WellMed Doctors helping patients for more than 25 years	**Effective Date:** 01/03/2023	**Revision Date(s):** 12/11/15, 8/24/16, 02/22/18, 11/20/19, 5/14/19, 7/8/19, 9/11/2019, 12/10/2020, 12/16/21, 12/15/2022
Department: PHARMACY	**MMC Review/ Approval Date(s):** 1/14/2020, 1/13/2021, 01/18/2022, 12/28/2022	**Page(s):** 18

Policy Number: 035.010
Title: Coverage Determination Policy for Antiemetics: Palonosetron (Aloxi), Fosnetupitant/Palonosetron (Akynzeo),Granisetron (Sustol) ,Aprepitant (Cinvanti),Fosaprepitant (Emend)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

Disclaimer:
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Title: Coverage Determination Policy for Antiemetics: Palonosetron (Aloxi), Fosnetupitant/Palonosetron (Akynzeo), Granisetron (Sustol), Aprepitant (Cinvanti), Fosaprepitant (Emend)

Coverage Policy Number: 035.010

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Step Therapy Criteria

Preferred drugs: **Aloxi** (Palonosetron)**, Emend** (Aprepitant)**, Granisetron HCl, Ondansetron**

Non-preferred drugs: Akynzeo, Cinvanti, Sustol

Non-Preferred Drug Step Therapy Criteria

Akynzeo, Cinvanti, or Sustol, may be covered when one of the criteria listed under Sections A, B, or C are satisfied:

A. History of use of Aloxi, Emend, Granisetron, or Ondansetron resulting in minimal clinical response to therapy **or**
B. History of intolerance or adverse event to Aloxi, Emend, Granisetron HCl, or Ondansetron **or**
C. Continuation of prior therapy within the past 365 days

Coverage Determination:

Coverage Determination (Initial/New Requests)

1. WellMed Medical Management will cover **palonosetron (Aloxi)** as medically necessary for all of the following indications:
   a. chemotherapy induced nausea and vomiting (CINV) in adults receiving a moderately or highly emetogenic chemotherapy agent(s) (see tables below)
   b. prevention of postoperative nausea and vomiting for up to 24 hours following surgery.

2. WellMed Medical Management will cover **fosaprepitant (Emend) in combination with other antiemetics** as medically necessary the following indication:
   a. chemotherapy induced nausea and vomiting (CINV) in adults receiving a moderately or highly emetogenic chemotherapy agent(s) (see tables below)

3. WellMed Medical Management will cover **granisetron XR (Sustol)** in combination with other antiemetics as medically necessary for all of the following indications:
   a. chemotherapy induced nausea and vomiting (CINV) in adults receiving a moderately or highly emetogenic chemotherapy agent(s) OR anthracycline and cyclophosphamide combination chemotherapy regimens (see tables below)

4. WellMed Medical Management will cover **aprepitant (Cinvanti),** in combination with a 5-HT3 antagonist and a corticosteroid, as medically necessary for the following indication:
   a. chemotherapy induced nausea and vomiting (CINV) in adults receiving a moderately or highly emetogenic chemotherapy agent(s) (see tables below)

5. Wellmed Medical Management will cover **fosnetupitant/palonosetron (Akynzeo)** in combination with dexamethasone as medically necessary for the following indication:

a. chemotherapy induced nausea and vomiting (CINV) in adults receiving a moderately or highly emetogenic chemotherapy agent(s) (see tables below).

Per NCCN, for moderate emetic risk parenteral chemotherapy, an NK1 RA should be added (to dexamethasone and a 5-HT3 RA regimen) for select patients with one or more risk factors, or previous treatment failure with a corticosteroid + 5-HT3 RA alone.

Patient risk factors for anticancer agent-induced nausea/vomiting include: (reference NCCN, 22)

- Younger age (<60 years)
- Female sex
- Previous history of CINV
- Little or no previous alcohol use
- Prone to motion sickness
- History of morning sickness during pregnancy
- Anxiety/high pretreatment expectation of nausea

Chemotherapy regimens with High Emetogenic Risk (> 90% frequency of emesis)[12]

Carboplatin AUC ≥4	Epirubicin > 90 mg/m^2
Carmustine ≥ 250 mg/m^2	Ifosfamide ≥ 2 g/m^2 per dose
Cisplatin	Mechlorethamine
Cyclophosphamide > 1,500 mg/m^2	Melphalan ≥ 140 mg/m2
Dacarbazine	Sacituzumab govitecan-hziy
Doxorubicin ≥ 60 mg/m^2	Streptozocin
Doxorubicin or Epirubicin with cyclophosphamide	

Chemotherapy regimens with Moderate Emetogenic Risk (> 30% - 90% frequency of emesis)[12]

Aldesleukin > 12-15 million IU/m^2	Epirubicin[a] ≤ 90 mg/m^2
Amifostine > 300 mg/m^2	Amivantamab-vmjw
Azacitidine	Fam-trastuzumab deruxtecan-nxki
Bendamustine	Idarubicin[a]
Busulfan	Ifosfamide[a] < 2 g/m^2 per dose
Carboplatin AUC[a] <4	Irinotecan (liposomal)
Carmustine[a] ≤ 250 mg/m^2	Irinotecan[a]
Clofarabine	Lurbinectedin
Cyclophosphamide[a] ≤ 1500 mg/m^2	Melphalan < 140 mg/m2
Cytarabine > 200 mg/m^2	Methotrexate[a] ≥ 250 mg/m^2
Dactinomycin[a]	Naxitamab-gqgk
Danuorubicin[a]	Oxaliplatin[a]
DAUNOrubicin and Cytarabine, Liposome	Romidepsin
Dinutuximab	Temozolomide
Doxorubicin[a] < 60 mg/m^2	Trabectedin[a]
Dual-drug liposomal encapsulation of cytarabine and daunorubicin	

[a] These agents may be highly emetogenic in certain patients

WellMed Medical Management **will NOT cover** palonosetron (**Aloxi**), fosnetupitant/palonosetron (**Akynzeo**), fosaprepitant (**Emend**), or aprepitant (**Cinvanti**) for any indication not approved by FDA or not recommended by NCCN such as any of the following conditions:

1. Chemotherapy induced nausea and vomiting in patients receiving chemotherapy agent with minimal to low (10-30%) emetogenic risk
2. Breakthrough emesis
3. Repeat dosing in multi-day emetogenic chemotherapy regimens
4. Pregnancy-related nausea and vomiting
5. Motion Sickness
6. Radiation-induced nausea and vomiting

Coverage Determination (Renewal/Continuation of Therapy Requests)

For RENEWAL of antiemetics

1. Patients must meet the same criteria for initiation, and dosing must be consistent with FDA approved labeling

FDA Approved Dose and Indication:

Product	Indication	Dosing*
Aloxi®	For prevention of Acute chemotherapy-induced nausea and vomiting associated with highly emetogenic chemotherapy	• 0.25 mg IV over 30 seconds approximately 30 minutes prior to the start of chemotherapy
	For prevention of Acute or Delayed chemotherapy-induced nausea and vomiting, associated with moderately emetogenic chemotherapy	• 0.25 mg IV over 30 seconds approximately 30 minutes prior to the start of chemotherapy
	For prevention of Postoperative nausea and vomiting	• 0.075 mg IV as a single dose immediately before induction of anesthesia
	NOTE: When prior authorization request is approved for palonosetron (Aloxi), one injection (0.25 mg) may be authorized per chemotherapy cycle, not to exceed one injection per 7 days[3] * *No dosage adjustment is required in renal impairment, geriatric patients or hepatic impairment*	
Emend®	For acute and delayed chemotherapy induced nausea and vomiting (CINV) in adults receiving initial or repeat courses of highly emetogenic chemotherapy agent(s)	• 150mg IV over 20-30 minutes approximately 30 minutes prior to chemotherapy given with 12 mg PO dexamethasone and 5-HT3 antagonist
	For delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy(MEC)	
	**No dosage adjustment is required in mild to moderate hepatic impairment (Child Pugh score 5=9). There are no clinical or pharmacokinetic data in patients with severe hepatic impairment (Child-Pugh score greater than 9). No dosage adjustment is required in Renal impairment or hemodialysis. No dose adjustment is required in Geriatric or Obese patients.*	
Sustol®	For the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and	• 10 mg administered as a single subcutaneous injection at least 30 minutes before the start of emetogenic chemotherapy on Day 1.

	cyclophosphamide (AC) combination chemotherapy regimens	
	** In patients with moderate renal impairment (CrCl 30-59ml/min) administer Sustol no more frequently than every 14 days. Avoid Sustol in patients with severe renal impairment (CrCl <30ml/min).*	
Cinvanti®	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.	• 130 mg IV over 2 minutes or infused over 30 minutes approximately 30 minutes before chemotherapy on day 1
	For the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).	
	** No dosage adjustment is necessary for patients with mild to moderate hepatic impairment (Child-Pugh score 5 to 9). There are no clinical or pharmacokinetic data in patients with severe hepatic impairment (Child-Pugh score greater than 9). Renal impairment, including ESRD requiring dialysis: No adjustment necessary*	
Akynzeo®	For the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC). Per NCCN, Akynzeo can be used for prevention of acute and delayed nausea and vomiting associated with moderate emetic risk parenteral chemotherapy.	• The recommended dose is 235mg/0.25mg administered 30 minutes before the start of chemotherapy directly into the vein (IV infusion). It takes about 30 minutes to receive the full dose.
	**No dosage adjustment for AKYNZEO is necessary in patients with mild to moderate renal impairment (CrCl 30 to 60 mL/min). Avoid use in severe renal impairment or ESRD. Avoid use in patients with severe hepatic impairment (Child-Pugh score greater than 9)*	

General Background:

Nausea and vomiting remain two of the most problematic symptoms experienced by patients with cancer who are receiving chemotherapy. Inadequately controlled nausea and vomiting can often limit the ability to deliver chemotherapy, as well as impair a patient's functional status and quality of life. The severity and incidence of nausea and vomiting in patients receiving chemotherapy can be influenced by several factors to include the specific type of chemotherapy agents being used, dosage of the chemotherapy agents, individual patient variability (i.e. age, sex, prior exposure to chemotherapy, and history of alcohol use) and the schedule and route of administration of the agents12.

Chemotherapy-induced nausea and vomiting (CINV) can occur within a few hours of treatment and may persist for several days. The three phases of CINV include:
- Acute emesis which usually occurs within the first 24 hours after receiving chemotherapy
- Delayed emesis usually occurs after 24 hours of receiving treatment and can persist for up to 7 days
- Anticipatory emesis usually occurs prior to the administration of chemotherapy in patients with poorly controlled emesis from previous cycles of chemotherapy.

More than 90% of patients receiving highly emetogenic chemotherapy will experience episodes of vomiting. However, only 30% of these patients will vomit if adequate prophylactic antiemetic regimen is given prior to receiving highly emetogenic chemotherapy 11. Thus, it is imperative that patients receive adequate prophylactic antiemetics to prevent chemotherapy-induced nausea and vomiting (CINV).

Post-operative nausea and vomiting (PONV) continues to be a common complication of surgery and if not controlled, can be a limiting factor for early discharge of ambulatory surgical patients. PONV can lead to an increase in total health care cost through increased recovery room time, expanded nursing care and unanticipated hospitalizations. The general incidence of vomiting is about 30% while the incidence of nausea is estimated to be 50% and can be as high as 80% in high risk patients 7. Prophylaxis with antiemetics can help decrease the incidence of PONV, thereby alleviating patient-related stress and ultimately reduce total health care cost7. However, routine prophylaxis is not recommended when there is little expectation that nausea and vomiting will occur postoperatively.

Serotonin (5-HT3) receptor antagonists have been widely studied in the management of CINV and PONV. There are currently three first-generation 5-HT3 receptor antagonists ondansetron (Zofran®), dolasetron (Anzemet®), granisetron (Kytril®), granisetron XR (Sustol®) and one second-generation agent Palonosetron (Aloxi®) commercially available in the United States.

All of these agents have been shown to be effective in controlling nausea and vomiting associated with cancer chemotherapy or surgery. Although 5-HT3 receptor antagonists are the current standard of care for the prevention of CINV, not all patients achieve adequate control of nausea and vomiting, and more than 50% of patients continue experience emesis after administration of highly emetogenic chemotherapy 10.

Palonosetron (Aloxi) differs from the first-generation 5-HT3 receptor antagonists (granisetron, dolasetron and ondansetron) in that it has a longer elimination half-life of 40 hours, which is 4-5 times more than the half-life of the first-generation 5-HT3 antagonists. It has a 30- to 100-fold higher binding affinity for the 5-HT3 receptor. Due to its potency and higher binding affinity, palonosetron triggers receptor internalization and exhibits prolonged inhibition of receptor function10. All 5-HT3 receptor antagonists have been shown to be effective in controlling post-operative nausea and vomiting and are FDA approved for prevention of PONV.

Cinvanti® is a substance P/neurokinin-1 (NK1) 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).

Emend® 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. It is also indicated for delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). Both of these agents have not been studied for treatment of established nausea and vomiting.

Concurrent use of Substance P/neurokinin-1(NK1) receptor antagonists and pimozide is contraindicated. Use of Cinvanti® and Emend® is contraindicated if a patient has any known hypersensitivity to any component of the drug.

Akynzeo® is a combination of palonosetron, a serotonin-3 (5-HT3) receptor antagonist, and netupitant or fosnetupitant, substance P/neurokinin-1 (NK-1) receptor antagonists: palonosetron prevents nausea and vomiting during the acute phase and netupitant/fosnetupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Medicare does not have a National Coverage Determination (NCD) for Aloxi(palonosetron), Emend® (fosaprepitant), Sustol (granisetron). A National Coverage Determination for Aprepitant for Chemotherapy-Induced Emesis is current; refer to the NCD for oral Aprepitant. Local Coverage Determinations (LCDs) do not exist at this time for Aloxi (palonosetron), Emend (fosaprepitant), Sustol (granisetron) and Cinvanti (aprepitant) for Colorado, Texas and Florida.

NCCN Antiemesis Guidelines:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Antiemesis

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Discussion

HIGH EMETIC RISK PARENTERAL ANTICANCER AGENTS — ACUTE AND DELAYED EMESIS PREVENTION[f,g,h,i,j]

DAY 1: Select treatment option A, B, or C All treatment options are category 1 and should be started before anticancer therapy[h]	DAYS 2, 3, 4:
Treatment option A (preferred), use the following combination[l]: 1. Olanzapine 5–10 mg oral (PO) once[k] 2. NK1 receptor antagonist (RA) (choose one): ◊ Aprepitant 125 mg PO once ◊ Aprepitant injectable emulsion 130 mg intravenous (IV) once[m] ◊ Fosaprepitant 150 mg IV once ◊ Netupitant 300 mg / palonosetron 0.5 mg (available as fixed combination product only) PO once[n] ◊ Fosnetupitant 235 mg / palonosetron 0.25 mg (available as fixed combination product only) IV once[n] ◊ Rolapitant 180 mg PO once[o] 3. 5-HT3 RA (choose one)[p,q]: ◊ Dolasetron 100 mg PO once ◊ Granisetron 10 mg subcutaneous (SQ) once,[r] or 2 mg PO once, or 0.01 mg/kg (max 1 mg) IV once, or 3.1 mg/24-h transdermal patch applied 24–48 h prior to first dose of anticancer therapy ◊ Ondansetron 16–24 mg PO once, or 8–16 mg IV once ◊ Palonosetron 0.25 mg IV once 4. Dexamethasone 12 mg PO/IV once[s,t]	**Treatment option A:** • Olanzapine 5–10 mg PO daily on days 2, 3, 4[k] • Aprepitant 80 mg PO daily on days 2, 3 (if aprepitant PO is used on day 1) • Dexamethasone 8 mg[s,t] PO/IV daily on days 2, 3, 4
Treatment option B, use the following combination: 1. Olanzapine 5–10 mg PO once[k] 2. Palonosetron 0.25 mg IV once 3. Dexamethasone 12 mg PO/IV once[s,t]	**Treatment option B:** • Olanzapine 5–10 mg PO daily on days 2, 3, 4[k]
Treatment option C, use the following combination: 1. NK1 RA (choose one): ◊ Aprepitant 125 mg PO once ◊ Aprepitant injectable emulsion 130 mg IV once[m] ◊ Fosaprepitant 150 mg IV once ◊ Netupitant 300 mg / palonosetron 0.5 mg (available as fixed combination product only) PO once[n] ◊ Fosnetupitant 235 mg / palonosetron 0.25 mg (available as fixed combination product only) IV once[n] ◊ Rolapitant 180 mg PO once[o] 2. 5-HT3 RA (choose one)[p,q]: ◊ Dolasetron 100 mg PO once ◊ Granisetron 10 mg SQ once,[r] or 2 mg PO once, or 0.01 mg/kg (max 1 mg) IV once, or 3.1 mg/24-h transdermal patch applied 24–48 h prior to first dose of anticancer therapy ◊ Ondansetron 16–24 mg PO once, or 8–16 mg IV once ◊ Palonosetron 0.25 mg IV once 3. Dexamethasone 12 mg PO/IV once[s,t]	**Treatment option C:** • Aprepitant 80 mg PO daily on days 2, 3 (if aprepitant PO is used on day 1) • Dexamethasone 8 mg[s,t] PO/IV daily on days 2, 3, 4

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

See Footnotes on AE-5A

AE-4

MODERATE EMETIC RISK PARENTERAL ANTICANCER AGENTS — ACUTE AND DELAYED EMESIS PREVENTION[f,g,h,i,j]

DAY 1: Select treatment option D, E, or F All treatment options are category 1 and should be started before anticancer therapy[h]	DAYS 2, 3:
Treatment option D, use the following combination: 1. 5-HT3 RA (choose one): ◊ Dolasetron 100 mg PO once ◊ Granisetron 10 mg SQ once[r] (preferred), or 2 mg PO once, or 0.01 mg/kg (max 1 mg) IV once, or 3.1 mg/24-h transdermal patch applied 24–48 h prior to first dose of anticancer therapy ◊ Ondansetron 16–24 mg PO once, or 8–16 mg IV once ◊ Palonosetron 0.25 mg IV once (preferred) 2. Dexamethasone 12 mg PO/IV once[s,t]	**Treatment option D:** • Dexamethasone 8 mg[s,t] PO/IV daily on days 2, 3 OR • 5-HT3 RA monotherapy[u]: ◊ Granisetron 1–2 mg (total dose) PO daily or 0.01 mg/kg (max 1 mg) IV daily on days 2, 3 ◊ Ondansetron 8 mg PO twice daily or 16 mg PO daily or 8–16 mg IV daily on days 2, 3 ◊ Dolasetron 100 mg PO daily on days 2, 3
Treatment option E, use the following combination[v]: 1. Olanzapine 5–10 mg PO once[k] 2. Palonosetron 0.25 mg IV once 3. Dexamethasone 12 mg PO/IV once[s,t]	**Treatment option E:** • Olanzapine 5–10 mg PO daily on days 2, 3[k]
Treatment option F, use the following combination[v]: 1. NK1 RA (choose one): ◊ Aprepitant 125 mg PO once ◊ Aprepitant injectable emulsion 130 mg IV once[m] ◊ Fosaprepitant 150 mg IV once[n] ◊ Netupitant 300 mg/palonosetron 0.5 mg (available as fixed combination product only) PO once[n] ◊ Fosnetupitant 235 mg / palonosetron 0.25 mg (available as fixed combination product only) IV once[n] ◊ Rolapitant 180 mg PO once[o] 2. 5-HT3 RA (choose one)[p,q]: ◊ Dolasetron 100 mg PO once ◊ Granisetron 10 mg SQ once,[r] or 2 mg PO once, or 0.01 mg/kg (max 1 mg) IV once, or 3.1 mg/24-h transdermal patch applied 24–48 h prior to first dose of anticancer therapy. ◊ Ondansetron 16–24 mg PO once, or 8–16 mg IV once ◊ Palonosetron 0.25 mg IV once 3. Dexamethasone 12 mg PO/IV once[s,t]	**Treatment option F:** • Aprepitant 80 mg PO daily on days 2, 3 (if aprepitant PO used on day 1) • ± Dexamethasone 8 mg[s,t] PO/IV daily on days 2, 3

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

See Footnotes on AE-5A

Clinical Evidence:

Prevention of Chemotherapy-induced nausea and vomiting (CINV)

Jin Y et. al analyzed the outcomes of nine randomized controlled trials conducted in a total of 3,463 patients comparing palonosetron with the first-generation 5-HT3 receptor antagonists (ondansetron, granisetron and dolasetron) for the prevention of CINV in cancer patients. Patients either received moderately emetogenic chemotherapy or moderately to highly emetogenic chemotherapy or highly emetogenic chemotherapy. Patients received a single dose of 0.25mg or 0.75mg in the palonosetron-treated groups and these were compared with patients treated with ondansetron 32mg, dolasetron 100mg or granisetron 3mg as a control group, with or without IV dexamethasone prior to initiation of chemotherapy. The investigators found a significant reduction in the cumulative incidence of emesis in the palonosetron (0.25mg IV) group on day 1 (RR=1.11, 95% CI: 1.05-1.17), from day 2 to 5 (RR= 1.26, 95% CI: 1.16-1.36) and the overall 5 days (RR= 1.23, 95% CI: 1.13-1.34). Subgroup analysis was conducted to evaluate its efficacy with use of moderately emetogenic chemotherapy versus highly emetogenic chemotherapy. A single dose of palonosetron showed similar efficacy to first-generation 5-HT3 antagonists with regards to the control of acute nausea and vomiting in patients receiving moderately emetogenic chemotherapy (RR= 1.06, 95% CI: 1.00-1.12, P= 0.054). The investigators analysis did not find superior efficacy with regards to control of acute CINV in the single dose palonosetron10.

A multicenter, randomized, double-blind phase III study conducted by Gralla et. al compared the efficacy and tolerability of single, fixed IV doses of palonosetron 0.25mg and 0.75mg with a single IV dose of ondansetron 32mg in the prevention of acute and delayed CINV following administration of moderately emetogenic chemotherapy in 563 patients (palonesetron 0.25mg (n) = 189; palonesetron 0.75mg (n)=n 189; Ondansetron 32mg (n) = 185) . The investigators found palonosetron 0.25mg (81%) to have a statistically significant superiority over ondansetron 32mg (69%) for the prevention of acute emesis (97.5% CI 1.8 – 22.8, p-value = 0.009). Also, for the delayed (24-120 hrs) and overall (0-120hrs) time periods, there was a higher proportion of patients in the palonosetron 0.25mg arm that achieved a complete response as compared to the ondansetron arm (97.5% CI 7.5 – 30.3, p-value <0.001 for delayed; 97.5% CI 7.4 -30.7, p-value <0.001 for overall). Both doses of palonosetron had significantly higher complete control (defined as no emetic episode, no need for rescue medication and no more than mild nausea) rates compared to ondansetron during the delayed (24-120 hrs) period (66.7% vs. 50.3%, p=0.001) and the overall (0-120hrs) time period (63.0% vs. 44.9%, p=0.001)8.

Eisenberg et. al conducted a phase III, single dose trial in 592 patients randomized to either receive IV palonosetron 0.25mg (n=189), IV palonosetron 0.75mg (n= 189) or IV dolasetron 100mg (n=191), 30 minutes prior to receiving moderately emetogenic chemotherapy. They found higher complete response rates in both palonosetron groups during the delayed (24-120 hrs) and overall (0-120hrs) time periods. Complete control rates were also higher in the palonosetron 0.25mg and palonosetron 0.75mg treatment arms during the delayed (24-120hrs) period compared to the dolasetron treatment arm (48.1%, 51.9%, and 36.1% respectively; p= 0.018 and p=0.002 for palonosetron 0.25mg and 0.75mg vs. respectively) and during the overall (0-120hrs) time period (41.8%, 42.9%, 30.9%, respectively; p=0.027 and p= 0.016 for

palonosetron 0.25mg and 0.75mg versus dolasetron respectively). Superiority of palonosetron compared with dolasetron was observed throughout the study for both the primary endpoints and secondary endpoints6.

Prevention of post-operative nausea and vomiting (PONV)

Park et. al conducted a randomized, double-blind study to evaluate the efficacy of palonosetron compared with ondansetron for the prevention of PONV in patients undergoing laparoscopic gynecological surgery. 90 female patients who had at least two risk factors for PONV were randomized to receive either single-dose IV palonosetron 0.075mg or IV ondansetron 8mg, immediately before induction of anesthesia. There were no statistically significant differences found in both treatment groups with regards to patient characteristics. The incidence of PONV and nausea (not vomiting) was found to be significantly lower in the palonosetron group than in the ondansetron group during the overall 0 – 24 hrs time interval (p-value < 0.05). The investigators also found that more patients in the palonosetron group had a complete response (no PONV and no rescue antiemetic) compared with the ondansetron group (42.2% versus 66.7% respectively; p-value < 0.05)13.

Laha et. al conducted a randomized, single-blind, parallel study in 98 patients undergoing laparoscopic cholecystectomy. Patients were randomized to receive a single pre-induction IV dose of palonosetron 75 mcg fixed dose (n=49) or ondansetron 4 mg fixed dose (n=49). The investigators found that the frequency of all PONV episodes in the 24hrs period following the surgical procedure, did not show any statistically significant difference between the two groups (p=0.506). In the palonosetron arm, 14 (28.6%) patients required at least one dose of rescue medication while 13 (26.5%) did in the other arm. The number of complete responders (no PONV episodes and no rescue) was 14 (28.6%) in palonosetron arm and 16 (32.7%) in the ondansetron arm. Both these differences were statistically non-significant 11

HCPCS Code:

Drug Description	HCPCS Code
Palonosetron, 25 MCG Injection	J2469
Fosnetupitant/Palonosetron, 0.25 MG Injection	J1454
Granisetron, xr, 0.1 MG Injection	J1627
Aprepitant, 1 MG Injection	J0185
Fosaprepitant, 1 MG Injection	J1453

Acronyms:

CMS= Centers for Medicare and Medicaid Services, CINV = Chemotherapy-induced nausea and vomiting, PONV = Post-operative nausea and vomiting, 5-HT3 = Serotonin, NCCN = National Comprehensive Cancer Network, ASCO = American Society of Clinical Oncology, FDA = Food and Drug Administration, HEC = highly emetogenic cancer chemotherapy, MEC = moderately emetogenic cancer chemotherapy, LCD = Local Coverage Determination, NCD = National Coverage Determination

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