

Defense against CINV* for both adults and pediatric patients

FDA-APPROVED in pediatric patients ≥ 1 month and < 17 years old

*CINV=chemotherapy-induced nausea and vomiting.

Indication in pediatrics

ALOXI[®] injection 20 mcg/kg (max 1.5 mg) is indicated in patients ≥ 1 month up to 17 years of age for the prevention of acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including highly emetogenic chemotherapy.

Indication in adults

ALOXI injection is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy, and the prevention of acute nausea and vomiting associated with initial and repeat courses of highly emetogenic chemotherapy.

Important Safety Information

Contraindications

- ALOXI is contraindicated in patients known to have hypersensitivity to the drug or any of its components

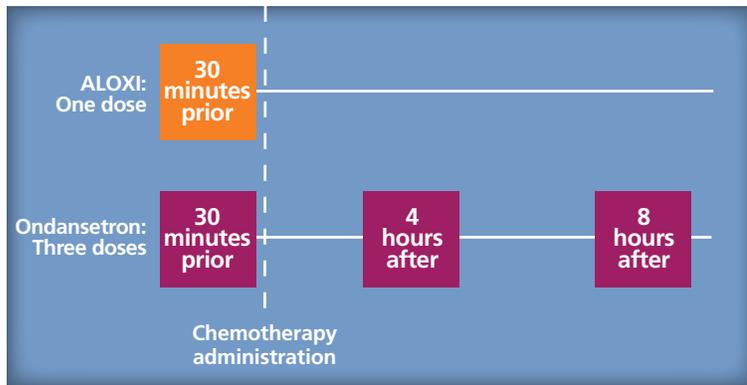
Please see Important Safety Information throughout and accompanying Full Prescribing Information.

Aloxi[®]
palonosetron HCl injection
0.25 mg/5 mL

A Proven Option for Pediatric Patients

One dose of ALOXI® provided CINV prevention for the first 24 hours¹

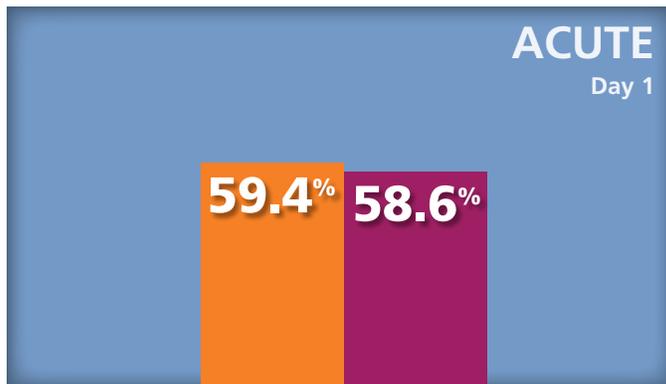
Dosing during chemotherapy



■ ALOXI 20 mcg/kg IV ■ Ondansetron 0.15 mg/kg IV

Complete response demonstrated in patients aged 1 month to less than 17 years¹

Prevention of Acute Nausea and Vomiting (0-24 hours): Complete response rates



■ ALOXI 20 mcg/kg IV (n=165) ■ Ondansetron 0.15 mg/kg IV x 3 (n=162)

- Double-blind, active-controlled non-inferiority clinical trial in 327 pediatric cancer patients comparing single doses of ALOXI with ondansetron following emetogenic chemotherapy. Emetogenic chemotherapies administered included doxorubicin, cyclophosphamide (<1500 mg/m²), ifosfamide, cisplatin, dactinomycin, carboplatin, and daunorubicin
- Complete Response in the acute phase of the first cycle of chemotherapy was defined as no vomiting, no retching, and no rescue medication in the first 24 hours after chemotherapy
- Non-inferiority criteria were met if the lower bound of the 97.5% confidence interval for the difference in Complete Response rates of intravenous palonosetron minus intravenous ondansetron was larger than -15%. The non-inferiority margin was 15%

Safety in Pediatric Patients

Treatment-related adverse reactions for pediatric patients¹

- In the clinical trial, adverse reactions were evaluated in pediatric patients receiving palonosetron for up to 4 chemotherapy cycles

	ALOXI 20 mcg/kg IV (n=163)
Event	
Headache	<1%
Dizziness	<1%
Dyskinesia	<1%
Infusion site pain	<1%
Allergic dermatitis	<1%
Skin disorder	<1%

Pediatric Pharmacokinetics¹

Parameters in pediatric patients following infusion of ALOXI at 20 mcg/kg over 15 minutes include:

- Median half-life of 29.5 hours, compared to 40 hours in adults
- Peak plasma concentrations variable among age groups after administration, tending to be lower in patients younger than 6 years

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Warnings and Precautions

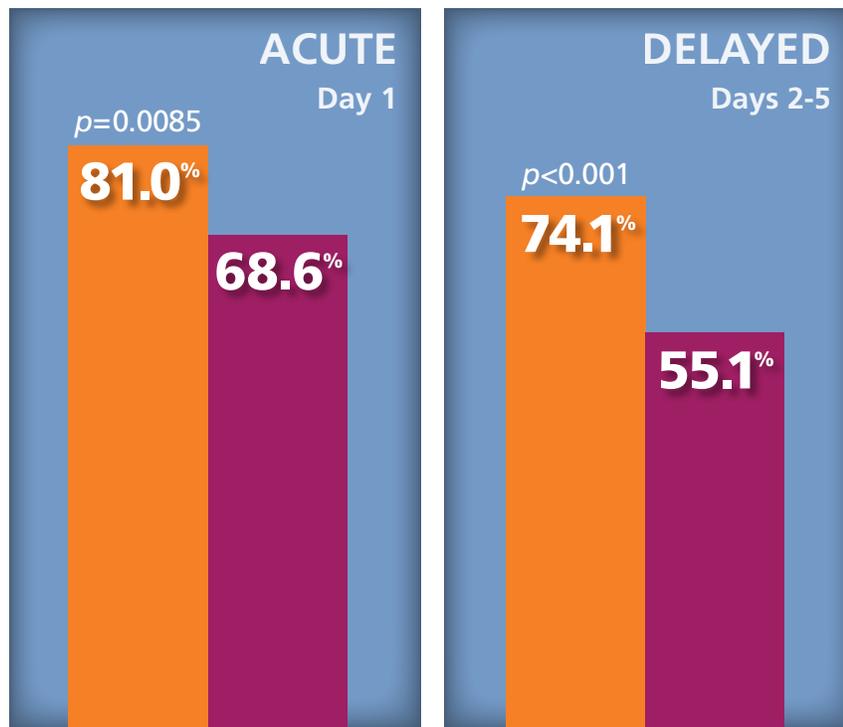
- Hypersensitivity reactions, including anaphylaxis, have been reported with or without known hypersensitivity to other 5-HT₃ receptor antagonists
- Serotonin syndrome has been reported with 5-HT₃ receptor antagonists alone, but particularly with the use of serotonergic drugs. Serotonin syndrome can be life threatening. Symptoms may include the following combination of signs and symptoms: mental status changes, autonomic instability, neuromuscular symptoms, seizures, and gastrointestinal symptoms. Patients should be monitored for the emergence of serotonin syndrome, and if symptoms occur, discontinue ALOXI and initiate supportive treatment. Patients should be informed of the increased risk of serotonin syndrome, especially if ALOXI is used concomitantly with other serotonergic drugs

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Superior 5-Day Prevention in Adults Following MEC

Significantly greater complete response rates compared to ondansetron following MEC²



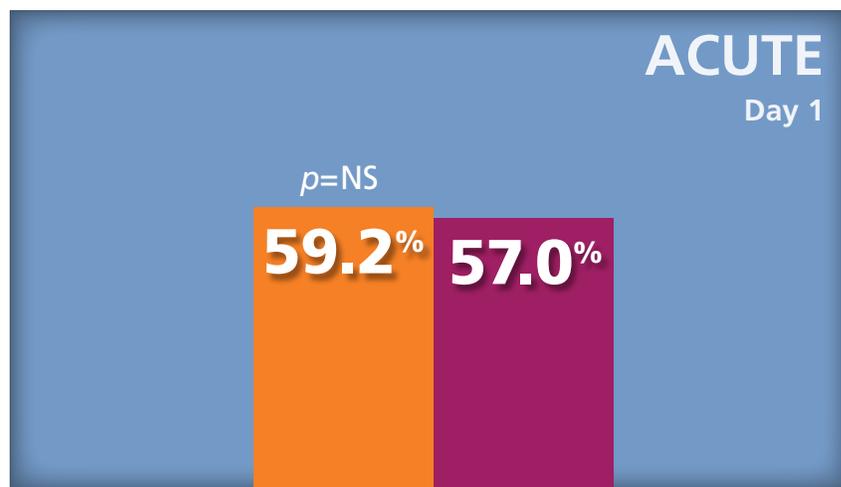
■ ALOXI® 0.25 mg IV (n=189) ■ Ondansetron 32 mg IV (n=185)*

*Intent-to-treat (ITT) cohort.

- Complete response was defined as no emetic episode and no rescue medication²
- Double-blind, randomized, Phase III noninferiority trial comparing single doses of ALOXI with ondansetron following MEC with a primary endpoint of CR during the acute phase (Day 1). P values represent adjusted post hoc, 2-sided, Fisher's exact test comparison of ALOXI with ondansetron. Significance level = 0.025, 97.5% CI²

Prevention of Acute CINV in Adults Following HEC

Complete response rates compared to ondansetron in the first 24 hours following HEC³



■ ALOXI 0.25 mg IV (n=223) ■ Ondansetron 32 mg IV (n=221)*

*Intent-to-treat (ITT) cohort.

- Complete response was defined as no emetic episode and no use of rescue medication³
- Phase III, multinational, randomized, double-blind, double-dummy, stratified, parallel-group, active-comparator noninferiority trial comparing single doses of ALOXI with ondansetron following HEC with a primary endpoint of CR during the acute phase (Day 1). *P* values represent adjusted post hoc, 2-sided Fisher's exact test comparisons of ALOXI with ondansetron. Significance level = 0.025, 97.5% CI³

Important Safety Information (continued)

Adverse Reactions

- In pediatric patients, while they require a higher dose of palonosetron, the safety profile is consistent with the established profile in adults; however, adverse reactions were reported in <0.1% of pediatric patients
- In adults, the most commonly reported adverse drug reactions include headache (9%) and constipation (5%)

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0.25 mg/5 mL

Safety in Adults Following MEC and HEC

Treatment-related adverse reactions following HEC and MEC in pivotal studies^{2,3}

	MEC Study		HEC Study	
	ALOXI® 0.25 mg IV	Ondansetron 32 mg IV	ALOXI 0.25 mg IV	Ondansetron 32 mg IV
Event	(n=187)	(n=187)	(n=225)	(n=223)
Headache	5%	5%	8%	11%
Constipation	2%	2%	4%	2%
Dizziness	1%	3%	—	—
Diarrhea	—	—	1%	2%

References: 1. ALOXI® (palonosetron HCl) injection Full Prescribing Information. 2. Gralla R, Lichinitser M, Van der Vegt S, et al. Palonosetron improves prevention of chemotherapy-induced nausea and vomiting following moderately emetogenic chemotherapy: results of a double-blind randomized phase III trial comparing single doses of palonosetron with ondansetron. *Ann Oncol.* 2003;14:1570-1577. 3. Aapro MS, Grunberg SM, Manikhas GM, et al. A phase III, double-blind, randomized trial of palonosetron compared with ondansetron in preventing chemotherapy-induced nausea and vomiting following highly emetogenic chemotherapy. *Ann Oncol.* 2006;17:1441-1449. 4. Basch E, Prestrud AA, Hesketh PJ, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update 2011. ASCO Web site. <http://www.asco.org/ASCOv2/Department%20Content/Cancer%20Policy%20and%20Clinical%20Affairs/Downloads/Guideline%20Tools%20and%20Resources/Antiemetics/2011/Antiemetics%20Full%20Guideline%2010.14.11.pdf>. Accessed February 12, 2013.

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Dosing and Administration

Adults and Pediatric Patients¹

Patient Type ¹	Dosage*	Administration
Pediatric (≥1 month —up to 17 years)	20 mcg/kg (maximum 1.5 mg) x 1	<ul style="list-style-type: none">• 15-minute infusion• 30 minutes prior to start of chemotherapy
Adult (>18 years)	0.25 mg x 1	<ul style="list-style-type: none">• 30-second infusion• 30 minutes prior to start of chemotherapy

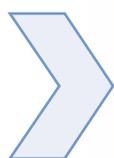
No dose adjustments in adults¹

- No dose adjustments are required for the elderly* or in adults with renal or hepatic impairment
 - Greater sensitivity in some older individuals cannot be ruled out

*Note different dosing units in pediatrics.

No significant effect on QTc intervals in adults¹

- A thorough QT/QTc study demonstrated no significant effect on any ECG parameters (including QT/QTc intervals) at doses up to 2.25 mg
 - Double-blind, randomized, parallel, placebo-, and positive- (moxifloxacin) controlled trial in 221 healthy adult patients



No restriction on repeat dosing¹

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Prevent CINV With One Dose: Proven Strength in Both Adult and Pediatric Patients

Powerful

- One dose is clinically proven to prevent CINV for up to 5 days following MEC in adults²
- One dose is clinically proven to prevent acute CINV in adults and pediatric patients, following chemotherapy including HEC regimens^{1,3}

Proven

- Efficacy and safety studied across a variety of patient types and chemotherapy regimens in multiple clinical trials, including pediatric patients aged 1 month to less than 17 years^{1,3}

Preferred

- Preferred 5-HT₃ receptor antagonist prior to MEC listed in the ASCO guidelines in adults⁴



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