POSFREA™
(palonosetron) Injection

Ordering Information

To order POSFREA™ (palonosetron) Injection, please contact one of these authorized specialty distributors and use the appropriate order #:

0.25 mg/5 mL (0.05 mg/mL)
NDC: 83831-0105-01

Institutions/Hospitals	0.25 mg/5 mL (0.05 mg/mL)
Cardinal Health Specialty	5945779
CENCORA - ASD Healthcare	10292116
Physician Offices	**0.25 mg/5 mL (0.05 mg/mL)**
Cardinal Health Specialty	5945779
Oncology Supply	10292154
McKesson Specialty Health	5018368

UNIQUE J-CODE

J2468

Highlights[1]

- Free from disodium edetate (EDTA)
- Free from sodium citrate
- Not made with natural rubber
- Unique J-Code: J2468

Please see Indications and Important Safety Information on pages 3 to 7and full Prescribing Information for POSFREA™.

AVYXASSIST™

Simplifying Patient Access, Providing Comprehensive Support.

AVYXASSIST™ can offer support to qualifying patients in need. The program provides the following services*

- Benefit verification
- Prior authorization requirements
- Appeals process information
- Referrals to 501(c)(3) foundations when applicable
- Free product assistance (uninsured or underinsured), bridge supply (coverage delays)
- Product replacement
- Copay assistance

COPAY ASSISTANCE PROGRAM

Eligible patients may pay as little as **$0** per dose*

TO ENROLL, PLEASE CHOOSE ONE OF THE FOLLOWING OPTIONS

Phone

866-939-8927
Monday through Friday
8 AM to 8 PM ET

CALL NOW

OR

Online

Click on the link below to begin your online enrollment

ENROLL NOW

OR

Fax

Download, print and fax the completed enrollment form to 833-852-3420

DOWNLOAD NOW

*For Eligibility Requirements Please Contact A Patient Access Specialist. Terms And Conditions Apply.

INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

Chemotherapy-Induced Nausea and Vomiting in Adults

POSFREA™ is indicated for:

- Moderately emetogenic cancer chemotherapy -- prevention of acute and delayed nausea and vomiting associated with initial and repeat courses
- Highly emetogenic cancer chemotherapy -- prevention of acute nausea and vomiting associated with initial and repeat courses

Postoperative Nausea and Vomiting in Adults

POSFREA™ is indicated for prevention of 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, POSFREA™ is recommended even where the incidence of postoperative nausea and/or vomiting is low.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

POSFREA™ is ontraindicated in patients known to have hypersensitivity to the drug or any of its components

WARNINGS AND PRECAUTIONS

Hypersensitivity

Hypersensitivity reactions, including anaphylaxis, have been reported with or without known hypersensitivity to other 5-HT_3 receptor antagonists.

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 POSFREA™ and other serotonergic drugs. If symptoms of serotonin syndrome occur, discontinue POSFREA™ and initiate supportive treatment. Patients should be informed of the increased risk of serotonin syndrome, especially if POSFREA™ is used concomitantly with other serotonergic drugs

IMPORTANT SAFETY INFORMATION (CONTINUED)

ADVERSE REACTIONS

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.

The safety of POSFREA™ has been established from adequate and well-controlled studies of another intravenous formulation of palonosetron HCl. Below is a display of the adverse reactions of palonosetron HCl in these adequate and well-controlled studies.

Chemotherapy-Induced Nausea and Vomiting:

In clinical trials for the prevention of nausea and vomiting induced by moderately or highly emetogenic chemotherapy, 633 adult patients received a single 0.25 mg dose of palonosetron HCl, 410 patients received a single 32 mg dose of ondansetron and 194 patients received a single 100 mg dose of dolasetron. Adverse reactions were similar in frequency and severity with intravenous palonosetron HCl, ondansetron or dolasetron. The following adverse reactions were reported by ≥ 2% of patients in these trials who received palonosetron HCL 0.25 mg intravenously, ondansetron 32 mg intravenously, or dolasetron 100 mg intravenously, respectively: headache (9%, 8%, 16%, respectively), constipation (5%, 2%, 6%, respectively), diarrhea (1%, 2%, 2%, respectively), dizziness (1%, 2%, 2%, respectively), fatigue (<1%, 1%, 2%, respectively), abdominal pain (<1%, <1%, 2%, respectively), insomnia (<1%, 1%, 2%, respectively).

In other studies, 2 subjects experienced severe constipation following a single palonosetron HCl dose of approximately 0.75 mg, three times the recommended dose.

In clinical trials, the following infrequently reported adverse reactions, assessed by investigators as treatment-related or causality unknown, occurred following administration of palonosetron HCl to adult patients receiving concomitant cancer chemotherapy:

Cardiovascular: 1%: non-sustained tachycardia, bradycardia, hypotension, < 1%: hypertension, myocardial ischemia, extrasystoles, sinus tachycardia, sinus arrhythmia, supraventricular extrasystoles and QT prolongation. In many cases, the relationship to palonosetron was unclear.

Dermatological: < 1%: allergic dermatitis, rash.

Hearing and Vision: < 1%: motion sickness, tinnitus, eye irritation and amblyopia.

Gastrointestinal System: 1%: diarrhea, < 1%: dyspepsia, abdominal pain, dry mouth, hiccups and flatulence.

General: 1%: weakness, < 1%: fatigue, fever, hot flash, flu-like syndrome.

Liver: < 1%: transient, asymptomatic increases in AST and/or ALT and bilirubin. These changes occurred predominantly in patients receiving highly emetogenic chemotherapy.

Metabolic: 1%: hyperkalemia, < 1%: electrolyte fluctuations, hyperglycemia, metabolic acidosis, glycosuria, appetite decrease, anorexia.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Musculoskeletal: < 1%: arthralgia.

Nervous System: 1%: dizziness, < 1%: somnolence, insomnia, hypersomnia, paresthesia.

Psychiatric: 1%: anxiety, < 1%: euphoric mood.

Urinary System: < 1%: urinary retention.

Vascular: < 1%: vein discoloration, vein distention.

Postoperative Nausea and Vomiting:

Adverse reactions occurred in adults receiving intravenous palonosetron HCl 0.075 mg immediately before induction of anesthesia in three randomized placebo-controlled trials. Rates of adverse reactions between palonosetron HCl 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. The following adverse reactions were reported by ≥ 2% of patients in these trials who received palonosetron HCL 0.075 mg intravenously (N=336) compared to placebo (N=369): electrocardiogram QT prolongation (5% vs. 3%), bradycardia (4% vs. 4%), headache (3% vs 4%), and constipation (2% vs 3%).

In these clinical trials, the following infrequently reported adverse reactions, assessed by investigators as treatment-related or causality unknown, occurred following administration of palonosetron HCl to adult patients receiving concomitant perioperative and intraoperative medications including those associated with anesthesia:

Cardiovascular: 1% electrocardiogram QTc prolongation, sinus bradycardia, tachycardia; <1%: 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: 1%: pruritus.

Gastrointestinal System: 1%: flatulence, < 1%: dry mouth, upper abdominal pain, salivary hypersecretion, dyspepsia, diarrhea, intestinal hypomotility, anorexia.

General: < 1%: chills.

Liver: 1%: increases in AST and/or ALT< 1%: hepatic enzyme increased.

Metabolic: < 1%: hypokalemia, anorexia.

Nervous System: : < 1%: dizziness.

Respiratory: < 1%: hypoventilation, laryngospasm.

Urinary System: 1%: urinary retention.

Postmarketing Experience

The following adverse reactions have been identified during post approval use of another intravenous formulation of palonosetron HCl. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Very rare cases (<1/10,000) of hypersensitivity reactions including anaphylaxis and anaphylactic shock and injection site reactions (burning, induration, discomfort and pain) were reported from postmarketing experience of palonosetron HCl 0.25 mg in the prevention of chemotherapy- induced nausea and vomiting.

DRUG INTERACTIONS

Serotonergic Drugs

Serotonin syndrome (including altered mental status, autonomic instability, and neuromuscular symptoms) has been described following the concomitant use of 5-HT3 receptor antagonists and other serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs). Monitor for the emergence of serotonin syndrome. If symptoms occur, discontinue POSFREA™ and initiate supportive treatment.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary:

There are no available data on palonosetron HCl use in pregnant women to inform a drug- associated risk. In animal reproduction studies, no effects on embryo-fetal development were observed with the administration of oral palonosetron HCl to rats and rabbits during organogenesis at doses up to 1894 and 3789 times the recommended human intravenous dose, respectively [see Data below].

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data:

Animal Data

In animal reproduction studies, no effects on embryo-fetal development were observed in pregnant rats given oral palonosetron HCl at doses up to 60 mg/kg/day (1894 times the recommended human intravenous dose based on body surface area) or pregnant rabbits given oral doses up to 60 mg/kg/day (3789 times the recommended human intravenous dose based on body surface area) during the period of organogenesis.

Lactation

Risk Summary:

There are no data on the presence of palonosetron in human milk, the effects of palonosetron on the breastfed infant, or the effects of palonosetron on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for POSFREA™ and any potential adverse effects on the breastfed infant from palonosetron or from the underlying maternal condition.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Pediatric Use

This product has not been approved for use in pediatric patients for prevention of chemotherapy- induced nausea and vomiting.

The safety and effectiveness of POSFREA™ for prevention of postoperative nausea and vomiting have not been established in pediatric patients.

Geriatric Use

Of the 1374 adult cancer patients in clinical studies of intravenously administered palonosetron HCl for CINV, 316 (23%) were aged 65 years and over, while 71 (5%) were aged 75 years and over. Of the 1520 adult patients in clinical studies of intravenously administered palonosetron HCl for PONV, 73 (5%) were age 65 years older. No overall differences in safety or effectiveness were observed between these subjects and the younger subjects, but greater sensitivity in some older individuals cannot be ruled out. Population pharmacokinetics analysis did not reveal any differences in palonosetron pharmacokinetics between cancer patients ≥ 65 years of age and younger patients. No dose adjustment or special monitoring are required for geriatric patients.

No overall differences in safety were observed between older and younger subjects in these studies, though the possibility of heightened sensitivity in some older individuals cannot be excluded. No differences in efficacy were observed in geriatric patients for the CINV indication and none are expected for geriatric PONV patients. However, palonosetron HCl efficacy in geriatric patients has not been adequately evaluated.

OVERDOSAGE

There is no known antidote to palonosetron HCl. Overdose should be managed with supportive care.

Dialysis studies have not been performed, however, due to the large volume of distribution, dialysis is unlikely to be an effective treatment for palonosetron HCl overdose. A single intravenous dose of palonosetron HCl at 30 mg/kg (947 and 474 times the human dose for rats and mice, respectively, based on body surface area) was lethal to rats and mice. The major signs of toxicity were convulsions, gasping, pallor, cyanosis and collapse.

Please see the full Prescribing Information for safety information, and dosing guidelines.

To report SUSPECTED ADVERSE REACTIONS, contact Avyxa Pharma, LLC at 1-888-520-0954 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.