Akynzeo® (fosnetupitant/palonosetron)
(Intravenous)

Document Number: EOCCO-0363

Last Review Date: 04/04/2024
Date of Origin: 05/01/2018
Dates Reviewed: 05/2018, 06/2018, 02/2019, 02/2020, 10/2020, 04/2021, 4/2022, 04/2023, 04/2024

I. Length of Authorization

Coverage is provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Akynzeo 235 mg/0.25 mg (fosnetupitant/palonosetron) single-dose vial: 1 vial per 7 days

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

- 1 billable unit per 7 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Prevention of chemotherapy-induced nausea and vomiting (CINV) † ‡ [1-5]

- Patient has failed**§** with another generically available 5-HT_3 receptor antagonist (e.g., ondansetron, granisetron, palonosetron, etc.) in combination with a NK-1 receptor antagonist (e.g., aprepitant, fosaprepitant, rolapitant, etc.) while receiving the current anticancer chemotherapy regimen; **AND**
  - Patient is receiving highly emetogenic anticancer chemotherapy (HEC)*****; **AND**
    - Used in combination with dexamethasone with or without olanzapine; **OR**
  - Patient is receiving moderately emetogenic anticancer chemotherapy (MEC)******; **AND**
    - Used in combination with dexamethasone; **AND**
      - Patient has additional risk factors for anticancer agent-induced nausea/vomiting **¥**; **OR**
      - Patient has experienced previous treatment failure with a combination of corticosteroid and 5-HT_3 receptor antagonist; **OR**

- Patient experienced emesis during a previous cycle of anticancer chemotherapy with a 3-drug regimen (olanzapine or NK-1 receptor antagonist-containing regimen); **AND**
  i. Used in combination with olanzapine and dexamethasone as a component of a 4-drug regimen if not previously given; **AND**

Akynzeo is NOT covered for any of the following:

- Breakthrough emesis
- Repeat dosing in multi-day emetogenic chemotherapy regimens
- CINV related to an anthracycline plus cyclophosphamide chemotherapy regimen

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

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

Highly Emetogenic Chemotherapy (HEC) [3]			
Carboplatin	Carmustine	Cisplatin	Cyclophosphamide
Dacarbazine	Doxorubicin	Epirubicin	Fam-trastuzumab deruxtecan-nxki
Ifosfamide	Mechlorethamine	Melphalan ≥140 mg/m^2	Sacituzumab govitecan-hziy
Streptozocin			
The following can be considered HEC in certain patients [3]			
Dactinomycin	Daunorubicin	Idarubicin	Irinotecan
Methotrexate ≥250mg/m^2	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 (HEC) [3]			
Aldesleukin >12–15 million IU/m^2	Amifostine >300 mg/m^2	Bendamustine	Busulfan
Clofarabine	Cytarabine >200 mg/m^2	Dinutuximab	Dual-drug liposomal encapsulation of cytarabine and daunorubicin
Irinotecan (liposomal)	Lurbinectedin	Melphalan <140 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

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

IV. Renewal Criteria [1-3]

Coverage can 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**
- Beneficial response as evidenced by reduction in nausea and/or vomiting; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hypersensitivity reactions (including anaphylaxis), serotonin syndrome (e.g., mental status changes, autonomic instability, neuromuscular symptoms, seizures, etc.)

V. Dosage/Administration [1-3]

Indication	Dose
Prevention of chemotherapy-induced nausea and vomiting (CINV)	Administer the contents of 1 vial, intravenously, on Day 1 of each chemotherapy cycle approximately 30 minutes prior to the start of chemotherapy

VI. Billing Code/Availability Information

HCPCS Code:

- J1454 – Injection, fosnetupitant 235 mg and palonosetron 0.25 mg; 1 billable unit = fosnetupitant 235 mg and palonosetron 0.25 mg

NDC(s):

- Akynzeo (235 mg fosnetupitant/0.25 mg palonosetron); single-dose vial for injection (lyophilized powder): 69639-0102-xx
- Akynzeo (235 mg fosnetupitant/0.25 mg palonosetron per 20 mL); single-dose vial for injection (solution; to-be-diluted): 69639-0105-xx
- Akynzeo (235 mg fosnetupitant/0.25 mg palonosetron per 20 mL); single-dose vial for injection (solution; ready-to-use): 69639-0106-xx

VII. References

1. Akynzeo [package insert]. Helsinn Therapeutics (U.S.), Inc., Iselin, NJ, under license of Helsinn Healthcare SA, Switzerland. February 2023. Accessed March 2024.
2. Referenced with permission from the NCCN Drugs and Biologics Compendium (NCCN Compendium®) fosnetupitant/palonosetron. National Comprehensive Cancer Network, 2024. 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 March 2024.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Antiemesis. Version 1.2024. National Comprehensive Cancer Network, 2024. 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 March 2024.
4. 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.
5. Hesketh PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Guideline Update. J Clin Oncol. 2020 Aug 20;38(24):2782-2797. Doi: 10.1200/JCO.20.01296.
6. Karthaus M, Szabo P, Voisin D, et al. Phase III study of palonosetron (PALO) given as 30-min IV infusion (IV inf) versus 30-sec IV bolus (IV bol) for prevention of chemotherapy-induced nausea and vomiting (CINV) associated with highly emetogenic chemotherapy (HEC). Journal of Clinical Oncology 35(31_suppl):227-227; November 2017. DOI: 10.1200/JCO.2017.35.31_suppl.227.

7. Schwartzberg L, Roeland E, Andric Z, et al. Phase III safety study of intravenous NEPA: a novel fixed antiemetic combination of fosnetupitant and palonosetron in patients receiving highly emetogenic chemotherapy. Ann Oncol. 2018 Jul 1;29(7):1535-1540. Doi: 10.1093/annonc/mdy169.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
R11.0	Nausea
R11.10	Vomiting, unspecified
R11.11	Vomiting without nausea
R11.12	Projectile vomiting
R11.2	Nausea with vomiting, unspecified
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
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 Government Benefit Administrators
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