Palonosetron: Aloxi®; Posfrea™ (Intravenous)

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I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months, unless otherwise specified.
  - Prevention of Post-Operative Nausea and Vomiting (PONV): Prior authorization validity will be provided for 1 dose
- Renewal: Prior authorization validity may be renewed every 6 months thereafter, unless otherwise specified.
  - Prevention of Post-Operative Nausea and Vomiting (PONV): Prior authorization validity may NOT be renewed

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

CINV:

- 10 billable units per 7 days

PONV:

- 3 billable units x 1 dose only

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient must try and have an inadequate response, contraindication, or intolerance to Aloxi prior to approval of Posfrea; **AND**

Prevention of Chemotherapy Induced Nausea and Vomiting (CINV) in Adults † ‡ [1-5,7]

- Patient meets one of the following criteria:
  b. Patient is receiving highly or moderately emetogenic anticancer chemotherapy (HEC*/MEC***); **OR**
  c. Patient has failed**§** with another 5HT3-antagonist (i.e., ondansetron or granisetron) while receiving the current anticancer chemotherapy regimen; **OR**
  d. Used in combination with olanzapine, neurokinin-1 receptor antagonist (NK-1 RA), and dexamethasone as a component of a 4-drug regimen if not previously given; **AND**
    - Patient experienced emesis during a previous cycle of anticancer chemotherapy with a 3-drug regimen (olanzapine or NK-1 RA-containing regimen); **OR**
    - Patient has additional risk factors for anticancer agent-induced nausea/vomiting **¥**; **AND**
- Palonosetron is NOT covered for any of the following:
  - Breakthrough emesis
  - Repeat dosing in multi-day emetogenic chemotherapy regimens

§ NOTE: Failure is defined as two or more documented episodes of vomiting attributed to the current chemotherapy regimen

Prevention of Chemotherapy Induced Nausea and Vomiting (CINV) in Pediatric Patients † [1-5,7]

- Patient is at least 1 month old and less than 17 years old; **AND**
- Patient is receiving emetogenic chemotherapy; **AND**
- Palonosetron is NOT covered for:
  - Breakthrough emesis; **OR**
  - Repeat dosing in multi-day emetogenic chemotherapy regimens

Prevention of Post-Operative Nausea and Vomiting (PONV) in Adults † [1]

***Highly emetogenic chemotherapy (HEC)**:

Highly Emetogenic Chemotherapy (HEC) [3]			
Carboplatin AUC ≥4	Carmustine >250 mg/m^2	Cisplatin	Cyclophosphamide >1500 mg/m^2
Dacarbazine	Datopotamab deruxtecan-dlnk	Doxorubicin ≥60 mg/m^2	Epirubicin >90 mg/m^2

Fam-trastuzumab deruxtecan-nxki	Ifosfamide ≥2 g/m^2 per dose	Mechlorethamine	Melphalan ≥140 mg/m^2
Sacituzumab govitecan-hziy	Streptozocin	Zolbetuximab-clzb	
The following can be considered HEC in certain patients [3]			
Dactinomycin	Daunorubicin	Doxorubicin <60 mg/m^2	Epirubicin ≤90 mg/m^2
Idarubicin	Ifosfamide <2 g/m^2 per dose	Irinotecan	Oxaliplatin
Trabectedin			
The following regimens can be considered HEC [3]			
FOLFOX	FOLFIRI	FOLFIRINOX; FOLFOXIRI	AC (any anthracycline + cyclophosphamide)

****Moderately emetogenic chemotherapy (MEC)**:

Moderately Emetogenic Chemotherapy (MEC) [3]			
Aldesleukin >12–15 million IU/m^2 or 600,000 IU/kg	Amifostine >300 mg/m^2	Bendamustine	Busulfan
Carboplatin AUC <4	Carmustine ≤250 mg/m^2	Clofarabine	Cyclophosphamide ≤1500 mg/m^2
Cytarabine >200 mg/m^2	Dinutuximab	Dual-drug liposomal encapsulation of cytarabine and daunorubicin	Irinotecan (liposomal)
Lurbinectedin	Melphalan <140 mg/m^2	Methotrexate ≥250 mg/m^2	Mirvetuximab soravtansine-gynx
Naxitamab-gqgk	Romidepsin	Temozolomide	

¥ Patient risk factors for anticancer agent-induced nausea/vomiting [3]

- Younger age
- Female sex
- Previous history of anticancer agent-induced nausea and vomiting (chemotherapy-induced nausea and vomiting [CINV])
- Little or no previous alcohol use
- Prone to motion sickness
- History of morning sickness during pregnancy
- Anxiety/high pretreatment expectation of nausea
- Partial or complete bowel obstruction
- Vestibular dysfunction
- Brain metastases
- Electrolyte imbalance: hypercalcemia, hyperglycemia, or hyponatremia
- Uremia
- Concomitant drug treatments, including opioids
- Gastroparesis: tumor or chemotherapy (e.g., vincristine) induced or other causes (e.g., diabetes)

- Excessive secretions (e.g., seen in patients with head and neck cancers)
- Malignant ascites
- Psychophysiologic: Anxiety or anticipatory nausea/vomiting
- Cannabinoid hyperemesis syndrome
- Rapid opioid withdrawal
- Pancreatitis
- Dysmotility
- Concomitant radiation therapy (RT), especially total body irradiation and RT directed at the abdomen or brain

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-4]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Duration of authorization has not been exceeded *(refer to Section I)*; **AND**
- Beneficial response as evidenced by reduction in nausea and/or vomiting; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serotonin syndrome (e.g., mental status changes, autonomic instability, neuromuscular symptoms, etc.), severe hypersensitivity reactions (including anaphylaxis and anaphylactic shock), etc.

V. Dosage/Administration [1,2]

Indication	Dose
Prevention of chemotherapy-induced nausea and vomiting in adults	Administer 0.25 mg intravenously, no more frequently than weekly, prior to emetogenic chemotherapy
Prevention of chemotherapy-induced nausea and vomiting in pediatric patients (1 month to less than 17 years of age)	Administer 20 mcg/kg (max of 1.5 mg) intravenously, no more frequently than weekly, prior to emetogenic chemotherapy
Post-operative nausea and vomiting	Administer 0.075 mg intravenously immediately before the induction of anesthesia

VI. Billing Code/Availability Information

HCPCS Code(s):

- J2469 – Injection, palonosetron hcl, 25 mcg: 1 billable unit = 25 mcg (0.025 mg)
- J2468 – Injection, palonosetron hydrochloride (posfrea), 25 micrograms; 1 billable unit = 25 mcg (0.025 mg) Ψ (Posfrea only)

NDC(s):

- Aloxi 0.25 mg/5 mL solution for injection in a single-dose vial: 69639-103-xx **§**
- Aloxi 0.075 mg/1.5 mL solution for injection in a single-dose vial: 69639-103-xx (not commercially available)
- Posfrea 0.25 mg/5 mL solution for injection in a single-dose vial: 83831-0105-xx **Ψ**
- Posfrea 0.075 mg/1.5 mL solution for injection in a single-dose vial: 83831-0104-xx **Ψ**

– ***§*** *Available as a multi-sourced generic;*

– ***Ψ*** *Designated products approved by the FDA as a 505(b)(2) NDA of the innovator product. These products are not rated as therapeutically equivalent to their reference listed drug in the Food and Drug Administration's (FDA) Orange Book and are therefore considered single source products based on the statutory definition of "single source drug" in section 1847A(c)(6) of the Act. For a complete list of all approved 505(b)(2) NDA products please reference the latest edition of the Orange Book:*

Approved Drug Products with Therapeutic Equivalence Evaluations | Orange Book | FDA

VII. References

1. Aloxi [package insert]. Switzerland; Helsinn Healthcare SA; April 2020. Accessed June 2025.
2. Posfrea [package insert]. New Jersey, USA; Avyxa Pharma, LLC; April 2025. Accessed June 2025.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) palonosetron. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2025.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Antiemesis. Version 2.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2025.
5. Roila F, Molassiotis A, Herrstedt J, et al. MASCC and ESMO Consensus Guidelines for the Prevention of Chemotherapy and Radiotherapy-Induced Nausea and Vomiting: ESMO Clinical Practice Guidelines. Ann Oncol (2016) 27 (suppl 5): v119-v133.
6. Hesketh PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2017 Oct 1;35(28):3240-3261.
7. Hesketh PJ, Kris MG, Basch E, et al. Antiemetics: ASCO Guideline Update. Journal of Clinical Oncology 2020 38:24, 2782-2797.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
R11.0	Nausea

ICD-10	ICD-10 Description
R11.10	Vomiting, unspecified
R11.11	Vomiting without nausea
R11.12	Projectile vomiting
R11.2	Nausea with vomiting, unspecified
T41.0X5A	Adverse effect of inhaled anesthetics, initial encounter
T41.1X5A	Adverse effect of intravenous anesthetics, initial encounter
T41.205A	Adverse effect of unspecified general anesthetics, initial encounter
T41.295A	Adverse effect of other general anesthetics, initial encounter
T41.45XA	Adverse effect of unspecified anesthetic, initial encounter
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
T45.95XD	Adverse effect of unspecified primarily systemic and hematological agent, subsequent encounter
T45.95XS	Adverse effect of unspecified primarily systemic and hematological agent, sequela
T50.905A	Adverse effect of unspecified drugs, medicaments and biological substances, initial encounter
T50.905D	Adverse effect of unspecified drugs, medicaments and biological substances, subsequent encounter
T50.905S	Adverse effect of unspecified drugs, medicaments and biological substances, sequela
T50.995A	Adverse effect of other drugs, medicaments and biological substances, initial encounter
T88.59XA	Other complications of anesthesia, initial encounter
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA,HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC