RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	palonosetron
Policy Number:	RxA.387
Drug(s) Applied:	Aloxi®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Palonosetron (Aloxi®) is a serotonin-3 (5-HT_3) receptor antagonist. Palonosetron is indicated in adults 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.
- 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, Aloxi® is recommended even where the incidence of postoperative nausea and/or vomiting is low.

Aloxi® is indicated in 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Palonosetron (Aloxi®)	Prevention of nausea and vomiting associated with cancer chemotherapy	Adults: 0.25 mg IV given 30 min prior to chemotherapy Pediatrics (1 month to less than 17 years): 20 mcg/kg (max 1.5 mg) IV given 30 min prior to chemotherapy	Adults: 0.25 mg/dose Pediatrics: 1.5 mg/dose
	Prevention and treatment of postoperative nausea and vomiting	Adults: 0.075 mg IV immediately before the induction of the anesthesia Efficacy beyond 24 hours has not been demonstrated.	0.075 mg/dose

Dosage Forms

- Single-use vial for injection: 0.25 mg/5 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Prevention of Nausea and Vomiting Associated with Cancer Chemotherapy (must meet all)**:**

1. Prescribed for the prevention of chemotherapy-induced nausea/vomiting;
2. Failure of a formulary 5-HT_3 receptor antagonist (ondansetron is preferred) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed one of the following (a or b):
   a. Adults (age ≥ 17 years): 0.25 mg per chemotherapy cycle;
   b. Pediatrics (age < 17 years): 1.5 mg per chemotherapy cycle.

Approval duration
Commercial: Projected course of chemotherapy
Medicaid: Projected course of chemotherapy

B. Prevention of Postoperative Nausea and Vomiting (must meet all):

1. Prescribed for the prevention of postoperative nausea/vomiting;
2. Member is scheduled to receive surgery;
3. Age 18 years of age or older;
4. Failure of a formulary 5-HT_3 receptor antagonist (ondansetron is preferred) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 0.075 mg once.

Approval duration
Commercial: One-time approval (3 days)
Medicaid: One-time approval (3 days)

II. Continued Therapy Approval

A. Prevention of Nausea and Vomiting Associated with Cancer Chemotherapy (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Member continues to receive cancer chemotherapy;
4. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Adults (age ≥ 17 years): 0.25 mg per chemotherapy cycle;
   b. Pediatrics (age < 17 years): 1.5 mg per chemotherapy cycle.

Approval duration
Commercial: Projected course of chemotherapy
Medicaid: Projected course of chemotherapy

B. Prevention of Postoperative Nausea and Vomiting

1. Re-authorization is not permitted. Members will need to meet the initial approval criteria.

Approval duration
Not applicable

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
5-HT_3: serotonin 5-hydroxytryptamine, type 3
ASCO: American Society of Clinical Oncology
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
PONV: postoperative nausea and vomiting

B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
5HT_3 Serotonin Antagonists		
Akynzeo® (fosnetupitant/ palonosetron)	**Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** 1 vial IV given 30 min prior to chemotherapy on day 1	1 vial/chemotherapy cycle
Akynzeo® (netupitant/ palonosetron)	**Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** 1 capsule PO given 1 hour prior to initiation of chemotherapy on day 1 (in combination with dexamethasone) or 1 vial IV given 30 min prior to initiation of chemotherapy on day 1	1 capsule or vial/chemotherapy cycle
Anzemet® (dolasetron)	**Prevention of nausea and vomiting associated with chemotherapy** 100 mg PO within 1 hr prior to chemotherapy	100 mg/day PO
granisetron	**Prevention of nausea and vomiting associated with chemotherapy** Tablet: 2 mg PO QD given 1 hr prior to chemotherapy, or 1 mg PO BID (one dose given 1 hr prior to chemotherapy and then 12 hours later) Injection: 10 mcg/kg IV given within 30 min prior to chemotherapy (on days chemotherapy is given) **Prevention of PONV*** 0.35 to 3 mg (5 to 20 mcg/kg) IV at the end of surgery	PO: 2 mg/day IV: 40 mcg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ondansetron (Zofran®, Zuplenz®)	**Prevention of nausea and vomiting associated with moderately emetogenic chemotherapy** Age 12 years or older: 8 mg PO given 30 min prior to chemotherapy, then repeat dose 8 hrs after initial dose, then 8 mg PO BID for 1 to 2 days after chemotherapy completion Age 4 to 11 years: 4 mg PO given 30 min prior to chemotherapy, then repeat dose 4 and 8 hrs after initial dose, then 8 mg PO TID for 1 to 2 days after chemotherapy completion **Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** 24 mg PO given 30 min prior to start of single-day chemotherapy	PO: 24 mg/day PO IV: 16 mg/dose (up to 3 doses/day)
	Prevention of nausea and vomiting associated with emetogenic chemotherapy: 0.15 mg/kg/dose IV given 30 min prior to chemotherapy, then repeat dose 4 and 8 hrs after initial dose **Prevention of PONV:** 16 mg PO given 1 hr prior to anesthesia or 4 mg IM/IV as a single dose given 30 min before end of anesthesia	PO: 24 mg/day PO IV: 16 mg/dose (up to 3 doses/day)
Sancuso® (granisetron)	**Prevention of nausea and vomiting associated with chemotherapy** Apply 1 patch at least 24 hrs prior to chemotherapy; may be applied up to 48 hrs after chemotherapy	1 patch/7 days
Sustol® (granisetron)	**Prevention of moderately emetogenic chemotherapy or anthracycline/cyclophosphamide chemotherapy:** 10 mg SC given 30 min prior to chemotherapy on day 1 (in combination with other agents). Do not administer more frequently than once every 7 days.	10 mg/7 days

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic. *Off-label

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Aloxi® is contraindicated in patients known to have hypersensitivity to the drug or any of its components.

- Boxed warning(s):
  - None reported

APPENDIX D: American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) Recommendations in Oncology

- **Minimal emetic risk chemotherapy**: No routine prophylaxis is recommended.
- **Low emetic risk chemotherapy**: Recommended options include dexamethasone, metoclopramide, prochlorperazine, or a 5-HT_3 receptor antagonist. NK_1 receptor antagonists are not included in low risk antiemetic recommendations.
- **Moderate emetic risk chemotherapy**: 5-HT_3 receptor antagonists and dexamethasone may be used in combination and with or without NK_1 receptor antagonists. Olanzapine may also be used in combination with palonosetron and dexamethasone.
  - Examples of moderate emetic risk chemotherapy: azacitidine, alemtuzumab, bendamustine, carboplatin, clofarabine, cyclophosphamide < 1,500 mg/m^2, cytarabine < 1,000 mg/m^2, daunorubicin, doxorubicin, epirubicin, idarubicin, ifosfamide, irinotecan, oxaliplatin
- **High emetic risk chemotherapy**: NK_1 receptor antagonists are recommended for use in combination with 5-HT_3 receptor antagonists and dexamethasone. Olanzapine may also be used in combination with 5-HT_3 receptor antagonists, dexamethasone, and/or NK_1 receptor antagonists.
  - Examples of high emetic risk chemotherapy: carmustine, cisplatin, cyclophosphamide $\geq$ 1,500 mg/m^2, dacarbazine, dactinomycin, mechlorethamine, streptozocin.
- **Breakthrough emesis**: Addition of an agent from a different drug class to the current antiemetic regimen is recommended for breakthrough emesis. Applicable drug classes include atypical antipsychotics (olanzapine), benzodiazepines (lorazepam), cannabinoids (dronabinol, nabilone), phenothiazines (prochlorperazine, promethazine), 5-HT_3 receptor antagonists (dolasetron, ondansetron, granisetron), steroids (dexamethasone), or other (haloperidol, metoclopramide, scopolamine). The recommendation includes addition of an NK_1 receptor antagonist to the prophylaxis regimen of the next chemotherapy cycle if not previously included.

References

1. Aloxi® Prescribing Information. Lugano, Switzerland: Helsinn Healthcare; April 2020. Available at: www.aloxi.com. Accessed July 30, 2020.
2. Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2014;118(1):85-113. Accessed July 30, 2020.
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4. National Comprehensive Cancer Network. Antiemesis Version 2.2020. Available at: https://www.nccn.org. Accessed July 30, 2020.
5. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed July 30, 2020.
6. Palonosetron, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed July 30, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to "palonosetron"; Drug(s) Applied was updated to "Aloxi®"; Line of Business Policy Applies to was updated to "All". 2. Dosage forms was updated: Discontinued drug strength 0.075 mg/1.5 mL was removed. 3. Clinical policy was updated: Approval duration was updated for both Initial and Continued Approval Criteria; Continued Approval was rephrased to "Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy".; Changed 18 to 17 for age range; Removed additional 3 days after cycle from approval duration. 4. References were updated.	07/30/2020	09/14/2020