HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ALOXI INJECTION safely and effectively. See full prescribing information for ALOXI INJECTION.

ALOXI® (palonosetron HCl) injection, for intravenous use
Initial U.S. Approval: 2003

----------INDICATIONS AND USAGE----------
ALOXI is a serotonin-3 (5-HT_3) receptor antagonist indicated in:
Adults for prevention of:
- acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). (1)
- acute nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC). (1)
- postoperative nausea and vomiting (PONV) for up to 24 hours following surgery. Efficacy beyond 24 hours has not been demonstrated (1)

Pediatric patients aged 1 month to less than 17 years for prevention of:
- acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including highly emetogenic cancer chemotherapy (HEC). (1)

----------DOSAGE AND ADMINISTRATION----------
Chemotherapy-Induced Nausea and Vomiting (2.1)

Age	Dose*	Infusion Time
Adults	**0.25 mg** as a single dose	Infuse over **30 seconds** beginning approximately 30 minutes before the start of chemotherapy
Pediatrics (1 month to less than 17 years)	**20 micrograms per kilogram** (maximum 1.5 mg) as a single dose	Infuse over **15 minutes** beginning approximately 30 minutes before the start of chemotherapy

*Note different dosing units in pediatrics

Postoperative Nausea and Vomiting (2.1)
- The recommended adult dosage is 0.075 mg as a single intravenous dose administered over 10 seconds immediately before the induction of anesthesia.

----------DOSAGE FORMS AND STRENGTHS----------
Injection:
- 0.25 mg palonosetron in 5 mL (0.05 mg/mL) in a single-dose vial (3)
- 0.075 mg palonosetron in 1.5 mL (0.05 mg/mL) single-dose vial (3)

----------CONTRAINDICATIONS----------
Hypersensitivity to palonosetron or any of its components (4)

----------WARNINGS AND PRECAUTIONS----------
- Hypersensitivity reactions, including anaphylaxis and anaphylactic shock: reported in patients with or without known hypersensitivity to other selective 5-HT_3 receptor antagonists. If symptoms occur, discontinue ALOXI and initiate appropriate medical treatment. (5.1)
- Serotonin syndrome: reported with 5-HT_3 receptor antagonists alone, but particularly with concomitant use of serotonergic drugs. (5.2, 7.1)

----------ADVERSE REACTIONS----------
Most common adverse reactions in
- chemotherapy-induced nausea and vomiting in adults (≥5%) are: headache and constipation (6.1)
- postoperative nausea and vomiting (≥ 2%) are: QT prolongation, bradycardia, headache, and constipation. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact HELSINN at 1-844-357-4668 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
Serotonergic Drugs: Monitor for serotonin syndrome; if symptoms occur, discontinue ALOXI and initiate supportive treatment. (7.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

ALOXI injection is indicated in adults for prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).
- acute nausea and vomiting associated with initial and repeat courses highly emetogenic cancer chemotherapy (HEC).
- postoperative nausea and vomiting (PONV) for up to 24 hours following surgery. Efficacy beyond 24 hours has not been demonstrated.

As with other antiemetics, routine prophylaxis is not recommended in patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and vomiting must be avoided during the postoperative period, ALOXI is recommended even where the incidence of postoperative nausea and/or vomiting is low.

ALOXI injection is indicated in pediatric patients 1 month to less than 17 years of age for prevention of:

- acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including highly emetogenic cancer chemotherapy.

2. DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

Prevention of Chemotherapy-Induced Nausea and Vomiting

The recommended dosage of ALOXI injection for prevention of nausea and vomiting associated with HEC and MEC in adults and associated with emetogenic chemotherapy, including HEC in pediatric patients 1 month to less than 17 years of age is shown in Table 1.

Table 1: Recommended Dosage of ALOXI Injection for the Prevention of Nausea and Vomiting Associated with Chemotherapy in Adults and Pediatric Patients 1 Month to Less than 17 Years

Age	Dose*	Infusion Time
Adults	**0.25 mg** as a single dose	Infuse over **30 seconds** beginning approximately 30 minutes before the start of chemotherapy
Pediatrics (1 month to less than 17 years)	**20 micrograms per kilogram** (max 1.5 mg) as a single dose	Infuse over **15 minutes** beginning approximately 30 minutes before the start of chemotherapy

*Note different dosing units in pediatrics

Postoperative Nausea and Vomiting

The recommended dosage of ALOXI injection in adults for PONV is 0.075 mg administered as a single intravenous dose over 10 seconds immediately before the induction of anesthesia.

2.2 Instructions for Intravenous Administration

- ALOXI injection is supplied ready for intravenous administration at a concentration of 0.05 mg/mL (50 mcg/mL).
- Do not mix ALOXI injection with other drugs.
- Flush the infusion line with normal saline before and after administration of ALOXI injection.
- Inspect ALOXI injection visually for particulate matter and discoloration before administration.
- Discard unused portion.

3. DOSAGE FORM AND STRENGTHS

ALOXI injection is sterile, clear, and colorless solution:

- 0.25 mg palonosetron in 5 mL (0.05 mg/mL) in a single-dose vial
- 0.075 mg palonosetron in 1.5 mL (0.05 mg/mL) in a single-dose vial

4. CONTRAINDICATIONS

ALOXI is contraindicated in patients known to have hypersensitivity to palonosetron *[see Warnings and Precautions (5.1)]*.

5. WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis and anaphylactic shock, have been reported with administration of ALOXI injection *[see Adverse Reactions (6.2)]*. These reactions occurred in patients with or without known hypersensitivity to other 5-HT_3 receptor antagonists. If hypersensitivity reactions occur, discontinue ALOXI injection and initiate appropriate medical treatment. Do not reinitiate ALOXI injection in patients who have previously experienced symptoms of hypersensitivity *[see Contraindications (4)]*.

5.2 Serotonin Syndrome

The development of serotonin syndrome has been reported with 5-HT_3 receptor antagonists. Most reports have been associated with concomitant use of serotonergic drugs (e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors, mirtazapine, fentanyl, lithium, tramadol, and intravenous methylene blue). Some of the reported cases were fatal. Serotonin syndrome occurring with overdose of another 5-HT_3 receptor antagonist alone has also been reported. The majority of reports of serotonin syndrome related to 5-HT_3 receptor antagonist use occurred in a post-anesthesia care unit or an infusion center.

Symptoms associated with serotonin syndrome may include the following combination of signs and symptoms: mental status changes (e.g. agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, with or without gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Patients should be monitored for the emergence of serotonin syndrome, especially with concomitant use of ALOXI and other serotonergic drugs. If symptoms of serotonin syndrome 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 *[see Drug Interactions (7.1)]*.

6. ADVERSE REACTIONS

Serious or otherwise clinically significant adverse reactions reported in other sections of labeling:

- Hypersensitivity Reactions [*see Warnings and Precautions (5.1)*]
- Serotonin Syndrome [*see Warnings and Precautions (5.2*)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Chemotherapy-Induced Nausea and Vomiting

Adults

In double-blind randomized clinical trials for the prevention of nausea and vomiting induced by MEC or HEC, 1374 adult patients received a single dose of ALOXI injection, ondansetron (Studies 1 and 3) or dolasetron (Study 2) administered 30 minutes prior to chemotherapy *[see Clinical Studies (14.1)*. Adverse reactions were similar in frequency and severity in all 3 treatment groups. Common adverse reactions reported in at least 2% of patients in these trials are shown in Table 2.

Table 2: Common Adverse Reactions* in Adults with Receiving MEC (Studies 1 and 2) or HEC (Study 3)

Adverse Reaction	ALOXI injection 0.25 mg intravenously (N=633)	Ondansetron 32 mg intravenously (N=410)	Dolasetron 100 mg intravenously (N=194)
Headache	9%	8%	16%
Constipation	5%	2%	6%
Diarrhea	1%	2%	2%
Dizziness	1%	2%	2%
Fatigue	< 1%	1%	2%
Abdominal Pain	< 1%	< 1%	2%
Insomnia	< 1%	1%	2%

* Reported in at least 2% of patients in any treatment group

Less common adverse reactions, reported in 1% or less of patients, in Studies 1, 2 and 3 were:

- Cardiovascular: non-sustained tachycardia, bradycardia, hypotension, hypertension, myocardial ischemia, extrasystoles, sinus tachycardia, sinus arrhythmia, supraventricular extrasystoles and QT prolongation.
- Dermatological: allergic dermatitis, rash
- Hearing and Vision: motion sickness, tinnitus, eye irritation and amblyopia
- Gastrointestinal System: diarrhea, dyspepsia, abdominal pain, dry mouth, hiccups and flatulence
- General: weakness, fatigue, fever, hot flash, flu-like syndrome
- Liver: transient, asymptomatic increases in AST and/or ALT and bilirubin. These changes occurred predominantly in patients receiving highly emetogenic chemotherapy
- Metabolic: hyperkalemia, electrolyte fluctuations, hyperglycemia, metabolic acidosis, glycosuria, appetite decrease, anorexia
- Musculoskeletal: arthralgia
- Nervous System: dizziness, somnolence, insomnia, hypersomnia, paresthesia
- Psychiatric: anxiety, euphoric mood
- Urinary System: urinary retention

In other studies, 2 subjects experienced severe constipation following a single ALOXI injection dose of approximately 0.75 mg (three times the recommended dose).

Pediatrics Aged 2 Months to 17 Years

In a pediatric clinical trial, 163 pediatric cancer patients with a mean age of 8 years received a single 20 mcg/kg (maximum 1.5 mg) intravenous infusion of ALOXI injection 30 minutes before beginning the first cycle of emetogenic chemotherapy *[see Clinical Studies (14.2)]*. Adverse reactions were evaluated in pediatric patients receiving ALOXI injection for up to 4 chemotherapy cycles. The following adverse reactions were reported in less than 1% of patients:

- Nervous System: headache, dizziness, dyskinesia.
- General: infusion site pain.
- Dermatological: allergic dermatitis, skin disorder.

Postoperative Nausea and Vomiting

The most common adverse reactions reported in at least 2% of adults receiving ALOXI injection 0.075 mg intravenously immediately before induction of anesthesia in 3 randomized placebo-controlled trials *[see Clinical Studies (14.3)]* are shown in Table 3. Rates of adverse reactions between ALOXI injection and placebo groups were similar. Some events are known to be associated with, or may be exacerbated by, concomitant perioperative and intraoperative medications administered in this surgical population. A thorough QT/QTc study demonstrated ALOXI injection does not prolong the QT interval to any clinically relevant extent *[see Clinical Pharmacology (12.2)]*.

Table 3: Common Adverse Reactions* in Trials of Adults with Postoperative Nausea and Vomiting

Adverse Reaction	ALOXI injection 0.075 mg intravenously (N=336)	Placebo (N=369)
Electrocardiogram QT prolongation	5%	3%
Bradycardia	4%	4%
Headache	3%	4%
Constipation	2%	3%

* Reported in at least 2% of patients in any treatment group

Less common adverse reactions, reported in 1% of less of patients, in these PONV clinical trials were:

- Cardiovascular: QTc prolongation, sinus bradycardia, tachycardia, blood pressure decreased, hypotension, hypertension, arrhythmia, ventricular extrasystoles, generalized edema, ECG T wave amplitude decreased, platelet count decreased. The frequency of these adverse effects did not appear to be different from placebo.
- Dermatological: pruritus
- Gastrointestinal System: flatulence, dry mouth, upper abdominal pain, salivary hypersecretion, dyspepsia, diarrhea, intestinal hypomotility, anorexia
- General: chills
- Liver: increases in AST and/or ALT, hepatic enzyme increased
- Metabolic: hypokalemia, anorexia
- Nervous System: dizziness
- Respiratory: hypoventilation, laryngospasm
- Urinary System: urinary retention

DOCKET ALARM

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