Drug Policy:

Antiemetics

POLICY NUMBER UM ONC_1468	**SUBJECT** Antiemetics: Zofran™ (ondansetron), Kytril™ (granisetron), Aloxi™ (palonosetron) Sancuso™ (granisetron patch), Sustol™ (granisetron extended release), Akynzeo™ (netupitant oral /fosnetupitant injection-palonosetron), Emend™ Aprepitant oral or Fosaprepitant), Cinvanti™ (aprepitant injection), and Varubi™ (rolapitant oral).	**DEPT/PROGRAM** UM Dept	**PAGE 1 of 3**
DATES COMMITTEE REVIEWED 12/14/22, 12/30/22, 01/11/23, 01/10/24	**APPROVAL DATE** January 10, 2024	**EFFECTIVE DATE** January 26, 2024	**COMMITTEE APPROVAL DATES** 12/14/22, 12/30/22, 01/11/23, 01/10/24
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee	
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**	**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Antiemetics usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The member has not experienced disease progression on the requested medication AND
2. The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
3. Additional medication(s) are not being added to the continuation request.

B. Antiemesis

1. Zofran (ondansetron), Kytril (granisetron), Aloxi (palonosetron), Sustol (granisetron extended release), Akynzeo (netupitant oral/fosnetupitant injection + palonosetron), Sancuso (granisetron PATCH) may be used as prophylaxis prior to the administration of low, moderate, or high emetogenic risk chemotherapy.
    a. Only Zofran (ondansetron) or Kytril (granisetron) can be used [see exclusion criteria for other antiemetics]:
        i. Before radiation to the upper abdomen or total body irradiation OR
        ii. Treatment for nausea/vomiting induced by radiation or anticancer therapy.
2. Emend (fosaprepitant injection or aprepitant oral), Cinvanti (aprepitant injection), or Varubi (rolapitant oral) should be used in combination with dexamethasone and one of the following serotonin (5-HT3) antagonists: Zofran (ondansetron) or Kytril (granisetron) or Aloxi (palonosetron) prior to the administration of low, moderate, or high emetogenic risk chemotherapy.

III. EXCLUSION CRITERIA

A. Aloxi (palonosetron), Akynzeo (netupitant oral /fosnetupitant injection-palonosetron), Sancuso (granisetron patch), Sustol (granisetron extended release), Emend (fosaprepitant injection/oral aprepitant), Cinvanti (aprepitant injection), or Varubi (rolapitant oral) is being used for the prevention or treatment of radiation or total body irradiation induced nausea and vomiting or for the treatment of breakthrough nausea/vomiting.

B. Emend (fosaprepitant injection/oral aprepitant), Cinvanti (aprepitant injection), or Varubi (rolapitant oral) is being used without a 5HT3 receptor antagonist [e.g., Zofran (ondansetron)/Kytril (granisetron)/Aloxi (palonosetron] and dexamethasone.

C. Dose exceeds the maximum single dose limits for IV Zofran 16 mg, Oral Zofran 24 mg, Granisetron 2 mg IV/PO, Sancuso 3.1 mg patch, Anzemet 100 mg, Aloxi 0.25 mg IV, Aloxi 0.5 mg PO, Akynzeo 300 mg/0.5 mg (oral) or 235 mg/0.25 mg (IV), and Sustol 10 mg.

D. Dosing exceeds the single dose limit of aprepitant oral 125 mg, fosaprepitant injection 150 mg, rolapitant oral 180 mg, or aprepitant injection 130 mg.

E. Investigational use of Antiemetics with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
    1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
    4. Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).

5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Zofran prescribing information. GlaxoSmithKline Research. Triangle Park, NC 2020.

B. Granisetron prescribing information. Roche Laboratories Inc. Nutley, New Jersey 2019.

C. Aloxi prescribing information. Eisai Inc. Woodcliff Lake, NJ 2020.

D. Sancuso prescribing information. Kyowa Kirin, Inc. Bedminister, NJ 2021.

E. Sustol prescribing information. Heron Therapeutics. Redwood City, CA 2017.

F. Akynzeo prescribing information. Helsinn Therapeutics (U.S.), Inc. Iselin, NJ 2021.

G. Cinvanti prescribing information. Heron Therapeutics, Inc., San Diego, CA. 2022.

H. Emend prescribing information. Merck & Co, Inc. Whitehouse Station, NJ. 2022.

I. Rolapitant prescribing information. Tersara Therapeutics, LLC Deerfield, IL 2020.

J. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs Bethesda, MD 2023.

K. Clinical Pharmacology Elsevier Gold Standard 2023.

L. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2023.

M. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.

N. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

O. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.

P. NCQA UM 2023 Standards and Elements.