Clinical Policy: Palonosetron (Aloxi)

Reference Number: CP.CPA.198
Effective Date: 11.16.16
Last Review Date: 08.19
Line of Business: Commercial

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Palonosetron (Aloxi®) is a serotonin (5-HT_3) receptor antagonist.

FDA Approved Indication(s)

Aloxi 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.

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that Aloxi is **medically necessary** when the following criteria are met:

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 ≥ 18 years): 0.25 mg per chemotherapy cycle;
   b. Pediatrics (age < 18 years): 1.5 mg per chemotherapy cycle.

Approval duration: projected course of chemotherapy up to 72 hours after completion 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;
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: one time approval (3 days)

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

II. Continued Therapy

A. Prevention of Nausea and Vomiting Associated with Cancer Chemotherapy (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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 ≥ 18 years): 0.25 mg per chemotherapy cycle;
   b. Pediatrics (age < 18 years): 1.5 mg per chemotherapy cycle.

Approval duration: projected course of chemotherapy up to 72 hours after completion 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

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial.

IV. Appendices/General Information

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

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
5-HT_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
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)	PO: 2 mg/day IV: 10 mcg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Prevention of PONV* 0.35 to 3 mg (5 to 20 mcg/kg) IV at the end of surgery	
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 **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 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**	10 mg/7 days

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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.	

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 ≥ 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 breathrough 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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

VI. Product Availability

Single-use vial for injection: 0.25 mg/5 mL, 0.075 mg/1.5 mL

VII. References

1. Aloxi Prescribing Information. Lugano, Switzerland: Helsinn Healthcare; September 2018. Available at: www.aloxi.com. Accessed April 30, 2019.
2. Gan TJ, Diemunsch, P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2014;118:85-113.
3. Hesketh, PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 2017: JCO2017744789.
4. National Comprehensive Cancer Network. Antiemesis Version 1.2019. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed April 30, 2019.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2469	Injection, palonosetron HCl, 25 mcg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2018 annual review: new policy created. Split from CP.CPA. 223 Antiemetics – 5-HT_3 Receptor Antagonist into individual policies; generalized trial and failure for all indications to a 5-HT_3 antagonist (ondansetron is preferred); added age requirement for PONV per FDA indication; modified approval duration for PONV to one time approval and limited to evaluation by initial criteria only; modified approval duration for chemotherapy-induced N/V to duration of chemotherapy up to 72 hours after completion; references reviewed and updated.	05.15.18	08.18
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.14.19	08.19

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise

professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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