Antiemetics for Oncology

Policy Number: CS2024D0093K
Effective Date: July 1, 2024

➲ Instructions for Use

Table of Contents **Page**

Commercial Policy

- Antiemetics for Oncology

Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

State	Policy/Guideline
Arizona	None
Florida	None
Indiana	None
Kansas	None
Louisiana	None
Minnesota	None
Nebraska	None
New Mexico	None
North Carolina	None
Ohio	None
Pennsylvania	None
Texas	None
Virginia	None
Washington	None
Wisconsin	None

Coverage Rationale

This policy refers to the following products used as antiemetics for oncology use:

- Akynzeo® (palonosetron/netupitant) capsule
- Akynzeo® (palonosetron/fosnetupitant) injection
- Aloxi® (palonosetron) injection
- Cinvanti™ (aprepitant) injectable emulsion
- Emend® (fosaprepitant) injection, capsule
- Sustol® (granisetron extended release) injection
- Kytril® (granisetron) injection, tablets
- Varubi® (rolapitant) tablet
- Zofran® (ondansetron) injection, tablets

Inclusion of oral antiemetics in this policy and application of the preferred product criteria to them is limited to when these are administered prior to the chemotherapy infusion and not when they are self-administered by the patient outside of the infusion.

Preferred Product(s)	Non-Preferred Product(s)
Neurokinin 1 Receptor Antagonist (NK1 RA)	
Emend injection	Cinvanti injectable emulsion
Emend capsules	Varubi tablets
5-Hydroxytryptamine Receptor Antagonist (5HT3 RA)	
Kytril injection	Sustol injection
Kytril tablets	
Zofran injection	
Zofran tablets	
Aloxi injection	
NK1 RA/5HT3 RA Combination	
	Akynzeo injection
	Akynzeo capsule

Coverage for antiemetics will be provided contingent on the coverage criteria in the Diagnosis-Specific Criteria section.

Preferred Product Criteria

Treatment with non-preferred NK1 RA, 5HT3 RA, or NK1 RA/5HT3 RA combination product is medically necessary for the indications specified in the policy when one of the following is met:

- **Both** of the following:
  - History of a trial of adequate dose and duration to one of the preferred NK1 RA or 5HT3 RA products, resulting in minimal clinical response; **and**
  - Physician attests that, in their clinical opinion, the clinical response would be expected to be superior with non-preferred NK1 RA, 5HT3 RA, or NK1 RA/5HT3 RA combination product than experienced with preferred NK1 RA or 5HT3 RA product

  or
- **Both** of the following:
  - History of intolerance, contraindication, or adverse event to one of the preferred NK1 RA or 5HT3 RA products; **and**
  - Physician attests that, in their clinical opinion, the same intolerance, contraindication, or adverse event would not be expected to occur with non-preferred NK1 RA, 5HT3 RA, or NK1 RA/5HT3 RA combination products

Diagnosis-Specific Criteria

For the coverage criteria below, in absence of specified drug products, the term “antiemetics” will be used in this policy where the coverage criteria apply to all products listed above.

Antiemetics are proven and medically necessary for the following indications:

- NK1 RA **(Emend, Cinvanti, Varubi) may be indicated when one of following are present**:
  - **Both** of the following:
    - Prevention of chemotherapy-induced nausea and vomiting due to **High Emetic Risk** parenteral anticancer agents[10]; **and**
    - In combination with a 5HT3 RA

    or
  - **All** of the following:
    - Prevention of chemotherapy-induced nausea and vomiting due to **Moderate Emetic Risk** parenteral anticancer agents; **and**
    - In combination with a 5HT3 RA; **and**
    - **One** of the risk factors for anticancer agent-induced nausea/vomiting:
      - Younger age (< 55 years); **or**
      - Female sex; **or**

- Previous history of chemotherapy-induced nausea or vomiting; **or**
- Little or no previous alcohol use; **or**
- History of motion sickness or morning sickness during pregnancy; **or**
- High anxiety

- **5HT3 RA (Aloxi, Kytril, Sustol, Zofran) may be indicated when one of the following are present**:
  - **Both** of the following:
    - Prevention of chemotherapy-induced nausea and vomiting due to **High Emetic Risk** parenteral anticancer agents[12]; **and**
    - In combination with a NK1 RA

    or
  - Prevention of chemotherapy-induced nausea and vomiting due to **Moderate Emetic Risk** parenteral anticancer agents[11]; **or**
  - **All** of the following:
    - Prevention of chemotherapy-induced nausea and vomiting due to **Moderate Emetic Risk** parenteral anticancer agents[11]; **and**
    - In combination with a NK1 RA; **and**
    - **One** of the risk factors for anticancer agent-induced nausea/vomiting:
      - Younger age (< 55 years); **or**
      - Female sex; **or**
      - Previous history of chemotherapy-induced nausea or vomiting; **or**
      - Little or no previous alcohol use; **or**
      - History of motion sickness or morning sickness during pregnancy; **or**
      - High anxiety

      or
    - Treatment of breakthrough nausea and/or vomiting due to anticancer agent(s)

- **NK1 RA/5HT3 RA combination product (Akynzeo) may be indicated when one of the following are present**:
  - **All** of the following:
    - Prevention of chemotherapy-induced nausea and vomiting due to **Moderate Emetic Risk** parenteral anticancer agents[11]; **and**
    - **One** of the risk factors for anticancer agent-induced nausea/vomiting:
      - Younger age (< 55 years); **or**
      - Female sex; **or**
      - Previous history of chemotherapy-induced nausea or vomiting; **or**
      - Little or no previous alcohol use; **or**
      - History of motion sickness or morning sickness during pregnancy; **or**
      - High anxiety

    or
  - Prevention of chemotherapy-induced nausea and vomiting due to **High Emetic Risk** parenteral anticancer agents[12]

Definitions

Acute Emesis: Nausea and/or vomiting that occurs within a few minutes to several hours after administration of certain anticancer agents and commonly resolves with the first 24 hours.

Delayed Emesis: Nausea and/or vomiting that occurs more than 24 hours after anticancer agents.

High Emetic Risk: More than 90% of patients experience Acute Emesis.

Low Emetic Risk: 10-30% of patients experience Acute Emesis.

Minimal Emetic Risk: Fewer than 10% of patients experience Acute Emesis.

Moderate Emetic Risk: More than 30% to 90% of patients experience Acute Emesis.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0185	Injection, aprepitant, 1 mg
J1434	Injection, fosaprepitant (Focinvez), 1 mg
J1453	Injection, fosaprepitant, 1 mg
J1454	Injection, fosnetupitant 235 mg and palonosetron 0.25 mg
J1456	Injection, fosaprepitant (teva)
J1626	Injection, granisetron hydrochloride, 100 mcg
J1627	Injection, granisetron, extended release, 0.1 mg
J2405	Injection, ondansetron hydrochloride, per 1 mg
J2469	Injection, palonosetron HCl, 25 mcg
J8501	Aprepitant, oral, 5 mg
J8655	Netupitant 300 mg and palonosetron 0.5 mg, oral
J8670	Rolapitant, oral, 1 mg
Q0162	Ondansetron 1 mg, oral, FDA approved prescription anti-emetic, for use as a complete therapeutic substitute for an IV anti-emetic at the time of chemotherapy treatment, not to exceed a 48-hour dosage regimen
Q0166	Granisetron hydrochloride, 1 mg oral, FDA-approved prescription anti-emetic, for use as a complete therapeutic substitute for an IV anti-emetic at the time of chemotherapy treatment, not to exceed a 24-hour dosage regimen

Diagnosis Code	Description
R11.0	Nausea
R11.10	Vomiting, unspecified
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
Z51.11	Encounter for antineoplastic chemotherapy

Background

Anticancer related-emesis can significantly affect patient's quality of life and lead to poor compliance of therapy.[1,2] The incidence and severity of nausea and/or vomiting in patients receiving anticancer agents and/or radiation therapy (RT) can be affected by many factors, including: 1) the specific therapeutic agents used; 2) dosage of the agents; 3) schedule and the route of administration of the agents; 4) target of the RT (e.g., whole body, upper abdomen); 5) individual patient variability (e.g., younger age, female sex, prior anticancer agents, history of alcohol use, morning sickness, motion sickness, anxiety).[3,4]

Neurokinin 1 Receptor Antagonist (NK1 RA)

Aprepitant is a highly selective antagonist of neurokinin 1 (NK1) receptors.[6,8,9] By blocking the activity of substance P at neurokinin 1 receptors, aprepitant is thought to prevent the onset of nausea and vomiting. Fosaprepitant is a prodrug of aprepitant that is rapidly converted to aprepitant.[5,6,7,8]

5-Hydroxytryptamine Receptor Antagonist (5HT3 RA)

Palonosetron, granisetron, and ondansetron are 5-hydroxytryptamine (5HT3) receptor antagonist. By blocking the activity of serotonin at 5HT3 receptors in the central nervous system and gastrointestinal tract, these agents are thought to prevent the onset of nausea and vomiting.[14,15,16,17,18,19,20]

NK1 RA and 5HT3 RA Combination

Akynzeo is a combination product of a 5HT3 receptor antagonist (palonosetron) and an NK1 receptor antagonist (netupitant or fosnetupitant).[21,22,23]

Clinical Evidence

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN) publishes clinical practice guidelines for Oncology (NCCN Guidelines®) specific to antiemesis related to cancer treatments.[25] National Comprehensive Cancer Network (NCCN) provides recommendations for antiemetic therapy regimens based on the emetogenic risk of the chemotherapy and if it is intravenous or oral. The emetogenic risk of intravenous anticancer agents is based on the frequency of emesis.

High emetic risk agents have a greater than 90% frequency of emesis. Moderate emetic risk has a 30-90% frequency of emesis while low emetic risk has 10-30% frequency of emesis, and minimal emetic risk have less than 10% frequency of emesis. For oral antineoplastic agents, the levels are divided into those with moderate to high emetic risk (greater than or equal to 30% frequency of emesis) and minimal to low emetic risk (less than 30% frequency of emesis). (NCCN, 2020).

For high emetic risk parenteral (IV) anticancer agents, NCCN recommends several options as category 1 for acute and delayed emesis prevention. Regimens recommended include either aprepitant oral or IV, fosaprepitant IV, or rolapitant oral in combination with a 5-HT3 receptor antagonist [palonosetron IV; granisetron subcutaneous (SQ), oral, IV or transdermal; or ondansetron oral or IV] with dexamethasone oral or IV. Other options include netupitant/palonosetron oral or fosnetupitant/palonosetron IV in combination with dexamethasone; olanzapine oral with palonosetron IV and dexamethasone oral or IV; or aprepitant oral or IV, fosaprepitant IV, or rolapitant oral in combination with a 5-HT3 receptor antagonist, dexamethasone oral or IV, and olanzapine. (NCCN, 2023). For moderate emetic risk parenteral anti-cancer agents, several options are recommended without preference for acute and delayed emesis prevention. One option recommends a 5-HT3 receptor antagonist in combination with dexamethasone oral or IV. NCCN notes a preference for palonosetron IV or granisetron extended-release injection when an NK1 antagonist is not used in combination with 5-HT3 antagonist. Other options include use of aprepitant oral or IV, fosaprepitant IV, rolapitant oral in combination with a 5-HT3 receptor antagonist and dexamethasone oral or IV; netupitant/palonosetron oral or fosnetupitant/palonosetron IV in combination with dexamethasone; or olanzapine oral with palonosetron IV and dexamethasone oral or IV (NCCN, 2023). For low emetic risk parenteral anticancer agents, NCCN recommends dexamethasone oral or IV; metoclopramide oral or IV; prochlorperazine oral or IV; or an oral 5-HT3 receptor antagonist. Routine prophylaxis is not recommended for minimal emetic risk parenteral anticancer agents (NCCN, 2023). For high to moderate emetic risk with oral anticancer agents, NCCN recommends a 5-HT3 receptor antagonist (dolasetron oral, granisetron oral or transdermal, or ondansetron oral). For low to minimal risk with oral anticancer agents, as needed treatment is recommended initially with recommendations to use either metoclopramide oral as needed, prochlorperazine oral as needed, or an oral 5-HT3 antagonist as needed provided when nausea/vomiting is experienced (NCCN, 2023). If breakthrough chemotherapy-induced nausea and vomiting occurs, recommendations for subsequent chemotherapy cycles include changing the antiemetic regimen to a higher level for primary treatment (NCCN, 2023).

NCCN listed high emetic risk regimens (> 90% frequency of emesis):

- AC combination defined as any chemotherapy regimen that contains anthracycline and cyclophosphamide
- Carboplatin AUC ≥ 4
- Carmustine > 250 mg/m^2
- Cisplatin
- Cyclophosphamide > 1,500 mg/m^2
- Dacarbazine
- Doxorubicin ≥ 60 mg/m^2
- Epirubicin > 90 mg/m^2
- Fam-trastuzumab deruxtecan-nxki
- Ifosfamide ≥ 2 g/m^2 per dose
- Mechlorethamine
- Melphalan ≥ 140 mg/m^2

- Streptozocin
- Sacituzumab govitecan-hziy

NCCN listed moderate emetic risk regimens (> 30-90% frequency of emesis):
- Aldesleukin > 12-15 million IU/m^2
- Amifostine > 300 mg/m^2
- Bendamustine
- Busulfan
- Carboplatin AUC < 4
- Carmustine ≤ 250 mg/m^2
- Clofarabine
- Cyclophosphamide ≤ 1,500 mg/m^2
- Cytarabine > 200 mg/m^2
- Dactinomycin
- Daunorubicin
- Dual-drug liposomal encapsulation of cytarabine and daunorubicin
- Dinutuximab
- Doxorubicin < 60 mg/m^2
- Epirubicin ≤ 90 mg/m^2
- Idarubicin
- Ifosfamide < 2 g/m^2 per dose
- Irinotecan
- Irinotecan (liposomal)
- Lurbinectedin
- Melphalan < 140 mg/m^2
- Methotrexate ≥ 250 mg/m^2
- Naxitamab-gqgk
- Oxaliplatin
- Romidepsin
- Temozolomide
- Trabectedin

American Society of Clinical Oncology (ASCO)[28]

The ASCO has published guidelines for antiemetics in oncology after conducting a systematic review by an expert panel of forty-one publications (35 randomized control trials and 6 meta-analysis). The guideline addresses the prevention and management and nausea and vomiting due to antineoplastic agents and/or radiation therapy in patients with cancer.

For high emetic risk antineoplastic agents, ASCO guidelines recommend four-drug combination (an NK1 receptor antagonist, a 5-HT3 receptor antagonist, dexamethasone, and olanzapine) with dexamethasone and olanzapine to be continued on days 2-4; high quality of evidence and strong strength of recommendations. In addition, patients who are treated with anthracycline and cyclophosphamide combination should be offered four-drug antiemetic combination (an NK1 receptor antagonist, a 5-HT3 receptor antagonist, dexamethasone, and olanzapine) with olanzapine continued on days 2-4; high quality of evidence and strong strength of recommendations.

For moderate emetic risk antineoplastic agents, especially those treated with carboplatin area under the curve (AUC) ≥ 4 mg/ml per minute, ASCO guidelines recommend a 3-drug combination (an NK1 receptor antagonist, a 5-HT3 receptor antagonist, and dexamethasone). Those treated with moderate emetic risk antineoplastic agents excluding carboplatin AUC ≥ 4 mg/ml per minute, ASCO guidelines recommend 2-drug combination (a 5-HT3 receptor antagonist and dexamethasone); high quality of evidence and strong strength of recommendations.

For low emetic risk antineoplastic agents, ASCO guidelines recommend single agents (a 5-HT3 receptor antagonist or dexamethasone); low quality of evidence and moderate strength of recommendations. For minimal emetic risk antineoplastic agents, ASCO guidelines recommend no routine antiemetic prophylaxis; low quality of evidence and moderate strength of recommendation.

For breakthrough nausea and vomiting, ASCO guidelines recommend evaluating emetic risk, disease status, concurrent illnesses, and medications, and ascertain that the best regimen is being administered for the emetic risk. Those who experience nausea or vomiting despite optimal prophylaxis, and who did not receive olanzapine prophylactically, should

be offered olanzapine in addition to continuing the standard antiemetic regimen; intermediate quality of evidence and moderate strength of recommendation. Additionally, those who experience nausea or vomiting despite optimal prophylaxis, and who have already received olanzapine, may be offered a drug of a different class – for example, an NK1 receptor antagonist, lorazepam or alprazolam, a dopamine receptor antagonist, dronabinol, or nabilone – in addition to continuing the standard antiemetic regimen; intermediate quality of evidence for dronabinol and nabilone and low otherwise and moderate strength of recommendation. (ASCO, 2017).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Akynzeo® (palonosetron/netupitant) capsule is a combination of selective 5-HT3 receptor antagonist and substance P/neurokinin-1 (NK 1) receptor antagonist indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

Akynzeo® (palonosetron/fosnetupitant) injection is a combination of selective 5-HT3 receptor antagonist and substance P/neurokinin-1 (NK 1) receptor antagonist 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. Akynzeo injection has not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

Cinvanti® (aprepitant) emulsion is a substance P/neurokinin-1 (NK 1) receptor antagonist, indicated in adults, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high dose cisplatin and nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). CINVANTI has not been studied for treatment of established nausea and vomiting.

EMEND® (fosaprepitant) injection is a substance P/neurokinin-1 (NK1) receptor antagonist, indicated in adults and pediatric patients 6 months of age and older, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). EMEND has not been studied for treatment of established nausea and vomiting.

Emend® (aprepitant) capsules is a substance P/neurokinin-1 (NK1) receptor antagonist, indicated in combination with other antiemetic agents, in patients 12 years of age and older for prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Focinvez (fosaprepitant injection) is a substance P/neurokinin-1 (NK1) receptor antagonist, indicated in adults and pediatric patients 6 months of age and older, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). Focinvez has not been studied for treatment of established nausea and vomiting.

Varubi® (rolapitant) tablet is a substance P/neurokinin-1 (NK1) receptor antagonist indicated in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

Aloxi® (palonosetron) injection is a serotonin subtype 3 (5-HT3) receptor antagonist 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, and prevention of postoperative nausea and vomiting (PONV) for up to 24 hours following surgery. Efficacy beyond 24 hours has not been demonstrated. Aloxi is also 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.

Aloxi® (palonosetron) capsule is a serotonin subtype 3 (5-HT3) receptor antagonist, indicated for moderately emetogenic cancer chemotherapy – prevention of acute nausea and vomiting associated with initial and repeat courses.

Sustol® (granisetron extended release) injection is a serotonin-3 (5-HT3) receptor antagonist indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.

Kytril® (granisetron) injection is a serotonin-3 (5-HT3) receptor antagonist indicated for the prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin and for the prevention and treatment of postoperative nausea and vomiting in adults.

Zofran® (ondansetron) oral solution, tablets, and orally disintegrating tablets are 5-HT3 receptor antagonists indicated for the prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including cisplatin greater than or equal to 50 mg/m^2, nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy, nausea and vomiting associated with radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen, or postoperative nausea and/or vomiting.

Zofran® (ondansetron) injection is a 5-HT3 receptor antagonist indicated for prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy and prevention of postoperative nausea and/or vomiting.

References

1. Navari RM, Aapro M. Antiemetic Prophylaxis for Chemotherapy-Induced Nausea and Vomiting. N Engl J Med. 2016;374(14):1356-1367. doi:10.1056/NEJMra1515442.
2. McDonagh M, Peterson K, Thakurta S. Consideration of Evidence on Antiemetic Drugs for Nausea and Vomiting Associated with Chemotherapy or Radiation Therapy in Adults. Rockville (MD): Agency for Healthcare Research and Quality (US); 2010.
3. Herrstedt J. Antiemetics: an update and the MASCC guidelines applied in clinical practice. Nat Clin Pract Oncol. 2008;5(1):32-43. doi:10.1038/ncponc1021.
4. Hesketh PJ, Grunberg SM, Herrstedt J, et al. Combined data from two phase III trials of the NK1 antagonist aprepitant plus a 5HT 3 antagonist and a corticosteroid for prevention of chemotherapy-induced nausea and vomiting: effect of gender on treatment response. Support Care Cancer. 2006;14(4):354-360. doi:10.1007/s00520-005-0914-4.
5. Emend (fosaprepitant) for injection. Physician Prescribing Information [Internet] Merck Sharp & Dohme Corp. May 2022 Accessed at: https://www.merck.com/product/oncology/home.html. Created 2008; Accessed April 10, 2023.
6. Rapoport B, Smit T. Clinical pharmacology of neurokinin-1 receptor antagonists for the treatment of nausea and vomiting associated with chemotherapy. Expert Opinion on Drug Safety 2017;16(6):697-710. DOI: 10.1080/14740338.2017.1325868.
7. Candelario N, Lu ML. Fosaprepitant dimeglumine for the management of chemotherapy-induced nausea and vomiting: patient selection and perspectives. Cancer Management and Research 2016;8:77-82. DOI: 10.2147/CMAR.S93620.
8. Garnock-Jones KP. Fosaprepitant dimeglumine: a review in the prevention of nausea and vomiting associated with chemotherapy. Drugs 2016;76(14):1365-72. DOI: 10.1007/s40265-016-0627-7.
9. Emend (aprepitant) capsules. Physician Prescribing Information [Internet] Merck Sharp & Dohme Corp. November 2022; Accessed at: https://www.merck.com/product/oncology/home.html. Accessed April 11, 2023.
10. Aapro M, Carides A, Rapoport BL, Schmoll HJ, Zhang L, Warr D. Aprepitant and fosaprepitant: a 10-year review of efficacy and safety. Oncologist 2015;20(4):450-8. DOI: 10.1634/theoncologist.2014-0229.
11. Jordan K, Jahn F, Aapro M. Recent developments in the prevention of chemotherapy-induced nausea and vomiting (CINV): a comprehensive review. Annals of Oncology 2015;26(6):1081-1090. DOI: 10.1093/annonc/mdv138.
12. Inui N. Antiemetic therapy for non-anthracycline and cyclophosphamide moderately emetogenic chemotherapy. Medical Oncology 2017;34(5):77. DOI: 10.1007/s12032-017-0937-y.

13. Isoda A, et al. Palonosetron, aprepitant, and dexamethasone for prevention of nausea and vomiting after high dose melphalan in autologous transplantation for multiple myeloma: A phase II study. International Journal of Hematology 2017;105(4):478-84. DOI: 10.1007/s12185-016-2152-6.
14. Aloxi (palonosetron HCl) injection. Physician Prescribing Information [Internet] Helsinn, April 2020. Accessed April 11, 2023. Accessed April 11, 2023.
15. Navari RM. 5-HT3 receptors as important mediators of nausea and vomiting due to chemotherapy. Biochimica et Biophysica Acta 2015;1848(10 Pt B):2738-46. DOI: 10.1016/j.bbamem.2015.03.020.
16. Zhou M, et al. Update on the management of chemotherapy-induced nausea and vomiting - focus on palonosetron. Therapeutics and Clinical Risk Management 2015;11:713-29. DOI: 10.2147/TCRM.S68130.
17. Zofran (ondansetron) injection [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; March 2017 Accessed April 11, 2023.
18. Zofran (ondansetron) tablets [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2017. Accessed April 11, 2023.
19. Granisetron injection [prescribing information]. Lake Zurich, IL: Fresenius Kabl; November 2022. Accessed April 11, 2023.
20. Granisetron tablet [prescribing information]. Berlin, CT: Breckenridge Pharmaceuticals; May 2022. Accessed April 11, 2023.
21. Akynzeo (netupitant/palonosetron) [prescribing information]. Iselin, NJ: Helsinn Therapeutics (U.S.) Inc.; June 2021. Accessed April 11, 2023.
22. Akynzeo (fosnetupitant and palonosetron) [prescribing information]. Iselin, NJ: Helsinn Therapeutics (US), Inc; June 2021. Accessed April 11, 2023.
23. Aapro M, Rugo H, Rossi G, et al. A randomized phase III study evaluating the efficacy and safety of NEPA, a fixed-dose combination of netupitant and palonosetron, for prevention of chemotherapy-induced nausea and vomiting following moderately emetogenic chemotherapy. Ann Oncol. 2014;25(7):1328-1333. doi:10.1093/annonc/mdu101.
24. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Antiemesis. v.1.2023. Accessed May 2, 2024.
25. Hesketh PJ, Kris MG, Basch E, et al: Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 38:2782-2792, 2020.
26. Focinvez (fosaprepitant injection) [prescribing information]. North Brunswick, NJ: Spes Pharmaceuticals Inc.; August 2023.

Policy History/Revision Information

Date	Summary of Changes
07/01/2024	**Application** ***Ohio*** • Removed reference link to state-specific policy version **Applicable Codes** • Added HCPCS code J1434 **Supporting Information** • Updated *FDA* and *References* sections to reflect the most current information • Archived previous policy version CS2024D0093J

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.