09-J0000-87

Original Effective Date: 02/15/09

Reviewed: 12/11/24

Revised: 01/15/25

Subject: Palonosetron Hydrochloride (Posfrea®)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Chemotherapy induced (or radiation therapy induced) vomiting and nausea can significantly affect a patient's quality of life, leading to poor compliance with further chemotherapy or radiation therapy treatment. The severity and incidence of chemotherapy or radiation therapy induced nausea and vomiting are affected by factors such as the selected agent and dose of chemotherapy, route of administration, location of radiation therapy, prior chemotherapy use, and patient age and sex.

In general, to provide maximal protection against chemotherapy induced nausea and vomiting, antiemetic therapy should be initiated before chemotherapy. The antiemetic therapy should also be continued for the same length of time as the duration of the emetic activity of the chemotherapeutic agent being used. However, daily use of antiemetics is not recommended for some therapeutic agents that are taken long term (e.g., imatinib, erlotinib). Antiemetic agents can be administered by the oral, rectal, IV, intramuscular, or transdermal route. It should be noted that oral and IV 5-HT3 antagonists have equivalent efficacy when used at the appropriate doses.

Palonosetron (Aloxi) was approved by the U.S. Food and Drug Administration (FDA) in 2003 for prevention of acute and delayed nausea and vomiting associated with cancer chemotherapy. Posfrea was recently FDA approved for the same indication. Palonosetron selectively blocks serotonin 5-HT3 receptors to prevent emesis. National Comprehensive Cancer Network (NCCN) Guidelines for antiemesis recommend palonosetron for acute and delayed emesis prevention in combination with a NK1 antagonist (e.g., aprepitant, fosaprepitant, rolapitant) and dexamethasone before intravenous antineoplastic therapy with high or moderate emetic risk. It is also recommended in combination with dexamethasone without an NK1 antagonist for chemotherapy with moderate emetic risk. It is also recommended in combination with olanzapine and dexamethasone for moderate or high risk antineoplastic therapy.

POSITION STATEMENT:

Palonosetron HCl (Posfrea®) IV **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:

1. Indication for use is one of the following:
    a. Prevention of acute or delayed chemotherapy induced nausea and vomiting associated with initial or repeat courses of moderately or highly emetogenic chemotherapy (See Table 1)
    b. Prevention of acute or delayed chemotherapy induced nausea and vomiting associated with initial or repeat courses of low emetogenic chemotherapy (See Table 1) when the member has an inadequate response or contraindication to ondansetron (Zofran), or granisetron (Kytril)[a]
    c. Prevention of post-operative nausea and vomiting when the member has an inadequate response or contraindication to intravenous granisetron (Kytril) or ondansetron (Zofran) at the FDA recommended dose[a]
2. Generic palonosetron is **NOT** available for use due to a national drug shortage[b] – documentation must be provided
3. Dose does not exceed 0.25 mg prior to chemotherapy or 0.075 mg prior to induction of anesthesia

Duration of approval: 1 year

[a] Step therapy requirement does not apply if the member was previously approved by Florida Blue or a prior health plan

[b] To verify non-availability, the status of palonosetron injection must be listed as "Currently in Shortage" on the ASHP Current Shortages webpage (Drug Shortages List (ashp.org)) AND all listed manufactures must have all strengths unavailable

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Chemotherapy-Induced Nausea and Vomiting

- Adults: 0.25 mg IV approximately 30 minutes before start of chemotherapy

Postoperative Nausea and Vomiting

- Adults: 0.075 mg IV administered over 10 seconds immediately before the induction of anesthesia

Dose Adjustments

- None

Drug Availability

- 0.25 mg/5 mL solution for injection
- 0.075 mg/1.5mL single use vial

PRECAUTIONS:

Contraindications:

- Hypersensitivity to the drug or any of its components

Precautions/Warnings

- Hypersensitivity reactions, including anaphylaxis, may occur in individuals who have exhibited hypersensitivity to other selective 5-HT3 receptor antagonists.
- Serotonin syndrome has been reported with 5-HT3 receptor antagonists alone but particularly with concomitant use of serotonergic drugs.

BILLING/CODING INFORMATION:

HCPCS Coding:

J2468	Injection, palonosetron HCl (avyxa), not therapeytically equivalent to J2469, 25 mcg

ICD-10 Diagnosis Codes That Support Medical Necessity:

R11.0	Nausea
R11.10	Vomiting, unspecified
R11.11	Vomiting without nausea
R11.12	Projectile vomiting
R11.2	Nausea with vomiting, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs, sequela
T45.95XA	Adverse effect of unspecified primarily systemic and hematological agent, initial encounter
T50.905A	Adverse effect of unspecified drugs, medicaments and biological substances, initial encounter
T50.905S	Adverse effect of unspecified drugs, medicaments and biological substances, sequela

T66.xxxS	Radiation sickness, unspecified, sequela
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic chemotherapy

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: Medical necessity is determined using any applicable NCD or LCD and then Step therapy Requirements for Medicare Outpatient (Part B) Medications outlined in Policy (09-J3000-39).

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

None

OTHER:

Table 1 - Emetogenic Potential of Antineoplastic Agents

	High emetic risk (>90% frequency of emesis)	Moderate emetic risk (30-90% frequency of emesis)
IV	AC combination (doxorubicin or epirubicin with cyclophosphamide) Carboplatin AUC ≥ 4 Carmustine (> 250 mg/m2) Cisplatin Cyclophosphamide (> 1500 mg/m2) Dacarbazine Doxorubicin (≥ 60 mg/m2) Epirubicin (> 90 mg/ m2) Fam-trastuzumab deruxtecan-nxki Ifosfamide (≥ 2 g/ m2) Mechlorethamine Melphalan (≥ 140 mg/m2) Sacituzumab govitecan-hziy Streptozocin	Aldesleukin (> 12-15 million IU/m2) Amifostine (> 300 mg/m2) Bendamustine Busulfan Carboplatin AUC < 4 Carmustine (≤ 250 mg/m2) Clofarabine Cyclophosphamide (≤ 1500 mg/m2) Cytarabine (> 200 mg/m2) Dactinomycin Daunorubicin Dinutuximab Doxorubicin (< 60 mg/m2) Dual-drug liposomal encapsulation of cytarabine and daunorubicin Epirubicin (≤ 90 mg/m2) Idarubicin

		Ifosfamide (< 2g/m2) Irinotecan Irinotecan (liposomal) Lurbinectedin Melphalan (< 140 mg/m2) Methotrexate (≥ 250 mg/m2) Mirvetuximab soravtansine-gynx Naxitamab-gqgk Oxaliplatin Romidepsin Temozolomide Trabectedin
	Low emetic risk (10 – 30% frequency of emesis)	
IV	Ado-trastuzumab emtansine Aldesleukin ≤ 12 million international units/m2 Amifostine ≤ 300 mg/m2 Amivantamab-vmjw Arsenic trioxide Axicabtagene ciloleucel Azacitidine Belinostat Brexucabtagene autoleucel Brentuximab vedotin Cabazitaxel Carfilzomib Ciltacabtagene autoleucel Copanlisib Cytarabine (low dose) 100 – 200 mg/m2 Docetaxel Doxorubicin (liposomal) Enfortumab vedotin-ejfv Eribulin Etoposide 5-FU Floxuridine Gemcitabine Gemtuzumab ozogamicin Idecabtagene vicleucel Inotuzumab ozogamicin Isatuximab-irfc Ixabepilone Lisocabtagene maraleucel Loncastuximab tesirine-lpyl Methotrexate > 50 mg/m2 - < 250 mg/m2 Mitomycin Mitomycin pyelocalyceal solution Mitoxantrone Mogamulizumab-kpkc Mosunetuzumab-axgb Necitumumab Omacetaxine Paclitaxel	

	Paclitaxel-albumin Pemetrexed Pentostatin Polatuzumab vedotin-piig Pralatrexate Tafasitamab-cxix Tagraxofusp-erzs Talimogene laherparepvec Tebentafusp-tebn Thiotepa Tisagenlecleucel Tisotumab vedotin-tftv Topotecan Ziv-aflibercept

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2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 2024 Nov 30]. Available from: http://www.clinicalpharmacology.com/.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2024 Nov 30].
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5. NCCN Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2024 [cited 2024 Nov 30]. Available from: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/11/24.

GUIDELINE UPDATE INFORMATION:

02/15/09	New Medical Coverage Guideline.
04/15/09	Revision; consisting of removing criteria for failure of other agents for highly emetogenic chemo and adding maximum dosage per cycle.
05/15/09	Revision; consisting of adding ICD-9 codes.
08/15/10	Review and revision; consisting of updating references.
11/15/10	Revision; consisting of formatting changes.
01/01/11	Revision; consisting of removing the use of dolasetron from the position statement, and added ICD-10 codes.

06/15/11	Revision to guideline, consisting of defining emetogenic failure.
07/15/11	Revision to guideline, consisting of adding note regarding administration.
08/15/11	Review and revision to guideline; consisting of updating references.
08/15/12	Review and revision to guideline; consisting of updating position statement and references.
10/15/12	Revision to guideline; consisting of modifying criteria for coverage of moderately emetogenic cancer chemotherapy.
08/15/13	Review and revision to guideline; consisting of description, position statement, dosing/administration, precautions, program exceptions, and references.
08/15/14	Review and revision to guideline; consisting of position statement, dosing/administration, moderately emetogenic cancer chemotherapy, references
11/01/15	Revision: ICD-9 Codes deleted.
09/15/17	Revision to guideline; consisting of updating position statement, coding and references.
03/15/18	Update to coding.
05/15/19	Revision to Table 1 and references
07/15/19	Update to Program Exceptions.
01/01/20	Revision to guideline; consisting of updating position statement.
05/15/21	Revision to Table 1 and references
01/15/25	Policy updated to include Posfrea.