Clinical Policy: Fosnetupitant and Palonosetron (Akynzeo IV)

Reference Number: LA.PMN.158
Effective Date:
Last Review Date: 06.21
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description

Fosnetupitant/palonosetron is a fixed combination product of netupitant, a substance P/neurokinin 1 (NK_1) receptor antagonist, and palonosetron hydrochloride, a serotonin (5-HT_3) receptor antagonist.

FDA Approved Indication(s)

Akynzeo for injection is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy.

Policy/Criteria

Prior authorization is required. 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 Louisiana Healthcare Connections that Akynzeo 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. **Age ≥ 18 years;**
3. **Member is scheduled to receive highly emetogenic cancer chemotherapy (*see Appendix D*);**
4. **Member meets one of the following (a or b):**
   a. **Both of the following (i and ii):**
      i. **Failure of a 5-HT_3 receptor antagonist (*ondansetron is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;**
      ii. **Failure of an NK_1 antagonist (*aprepitant is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;**
      Prior authorization may be required for aprepitant

b. Request is for Stage IV or metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy;

5. **Prescribed in combination with dexamethasone;**
6. **Dose does not exceed the following:**
   a. **Akynzeo for injection: fosnetupitant 235 mg/palonosetron 0.25 mg (1 vial) per chemotherapy cycle.**

Approval duration: Projected course of chemotherapy

B. **Other diagnoses/indications**
   1. **Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.**

II. **Continued Therapy**

A. **Prevention of Nausea and Vomiting Associated with Cancer Chemotherapy (must meet all):**
   1. **Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;**
   2. **Member is responding positively to therapy;**
   3. **If request is for Akynzeo for injection, member continues to receive highly emetogenic cancer chemotherapy (*see Appendix D*);**
   4. **Prescribed in combination with dexamethasone;**
   5. **If request is for a dose increase, new dose does not exceed the following:**
      a. **Akynzeo for injection: fosnetupitant 235 mg/palonosetron 0.25 mg (1 vial) per chemotherapy cycle.**

Approval duration: Projected course of chemotherapy

B. **Other diagnoses/indications (must meet 1 or 2):**
   1. **Currently receiving medication via Louisiana Healthcare Connections 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 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.**

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 policy –LA.PMN.53 for Medicaid or evidence of coverage documents.**

IV. **Appendices/General Information**

Appendix A: Abbreviation/Acronym Key

5HT$_3$: serotonin 5-hydroxytryptamine, type 3
ASCO: American Society of Clinical Oncology
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
NK$_1$: neurokinin 1

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
5-HT$_3$ Serotonin Antagonists		
Aloxi® (palonosetron)	Prevention of nausea and vomiting associated with chemotherapy 0.25 mg IV given 30 min prior to chemotherapy	0.25 mg/day
Anzemet® (dolasetron)	Prevention of nausea and vomiting associated with chemotherapy 100 mg PO within 1 hr prior to chemotherapy	100 mg/day
granisetron (Kytril®)	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 PO IV: 10 mcg/kg/day
ondansetron (Zofran®, Zofran® ODT, 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	PO: 24 mg/day IV: 16 mg/dose (up to 3 doses/day)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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	
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
NK_1 Antagonists		
aprepitant (Emend®)	Prevention of nausea and vomiting associated with moderately to highly emetogenic chemotherapy *Capsules:* 125 mg PO on day 1 and 80 mg PO on days 2 and 3 *Oral suspension*: 3 mg/kg PO on Day 1, then 2 mg/kg PO on Days 2 and 3	Day 1: 125 mg Days 2 and 3: 80 mg
Emend® (fosaprepitant)	Prevention of nausea and vomiting associated with moderately to highly emetogenic chemotherapy 150 mg IV on day 1 (for single dose chemo regimens)	Day 1: 150 mg
Varubi™ (rolapitant)	Prevention of nausea and vomiting associated with moderately to highly emetogenic chemotherapy 180 mg PO on day 1	Day 1: 180 mg

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.

Appendix C: Contraindications/Boxed Warnings

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 (recommended by both ASCO and NCCN) or metoclopramide, prochlorperazine, or a 5-HT_3 receptor antagonist (recommended by NCCN only). 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: Per NCCN, an agent from a different drug class is recommended to be added to the current antiemetic regimen. 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 (haloperidol, metoclopramide, scopolamine). An NK_1 receptor antagonist may be added to the prophylaxis regimen of the next chemotherapy cycle if not previously included.**

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Prevention of chemotherapy-induced nausea and vomiting	1 vial infused IV over 30 minutes starting 30 minutes before chemotherapy on Day 1, in combination with dexamethasone	1 vial on Day 1 of chemotherapy cycle

VI. Product Availability

- **Single dose vial, powder for reconstitution: 235 mg fosnetupitant/0.25 mg palonosetron**

- **Single dose vial, injection solution: 235 mg fosnetupitant/0.25 mg palonosetron per 20 mL**

VII. References

1. **Akynzeo Prescribing Information. Woodcliff Lake, NJ: Eisai, Inc.; June 2020. Available at: https://www.akynzeo.com/. Accessed November 13, 2020.**
2. **Hesketh, PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol.* 2017: JCO2017744789.**
3. **National Comprehensive Cancer Network. Antiemesis Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed November 13, 2020.**
4. **Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/.**
5. **Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 13, 2020.**

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
J1454	Injection, fosnetupitant 235 mg and palonosetron 0.25 mg

Reviews, Revisions, and Approvals	Date
Converted corporate to local policy	06.2021

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. LHCC makes no representations and accepts no liability with respect to the content of any

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