GUIDANCE ON THE MANAGEMENT OF NAUSEA AND VOMITING WITH VYLOY® (ZOLBETUXIMAB) ADMINISTRATION

Based on Expert Guidance: Anticipate, Administer, and Manage

The information summarized below is to assist in infusion clinic planning and help HCPs prevent and manage side effects of nausea and vomiting that will likely occur with zolbetuximab. Treatment decisions are left to the clinical discretion of the prescriber based on institutional protocol, practice guidelines, and patient-specific characteristics and response.
Please refer to the VYLOY® product monograph for full details: Link

What to Expect With Zolbetuximab Use?

- Administer first followed by chemotherapy[1]
  - Do not co-administer using the same infusion line[1]
- First infusion (cycle 1 day 1 [C1D1]) to take a minimum of ~3.5 hrs (range, 3.33-4.5 hrs)[1,2]
- Subsequent infusions[a] to take a minimum of ~2.5 hrs (range, 2.38-4.5 hrs)[1,2]
- **Timing does not take into consideration the potential infusion interruptions/rate modifications[1,2]**
- **Diluted infusion should not be kept for >12 hrs[b] at room temperature or >24 hrs[b] under refrigeration[1]**
- Any baseline nausea and/or vomiting should be resolved to Grade ≤1 (≤ mild)[c] before starting the first infusion[1]
- In two global Phase 3 trials:
  - Nausea and vomiting were the most frequently reported all-grade TEAEs[3,4]
    - **~3 out of 4** patients experienced nausea
    - **~2 out of 3** patients experienced vomiting
  - Occurrences of nausea/vomiting was highest during cycle 1 (C1) and decreased significantly thereafter[2]
    - **Median time to first occurrence of nausea/vomiting[d] was <1 hr[2]**
    - In some instances, vomiting occurred suddenly without prior nausea[2,e]

Management of Nausea and/or Vomiting

Zolbetuximab Infusion Rates Recommendations Per PI

- Start at a slower rate (100 mg/m²/hr) for the first infusion and then adjust as tolerated for subsequent infusions[1]
- Subsequent infusions can be at a rate of 100-265 mg/m²/hr as tolerated[1]

Zolbetuximab Dose		Infusion Rate	
		Initial Infusion Rate First 30-60 mins	Subsequent Infusion Rate
First	800 mg/m²	75 mg/m²/hr	150-300 mg/m²/hr
Subsequent	600 mg/m² every 3 weeks or 400 mg/m² every 2 weeks	75 mg/m²/hr or 50 mg/m²/hr	150-300 mg/m²/hr or 100-200 mg/m²/hr

Infusion Modifications for Zolbetuximab-Related Adverse Reactions Management, Including Nausea and Vomiting

- No dose reduction recommended[1]
  - Nausea and vomiting are managed by reducing infusion rate, infusion interruption, withholding the dose, and/or permanent discontinuation[1]
- Zolbetuximab should not be discontinued without first attempting to modify or temporarily interrupt the infusion and/or without providing additional treatment for nausea and vomiting[5]

Hypersensitivity or IRR	Anaphylaxis	Immediately stop and permanently discontinue
	Grade 3 or 4[c]	
	Grade 2[c]	Interrupt the infusion (until recovery to Grade ≤1[c])
Nausea	Grade ≥2[c,f]	
Vomiting	Grade 2 or 3[c]	
	Grade 4[c]	Immediately stop and permanently discontinue

- Resume infusion at a reduced rate for the remaining infusion
- For next infusion, **premedicate** and administer per infusion rate recommendations

Grade 1: mild; Grade 2: moderate; Grade 3: severe or medically significant but not immediately life-threatening; Grade 4: life-threatening consequences[6,c]

Antiemetic Prophylaxis Prior to Each Zolbetuximab Infusion

- Zolbetuximab is emetogenic and may cause severe nausea and/or vomiting[1]
- Premedicate with antiemetics (e.g., NK-1 receptor blockers and/or 5-HT3 receptor blockers, as well as other drugs per local and institutional guidelines)[1]
  - **Use of other antiemetics or regimens based on antiemetic recommendations may follow:**
    - **MASCC/ESMO Antiemetic Guidelines (2023 MASCC and ESMO Guidelines)**
    - **ASCO Antiemetics Guidelines**
    - **ONS, Putting Evidence Into Practice: Evidence-Based Interventions to Prevent, Manage, and Treat Chemotherapy-Induced Nausea and Vomiting**
- The most commonly used prophylactic antiemetic regimens during C1D1 were:[2]
  - 5-HT3 receptor blocker + NK-1 receptor blocker (~26%)
  - 5-HT3 receptor blocker + NK-1 receptor blocker + others (~13%)
  - 5-HT3 receptor blocker + NK-1 receptor blocker + steroids (~12%)
- Patients who received prophylactic corticosteroids had similar PFS and OS benefits as those in the overall population[2,g,h]

[a]Cycle 1 day 15+ (C1D15+)/cycle 1 day 21+ (C1D21+). [b]If not administered immediately, the prepared infusion bag should be stored: under refrigeration at 2°C to 8°C for no longer than 24 hours including infusion time from the end of the preparation of the infusion bag; or at room temperature for no longer than 12 hours including infusion time from when the prepared infusion bag is removed from the refrigerator. [c]Toxicity was graded per NCI-CTCAE v5.0. Per NCI-CTCAE v5.0, grade refers to the severity of the AE.
[d]Reported as an IRR. [e]Applicable to the mFOLFOX6 plus zolbetuximab regimen. [f]NCI-CTCAE v5.0 does not list Grade 4 nausea. [g]This analysis was not designed to evaluate effect of corticosteroids on efficacy/safety. [h]Overall, 44% of patients in the SPOTLIGHT study and 34% of patients in the GLOW study received corticosteroids.

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Modified Delphi Panel Consensus Guidance on the Prevention and Management of Nausea and Vomiting in Patients Treated With Zolbetuximab + Chemotherapy[5]

- An international RAND/UCLA modified Delphi panel included 15 clinicians
  - Panelists[a] were selected based on their experience in the zolbetuximab clinical trials

Prior to and During First Infusion

Prophylaxis prior to first infusion

Provide one of the following National Comprehensive Cancer Network® (NCCN®)-recommended high-risk antiemetic drug regimens[7] (oral/IV antiemetics may be appropriate based on individual patient circumstances)

- NK-1 receptor antagonist + 5-HT3 receptor antagonist + dexamethasone + olanzapine
- or
- NK-1 receptor antagonist + 5-HT3 receptor antagonist + dexamethasone
- or
- 5-HT3 receptor antagonist + dexamethasone + olanzapine

During first infusion, if the patient is experiencing

Nausea alone

Consider either making no modifications, or **stopping the infusion for 30-60 mins** and **restarting it at the same rate** prior to the stop if symptoms improve

and

After the first hour (for the subsequent infusion recommended rate), also consider slowing the infusion without stopping it first (Please see for additional information)

Any vomiting (Please see for additional information)

Stop the infusion for 30-60 mins and restart it at a slower rate if symptoms improve

(Please see for additional information)

KEY

- Zolbetuximab infusion rate
- Patient symptoms
- Antiemetic regimens

Note: If infusion was running at the PI rate, **slow the rate by 50%; if the infusion rate had already been slowed to 50%, slow by an additional 50% (i.e., 25% of the initial rate)**

Note: For vomiting, IV hydration may be appropriate depending on individual patient circumstances

Second and Subsequent Infusions

- When planning for second or subsequent infusions, adjust your plan for subsequent infusions based on the patient's symptoms during previous infusions
- Begin second and subsequent infusions at the rate that was best tolerated during previous infusion (e.g., if the previous infusion was tolerated at the PI rate, subsequent infusions should be given at the same rate; if the infusion rate was slowed to 50% of the PI rate and symptoms improved, start subsequent infusions at this rate)
- With second and/or subsequent infusions, the degree of nausea and vomiting is expected to diminish. In these cases, patients may tolerate titration of the infusion rate **by increments of 25% (e.g., if the infusion rate was slowed to 50% and the patient remained asymptomatic for 30-60 mins, consider increasing the rate to 75%) back to 100% or maximum tolerated rate.** Continue to closely monitor the patient for any recurrence of symptoms, and administer additional antiemetic medications as needed to manage symptoms effectively

Continuation of treatment

When planning for second or subsequent infusions, if the patient in previous infusion experienced

Nausea alone or one episode of vomiting (Please see for additional information)

Rate recommended in PI

and

Make no change or escalate from previous infusion

Repeated vomiting (Please see for additional information)

Slower than the recommended rate in PI (Please see for additional information)

and

Escalate from previous infusion

During second and subsequent infusions, if patient is experiencing

Nausea alone

Make no modifications

Stop the infusion for 30-60 mins and restart it at a slower rate if symptoms improve (Please see for additional information)

[a]Experts from the US, Europe, Japan, and South Korea reviewed 382 scenarios, reaching an agreement in 85% (n=324).

5-HT3, 5-hydroxytryptamine (serotonin); **AE**, adverse event; **ASCO**, American Society of Clinical Oncology; **C**, cycle; **D**, day; **ESMO**, European Society for Medical Oncology; **HCP**, healthcare provider; **IRR**, infusion-related reaction; **IV**, intravenous; **MASCC**, Multinational Association of Supportive Care in Cancer; **mFOLFOX6**, modified folinic acid, fluorouracil, and oxaliplatin regimen; **NCI-CTCAE v5.0**, National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0; **NK-1**, neurokinin-1; **ONS**, Oncology Nursing Society; **OS**, overall survival; **PFS**, progression-free survival; **PI**, prescribing information; **RAND/UCLA**, RAND Corporation/University of California, Los Angeles; **TEAE**, treatment-emergent adverse event; **US**, United States.

1. VYLOY® (zolbetuximab for injection) Product Monograph. 28 APR 2025. **2.** Shitara K, et al. *ASCO GI* 2024. Abstract #372. **3.** Shitara K, et al. *Lancet*. 2023;401(10389):1655-1668. **4.** Shah MA, et al. *Nat Med*. 2023;29(8):2133-2141. **5.** Klempner SJ et al. ESMO Gastrointestinal Oncology, Volume 7, 2025 https://doi.org/10.1016/j.esmogo.2024.100131. **6.** 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. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.1.2024.

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