Clinical Policy Title:	palonosetron
Policy Number:	RxA.387
Drug(s) Applied:	Aloxi®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
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 intravenously given 30 min prior to chemotherapy Pediatrics (1 month to <17 years): 20 mcg/kg (max 1.5 mg) intravenously 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 intravenously immediately before the induction of the anesthesia	0.075 mg/dose

		Efficacy beyond 24 hours has not been demonstrated.	

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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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-HT3 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-HT3 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. Member is 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

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
$5HT_3$ Serotonin Antagonists		
Fosnetupitant/ palonosetron (Akynzeo®)	**Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** 1 vial intravenously given 30 min prior to chemotherapy on day 1	1 vial/chemotherapy cycle
netupitant/ palonosetron(Akynzeo®)	**Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** 1 capsule orally given 1 hour prior to initiation of chemotherapy on day 1 (in combination with dexamethasone) or 1 vial intravenously given 30 min prior to initiation of chemotherapy on day 1	1 capsule or vial/chemotherapy cycle
granisetron	**Prevention of nausea and vomiting associated with chemotherapy** Tablet: 2 mg orally once daily given 1 hr prior to chemotherapy, or 1 mg orally twice daily (one dose given 1 hr prior to chemotherapy and then 12 hours later) Injection: 10 mcg/kg intravenously given within 30 min prior to chemotherapy (on days chemotherapy is given)	Orally: 2 mg/day Intravenously: 40 mcg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Prevention of PONV* 0.35 to 3 mg (5 to 20 mcg/kg) intravenously at the end of surgery	
ondansetron (Zofran®, Zuplenz®)	**Prevention of nausea and vomiting associated with moderately emetogenic chemotherapy** Age ≥ 12 years: 8 mg orally given 30 min prior to chemotherapy, then repeat dose 8 hrs after initial dose, then 8 m by mouth twice daily for 1 to 2 days after chemotherapycompletion. Age 4 - 11 years: 4 mg orally given 30 min prior to chemotherapy, then repeat dose 4 and 8 hrs after initial dose, then 8 mg orally three times daily for 1 to 2 days after chemotherapy completion. **Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** 24 mg orally given 30 min prior to start ofsingle-day chemotherapy.	Orally: 24 mg/day PO Intravenously: 16 mg/dose (up to 3 doses/day)
	Prevention of nausea and vomiting associated with emetogenic chemotherapy: 0.15 mg/kg/dose intravenously given 30 min prior to chemotherapy, then repeat dose 4 and 8 hrs after initial dose. **Prevention of PONV:** 16 mg orally given 1 hr prior to anesthesia or 4 mg intramuscularly/intravenously as a single dose given 30 min before end of anesthesia.	Orally: 24 mg/day Intravenously: 16 mg/dose (up to 3 doses/day)
granisetron (Sancuso®)	**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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
granisetron (Sustol®)	**Prevention of moderately emetogenic chemotherapy or anthracycline/cyclophosphamide chemotherapy:** 10 mg subcutaneously 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 generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.
*Off-label

APPENDIX C: Contraindications/Boxed Warnings

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

- Boxed warning(s):
  - None reported

- **APPENDIX D: General Information**<u>**Minimal emetic risk chemotherapy**</u>: No routine prophylaxis is recommended.
- <u>**Low emetic risk chemotherapy**</u>: 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.
- <u>**Moderate emetic risk chemotherapy**</u>: 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.
- <u>**High emetic risk chemotherapy**</u>: 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 ≥ 1,500 mg/m^2, dacarbazine, dactinomycin, mechlorethamine, streptozocin.
- <u>**Breakthrough emesis**</u>: 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. Iselin, NJ: Helsinn Therapeutics (U.S.), Inc.; April 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=795f386e-2b44-5092-e053-2991aa0a5820. Accessed May 31, 2021.
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 May 31, 2021.
3. Hesketh, PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 2017;35(28): 3240-3261. Accessed May 31, 2021.
4. National Comprehensive Cancer Network. Antiemesis Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed May 31, 2021.
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 May 31, 2021.
6. Palonosetron, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed May 31, 2021.

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
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Appendix B: Therapeutic Alternative verbiage was updated to *“Below are suggested therapeutic alternatives..”* 3. Appendix B: Therapeutic Alternatives was updated to remove discontinued brand Anzemet® unavailable generic dolasetron. 4. Appendix B footnote was updated to,” Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only”. 5. References were reviewed and updated.	05/31/2021	09/14/2021