2 weeks)	75 or 50	150 - 300 or 100 - 200

*Infusion rate can be increased as tolerated, in the absence of adverse reaction, after 30 - 60 minutes.

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G - Special Precautions

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components

Other Warnings/Precautions:

- Patients were excluded from clinical trials if they had certain medical conditions, including the following; assess benefit-risk of zolbetuximab treatment in these patients:
  - a complete or partial gastric outlet syndrome
  - positive test for human immunodeficiency virus (HIV) infection or known active hepatitis B or C infection
  - significant cardiovascular disease
  - or history of central nervous system metastases

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Mutagenicity: Unknown
- Embryotoxicity: Not demonstrated in animal studies
- Fetotoxicity: Not demonstrated in animal studies
- Crosses placental barrier: Documented in animals
- Pregnancy:
  Zolbetuximab is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for at least **6 months** (general recommendation) after the last dose.
- Breastfeeding:
  Breastfeeding is not recommended during treatment and for **8 months** after the last dose.
- Fertility effects: Unknown

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H - Interactions

Zolbetuximab is not a cytokine modulator and is not expected to have an effect on cytochrome P450 or drug transporters. No pharmacokinetic drug interaction studies have been performed.

No dose adjustment is required for zolbetuximab and mFOLFOX6 or CAPOX when used in combination.

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
CBC	Baseline and before each cycle
Liver function tests	Baseline and before each cycle
Renal function tests	Baseline and before each cycle
Clinical toxicity assessment for hypersensitivity, infusion-related reactions, fatigue, peripheral edema, nausea/ vomiting or other GI effects.	At each visit

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Supplementary Public Funding

New Drug Funding Program (NDFP Website)

- Zolbetuximab - First-line Treatment of Advanced Gastric and Gastroesophageal Junction Adenocarcinoma

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K - References

NCCN Practice Guidelines in Oncology (NCCN Guidelines) - Antiemesis v.2.2025. NCCN, May 2025.

Prescribing Information: Vyloy® (zolbetuximab). Astellas Pharma US, Inc. October 2024.

Product Information: Vyloy® (zolbetuximab). Astellas Pharma Europe B.V. January 1, 2025.

Product Monograph: Vyloy® (zolbetuximab). Astellas Pharma Canada, Inc. April 28, 2025.

Reimbursement recommendation: Zolbetuximab. Canada's Drug Agency. February 2025.

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.

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.

September 2025 New drug monograph

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L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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