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Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-2596

Drug Class Update with New Drug Evaluation: Antiemetics

Date of Review: December 2026

Date of Last Review: Conventional (January 2017)
Newer (December 2020)

Dates of Literature Search: Conventional 11/01/16 - 08/25/2026
Newer 10/01/2020 - 08/25/2026

Generic Name: tradipitant

Brand Name (Manufacturer): Nereus (Vanda Pharmaceuticals, Inc)

Dossier Received: no

Current Status of PDL Class:
See **Appendix 1**.

Purpose for Class Update:

- Evaluate new evidence published since the last reviews for conventional and newer antiemetics.
- Evaluate potential changes to preferred drug list (PDL) to accommodate Healthier Oregon population.
- Analyze the efficacy and safety data for the new antiemetic drug, tradipitant, and determine its appropriate place in therapy.

Plain Language Summary:

- Medicines that help treat and prevent nausea and vomiting are called antiemetics.
- Antiemetics are divided into different drug classes based on how they work in the body. There are several different classes of antiemetics and more than one medicine in each class.
- Antiemetics are commonly used for people receiving cancer drugs (e.g., chemotherapy) to help with symptoms of nausea and vomiting caused by chemotherapy. Updated guidelines from Multinational Association of Supportive Care in Cancer (MASCC) and the European Society for Medical Oncology (ESMO) and from the National Comprehensive Cancer Network (NCCN) recommend antiemetics for immediate treatment and preventative treatment of nausea and vomiting caused by chemotherapy. The fee-for-service (FFS) coverage policy pays for antiemetics for people with cancer receiving chemotherapy.
- An updated guideline for the use of antiemetics in children with cancer who are receiving chemotherapy aligns with FFS coverage policy.
- Guidance from North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition on the treatment of cyclic vomiting syndrome in children and teenagers, which is sudden repeated attacks of nausea and vomiting, recommends use of NK1 RAs, such as aprepitant, and 5HT3 RAs, such as ondansetron, to treat and prevent nausea and vomiting.
- Some people have a condition that slows or stops movement of food from the stomach to the small intestine called gastroparesis. A 2025 American Gastroenterological Association guideline recommends metoclopramide as a medicine for gastroparesis.

Author: Kathy Sentena, PharmD

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- Updated 2026 guidance for the treatment and prevention of nausea and vomiting in patients who just had surgery, recommends combination antiemetic therapy (e.g., 5-HT3 RAs + dexamethasone, 5-HT3 RAs + NK1 RAs, NK1 RAs + dexamethasone, 5-HT3 RAs + droperidol) for most adults because combinations work better than a single drug. In children, ondansetron or dexamethasone are listed as the first choice of medicines to prevent nausea and vomiting.
- A new drug called tradipitant was approved for the prevention of nausea and vomiting due to motion sickness. It was shown to work better than placebo at preventing vomiting due to movement for people taking a boat trip.
- Drug Use Research and Management recommends that Oregon Health Plan (OHP) pays for antiemetics that are on the preferred drug list with no recommendations for changes to the current policy.

Research Questions:

1. What is the comparative efficacy and effectiveness of different antiemetic treatments in reducing nausea or vomiting in patients with cancer, post-operatively, during pregnancy, or in patients with severe nausea and vomiting who require rescue treatment (i.e., emergency department visit or hospitalization)?
2. What are the comparative harms of different antiemetic treatments used in patients with nausea and vomiting?
3. Are there subpopulations of patients in which a particular antiemetic would be more effective or associated with less harm?
4. What is the evidence for efficacy and harms for tradipitant when used for nausea and vomiting caused by motion?

Conclusions:

- This review identified evidence from 7 high-quality guidelines, 4 new drug formulations, one new drug indication, and 4 safety alerts.

Guidelines

- Guidelines from the MASCC and the ESMO and from the NCCN updated treatment recommendations for chemotherapy-induced nausea and vomiting (CINV). [1–6] A new recommendation included adding olanzapine as core therapy for chemotherapy regimens with high emetic risk. Four drug treatment regimens with a neurokinin-1 receptor antagonist (NK1 RA), 5-hydroxytryptamine type 3 receptor antagonist (5HT3 RA), dexamethasone and olanzapine are recommended for highly emetic chemotherapy. Dexamethasone and 5HT3 RAs are recommended for moderate emetic risk, and one antiemetic of any class is recommended for low emetic risk. Recommendations are discussed in detail below.
- The American Society of Clinical Oncology (ASCO) guideline on cannabis and cannabinoid use in adults with cancer recommends that dronabinol and nabilone may be considered as augmentation therapy added to guideline recommended antiemetics for patients undergoing treatment with moderate or highly emetogenic chemotherapy who have refractory nausea and vomiting (moderate quality of evidence; weak strength of recommendation).[7]
- A clinical practice guideline on the management of prevention and treatment of acute and delayed CINV in pediatric patients was published in 2022. Recommendations are consistent with current policy for coverage of antiemetics.[8]
- The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition published guidance on the management of cyclic vomiting in children and adolescents. The use of NK1 RAs and 5HT3 RAs are recommended as acute and preventative therapy (conditional recommendation; very-low certainty of evidence).[9]
- The American Gastroenterological Association (AGA) published a guideline in 2025 on the management of gastroparesis. They recommend the use of metoclopramide for gastroparesis based on a conditional recommendation and low-quality evidence.[10]
- Recommendations for the management of post-operative nausea and vomiting (PONV) were updated in 2026.[11] Combination antiemetic therapy is recommended for most adults due to improved efficacy over monotherapy (Category A). First-line recommendation for prophylactic antiemetics in pediatrics include ondansetron and dexamethasone (Category A1).

Drug Updates

- There are 4 new drug formulations (e.g., GIMOTI, APONVIE, FOCINVEZ, and NAVIRUX) and one new drug indication (POSFREA) presented below. Four Food and Drug Administration (FDA) safety alerts are presented in **Table 11**.

New Drug Evaluation

- A new drug for the prevention of motion sickness, tradipitant, was approved in December of 2025.[12] Approval was based on two phase 3, placebo-controlled randomized controlled trials (RCTs) (**Table 13**). The Motion Syros study found low-quality evidence that tradipitant 85 mg and 170 mg were superior to placebo for the primary outcome of percentage of vomiting during boat travel, 19.5%, 18.3% and 44.3%, respectively. For the outcome of more than one incidence of vomiting, tradipitant was superior to placebo with a number needed to treat (NNT) of 5-6 with one dose of medication.[13] In a second study the percentage of participants with vomiting during boat travel was reduced with tradipitant 170 mg compared to placebo, 17.5% versus 39.7% (P=0.0039).[14]

Recommendations:

- No changes to the PDL are recommended based on review of the evidence.
- Maintain tradipitant as nonpreferred.
- Evaluate costs in executive session.

Summary of Prior Reviews and Current Policy

- There were no changes to the PDL after reviewing the evidence and costs for newer antiemetics in December 2020.
- There is no evidence to suggest clinically significant differences between the newer antiemetics used for PONV.
- The conventional antiemetic class was added after the last review in January 2017. The PA criteria for the newer antiemetics and dronabinol were merged into one policy which will also apply to non-preferred conventional antiemetics. Promethazine and prochlorperazine tablets, syrups, and rectal suppositories, metoclopramide tablets and oral solutions and phosphoric acid/dextrose/fructose were made preferred on the PDL
- Pyridoxine was recommended as first-line therapy for pregnancy related nausea and vomiting.

Background:

Antiemetics are commonly prescribed for CINV, PONV, and pregnancy-related nausea and vomiting. A multitude of medical conditions can also cause nausea and vomiting, such as acute gastroenteritis and foodborne illnesses. Risk factors for nausea and vomiting are female gender, history of motion sickness, and non-smoking history.[15,16] In addition to these risk factors, patients undergoing surgery are at increased risk if they have a previous history of PONV; receive post-operative opioids; receive general (versus regional) anesthesia, volatile anesthetics or nitric oxide; and certain types of surgery.[15]

Antiemetics used for nausea and vomiting and common indications are displayed in **Table 1**.[15] Drugs used for nausea and vomiting can be separated into conventional antiemetics (e.g., metoclopramide, prochlorperazine, promethazine, dimenhydrinate, dronabinol, meclizine, scopolamine, trimethobenzamide, and meclizine) and newer antiemetics (e.g., ondansetron, aprepitant, dolasetron, doxylamine/pyridoxine, granisetron, netupitant/palonosetron, tradipitant, fosaprepitant, and fosnetupitant/palonosetron, and palonosetron). The newer antiemetics are well tolerated and are associated with a lower incidence of adverse effects compared to conventional antiemetics.[17]

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Table 1. Antiemetics for Nausea and Vomiting[18]

Antiemetic class	Drugs in class	Examples of indications*
5-HT3 (serotonin) receptor antagonists	• Ondansetron • Granisetron • Palonosetron • Dolasetron	• Chemotherapy-induced nausea/vomiting (CINV) • Radiation-induced nausea/vomiting (RINV) • Postoperative nausea/vomiting (PONV) • Severe or refractory nausea/vomiting
NK1 (neurokinin-1) receptor antagonists	• Aprepitant • Fosaprepitant • Netupitant • Fosnetupitant (in combination with palonosetron) • Rolapitant • Tradipitant	• CINV, especially moderately/highly emetogenic Chemotherapy • Motion sickness • PONV (selected agents/settings)
Dopamine (D2) receptor antagonists / prokinetic agents	• Metoclopramide	• Migraine-associated nausea/vomiting • PONV • Opioid-induced nausea/vomiting • General acute nausea/vomiting • Gastroparesis-related nausea
Dopamine antagonists	• Prochlorperazine • Promethazine • Perphenazine	• General acute nausea/vomiting • Migraine-associated nausea/vomiting • Vestibular/vertigo-associated nausea • Mild-to-moderate CINV (alternative therapy)
H1 antihistamines	• Dimenhydrinate • Meclizine • Diphenhydramine • Promethazine	• Motion sickness • Vertigo/labyrinthine or vestibular nausea/vomiting • Selected postoperative nausea/vomiting
Anticholinergics (muscarinic antagonists)	• Scopolamine	• Motion sickness prevention • Vestibular nausea/vomiting • PONV prevention
Cannabinoids	• Dronabinol • Nabilone	• CINV that is refractory to or inadequately controlled by conventional antiemetics

Key: * Example indications may not apply to all agents in the class.
Abbreviations: 5-HT3 RA = 5-HT3 receptor antagonist; NK1 RA – neurokinin-1 receptor antagonist.

Chemotherapy induced nausea and vomiting is common with many antineoplastic therapies and highly dependent upon regimen, schedule, and route of treatment.[19] Antiemetic classes used to control CINV include dopamine receptor antagonists, serotonin 5-HT3 receptor antagonists, NK1 RAs and oral cannabinoids (e.g., droperidol). Corticosteroids are also commonly used. Radiation-induced nausea and vomiting (RINV) varies depending upon area and amount of the body exposed to treatment and the radiation dose.[5] Patient variables, such as age, sex, prior chemotherapy, and alcohol use may also influence degree of

CINV. Young female patients are at highest risk for CINV.[15] Incidence of vomiting can be reduced by about 60% when prophylactic antiemetics are used; however, nausea is much more difficult to control. CINV is classified into acute (0-24 hours), delayed (24-170 hour), anticipatory, breakthrough, or refractory.[6] Guidelines for CINV recommend antiemetic therapy based on emetogenic potential of chemotherapy regimen. Antiemetic regimens should be guided by the chemotherapeutic agent with the greatest emetic risk in the chemotherapy regimen.[6]

Post-operative nausea and vomiting occurs in 25-30% patients undergoing surgery and in up to 70-80% patients at high-risk who do not receive antiemetic prophylaxis.[20] In addition, PONV occurs in 30-50% patients discharged from surgery. Antiemetics recommended by the Society for Ambulatory Anesthesiology (SAA) recommend 5-HT3 RA, NK1 RA, corticosteroids, butyrophenones (e.g., droperidol), antihistamines, and anticholinergics.[21] Patients at medium to high risk for PONV should receive one or two antiemetics to prevent PONV. There is no evidence of clinically significant difference in effectiveness between antiemetics used for PONV and guidelines do not prefer one treatment over another.[20,21]

Pregnancy-related nausea and vomiting requires treatment in 10% of females. The National Institutes for Health and Care Excellence (NICE) recommends doxylamine/pyridoxine for pregnancy nausea and vomiting.[22] The 5-HT3 RAs are frequently prescribed for pregnancy-related nausea and vomiting, despite limited evidence to support their use due to lack of high quality clinical trial data.

Antiemetics can also be used for motion sickness, in which females are more often affected.[16] Medications used for symptom management of motion sickness include tradipitant, scopolamine, meclizine, and dimenhydrinate.[16]

Key efficacy outcomes when determining efficacy of antiemetics include complete response, defined as no emesis and no need for rescue antiemetic medication, complete control or total control when nausea is also incorporated, the proportion of patients with no vomiting, the proportion with no or minimal nausea, nausea severity, use of rescue medication, and time to treatment failure.[15] A difference of 10% in complete response rates are considered the minimal clinically important difference (MCID).[23] Patient-reported outcomes as measured by validated measures such as the MASCC Antiemesis Tool (MAT), Functional Living Index–Emesis (FLIE), or other validated nausea/vomiting scales can assist in quantifying symptoms and the effect on daily functioning and quality of life.

The conventional antiemetic class consists of 374 claims in the second quarter, resulting in a small amount of spend to the OHA (**Appendix 1**)(8/12). The newer antiemetics account for approximately 1500 claims and represent a small quarterly spend to the Oregon Health Authority (OHA) (Appendix 1).

Methods:
A Medline literature search for new systematic reviews and RCTs assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 3**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, Canada's Drug Agency (CDA-AMA), and the Scottish Intercollegiate Guidelines Network (SIGN) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high-quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

Systematic Reviews:
After review, 25 systematic reviews were excluded due to poor quality (e.g., indirect network-meta-analyses), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).

New Guidelines:
High-Quality Guidelines:

MASCC/ESMO – Antiemetic Guidelines for Chemotherapy-induced Nausea and Vomiting

In 2024 MASCC/ESMO updated 2015 guidance on antiemetics used for CINV, separated by degree of emetogenicity.[1–5] Literature was searched from June 1, 2015, to January 13, 2023 and up to February 2023 for antiemetics used for multiple-day chemotherapy, high-dose chemotherapy and breakthrough nausea and vomiting.[4] Evidence was graded from I-V with a grade of recommendation of A-E (adapted from the Infectious Disease Society of America grading system).

Treatment recommendations for the use of antiemetics are presented in **Table 2**. Olanzapine is now recommended as part of the core regimen for treatment of acute and preventative high-emetic chemotherapy and as treatment for breakthrough CINV. Shorter courses of dexamethasone are often routinely recommended dependent upon emetic risk of chemotherapy regimen. Dexamethasone is often given IV on day 1 with chemotherapy and then orally is usually preferred on following days, depending on the chemotherapy regimen. In patients without a history of nausea or vomiting receiving emetogenic chemotherapy that is at low or minimal emetic risk, should not routinely receive an antiemetic as preventative therapy (Level of evidence IV; Grade D).[1]

Table 2. Antiemetic Recommendations for Use with Antineoplastic Regimens based on Emetic Risk

Indication	Recommendation	Level of Evidence	Grade of Recommendation
High-emetic-risk antineoplastic agents[2]			
Acute N/V with non-AC HEC	Four-drug regimen given as a single dose before chemotherapy: - 5-HT3 RA - DEX - NK1 RA* - Olanzapine	I	A
Delayed N/V following a non-AC HEC	DEX and olanzapine on days 2 and 4 if treated with above regimen	II	B
Acute N/V prevention following AC-based chemotherapy with HEC	Women† should be treated with a four-drug regimen given as a single dose before chemotherapy: - 5-HT3 RA - DEX - NK1 RA* - Olanzapine	I	A
Delayed N/V following AC-based chemotherapy with high emetic risk	Women† should be treated with olanzapine on days 2 and 4 if treated with above regimen	II	B

Prevention of acute and delayed N/V following chemotherapy of HEC in olanzapine is indicated	Olanzapine 10 mg once daily for 4 days. There is insufficient evidence clarifying if olanzapine 5 mg is as effective as 10 mg	II	B
Moderate emetic risk antineoplastic agents[3]			
Carboplatin – dose dependent‡	Three-drug regimen should be given as a single dose before chemotherapy: - 5-HT3 RA - DEX - NK1 RA*	I	A
Oxaliplatin – risk factor dependent	Two-drug regimen given as a single dose before chemotherapy: - 5-HT3 RA - DEX Addition of NK1 RA for prophylaxis in women age < 50 years	III	B
Other moderate risk chemotherapy	Two-drug regimen given as a single dose before chemotherapy: - 5-HT3 RA - DEX	II	C
Steroid-sparing regimen	No steroid is recommended routinely after day 1	II	B
Olanzapine	No evidence for use in primary prophylaxis	II	C
Low or minimal emetic risk[1]			
Low risk chemotherapy prophylaxis	Single agent: - DEX - 5-HT3 RA - Dopamine RA	II	B
Multiple-day chemotherapy, high-dose chemotherapy and breakthrough nausea and vomiting[4]			
Multiple-day cisplatin therapy	Acute (given once daily on days of chemotherapy and until 2 days post-chemotherapy unless noted): - 5-HT3 RA (given on days of chemotherapy with palonosetron on days 1, 3, and 5) - DEX - Olanzapine - Aprepitant Delayed: - DEX - Olanzapine - Aprepitant	I II	A B
High-dose chemotherapy for stem cell transplant	- 5-HT3 RA - DEX - Aprepitant	I	A

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	Prophylactic: - Olanzapine once daily at bedtime and continued 2-3 days post-chemotherapy could be considered		
Breakthrough	- Olanzapine	II	B
Radiotherapy and chemotherapy[5]			
High risk	Prophylaxis: - 5-HT3 RA - DEX	II	B
Moderate risk	Prophylaxis: - 5-HT3 RA - DEX optional	IV	B
Low	Rescue with DEX	IV	B
Minimal	Rescue with: - 5-HT3 RA - DEX - Dopamine RA	IV	B
Concomitant radiation and weekly cisplatin 40 mg/m^2	Acute: - 5-HT3 RA - DEX - NK1 RA	II	B
Concomitant chemoradiotherapy	Base antiemetic therapy on chemotherapy regimen risk category unless risk is higher with radiation therapy	IV	B
Radiotherapy[5]			
High risk	Prophylaxis: - 5-HT3 RA - DEX	II	B
Moderate	Prophylaxis: - 5-HT3 RA - DEX optional	II	A
Low	Brain: - Rescue with DEX Head and neck, thorax, pelvis: - 5-HT3 RA *or* - DEX *or* - Dopamine RA	IV	B
Minimal	Rescue: - 5-HT3 RA *or*	II	B

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	- DEX *or* - Dopamine RA		
Concomitant radiation and weekly cisplatin 40 mg/m^2	Acute (prophylaxis day 1 before cisplatin administration): - 5-HT3 RA - DEX - NK1 RA Delayed: - DEX (days 2-4)	II	B
Concomitant chemoradiation therapy	Base antiemetic therapy on chemotherapy regimen risk category unless risk is higher with radiation therapy	IV	B
Key: * aprepitant, fosaprepitant, netupitant w/palonosetron, fosnetupitant w/ palonosetron, or rolapitant; † Based off data in women treated for breast cancer; ‡ No evidence to support the use of an NK_1 RA for carboplatin levels with AUC <5 Abbreviations: 5-HT3 RA = 5-HT3 receptor antagonist; AC = anthracycline-cyclophosphamide; DEX = dexamethasone; HEC = high emetic risk chemotherapy; NK1 RA = neurokin-1 receptor antagonists; N/V = nausea and vomiting; RA = receptor antagonist.			

Patel, et al - Prevention of Nausea and Vomiting in Pediatric Cancer Patients

A 2022 clinical practice guideline published recommendations for the management of pediatric cancer patients with CINV.[8] The literature was searched from January 1, 1989, to January 21, 2022, on prevention of acute and delayed phase CINV.[8] A total of 328 RCTs were included in the systematic review and meta-analysis providing evidence for this review. Recommendations for antiemetic therapy was based on emetogenicity of chemotherapy regimens (**Table 3**).[8]

Table 3. Recommendations for the Prevention of Acute and Delayed Phase CINV in Pediatric Patients[8]

Indication	Recommendation	Quality of Evidence	Strength of Recommendation
High emetogenic chemotherapy			
Acute phase CINV			
Acute phase CINV	- 5HT3 RA - DEX - (fos)aprepitant	High	Strong
Acute CINV and patient is unable to receive (fos)aprepitant	- Palonosetron - DEX	Moderate	Strong
Acute CINV and patient is unable to receive DEX	- Palonosetron - (fos)aprepitant	Low	Strong
Acute CINV and patient is unable to receive DEX and (fos)aprepitant	- Palonosetron	Moderate	Strong
Acute CINV	Consider adding olanzapine to other CPG-consistent antiemetics	Moderate	Conditional
Delayed phase CINV			

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Patients at high risk of delayed phase CINV	- Use palonosetron in the acute phase as the preferred 5HT3 RA	Moderate	Strong
If (fos)aprepitant started in the acute phase	- Use oral aprepitant in the delayed phase	High	Strong
If granisetron or ondansetron is used in the acute phase	- Add DEX in the delayed phase	Moderate	Strong
If palonosetron is used in the acute phase	- Consider adding DEX in the delayed phase	Moderate	Conditional
In patients unable to receive oral aprepitant	- Use DEX in the delayed phase	Moderate	Strong
If olanzapine is started in the acute phase	- Continue olanzapine in the delayed phase	Moderate	Strong
Not recommended for use	- Do not use 5HT3 RAs in the delayed phase	Low	Strong
Moderate emetogenic chemotherapy			
Acute phase CINV			
Prevention of acute phase CINV	- 5HT3 RA - DEX	Moderate	Strong
Patient is unable to receive DEX	- 5HT3 RA - (fos)aprepitant	Low	Strong
Patient is unable to receive DEX and (fos)aprepitant	- 5HT3 RA	Low	Strong
Patient is unable to receive DEX and (fos)aprepitant	- Consider palonosetron as the preferred 5HT3 RA	Low	Conditional
Patient is unable to receive DEX and (fos)aprepitant	- Consider adding olanzapine to other CPG-consistent antiemetic	Low	Conditional
Prevention of delayed phase CINV			
Delayed phase prevention	- DEX	Low	Conditional
Patients receiving single-day chemotherapy who received (fos)aprepitant in the acute phase	- Continue oral aprepitant in the delayed phase	Moderate	Strong
Patients receiving multi-day chemotherapy (>3 days) who received (fos)aprepitant in the acute phase	- Oral aprepitant is not recommended in the delayed phase	Low	Conditional
If olanzapine is started in the acute phase	- Continue olanzapine in the delayed phase	Low	Strong
Low emetogenic chemotherapy			
Prevention of acute phase CINV	- 5HT3 RA	Low	Strong
Prevention of delayed phase CINV	- Do not use prophylaxis routinely	Very Low	Strong
Minimally emetogenic chemotherapy			

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Prevent acute phase CINV	- Do not use prophylaxis routinely	Very low	Strong
Prevent delayed phase CINV	- Do not use prophylaxis routinely	Very low	Strong

Abbreviations: 5-HT3 RA = 5-HT3 receptor antagonist; CINV = chemotherapy-induced nausea and vomiting; CPG = clinical practice guideline; DEX = dexamethasone; RA = receptor agonist.

NCCN – Antiemesis Clinical Practice Guidelines in Patients with Chemotherapy-induced Nausea and Vomiting

In 2026 NCCN updated guidance on the use of antiemetics for CINV.[6] Evidence was evaluated and assigned a category recommendation based on Table 4.

Table 4 . NCCN Categories of Evidence and Consensus[6]

Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Overview on use of antiemetics for CINV[6]:

- Antiemetic therapies are categorized as: acute, delayed, anticipatory, breakthrough or refractory.
- The emetogenic potential of the chemotherapy or radiation regimen dictates the appropriate antiemetic therapy. Risk categories are as follows: high, moderate, low and minimal.
- Evidence demonstrates that antiemetics are equally effective and individual antiemetic selection should be based on drug-drug interactions, patient-specific factors and individual experience.
- Selection of antiemetic regimen should always be based on the drug with the highest emetic risk.
- Antiemetic treatment recommendations for parenteral anticancer therapies are provided in Tables 5, 6 and 7.
- Parenteral anticancer therapies with minimal emetic potential require no routine prophylaxis.

Table 5. NCCN Recommendations for Acute and Delayed Emesis Prevention for High Emetic Risk Parenteral Anticancer Agents*[6]

Day 1 (Select option A, B or C)	Days 2, 3, 4
Treatment option A (preferred) use the following combination: • Olanzapine orally once daily (bedtime) • NK1 RA once (PO or IV) • 5-HT3 RA once (PO, SQ or IV) • Dexamethasone once (PO or IV)	Treatment option A: • Olanzapine orally (bedtime) on days 2, 3 and 4 • Aprepitant 80 mg orally on days 2, 3 (if aprepitant orally was used on day 1) • Dexamethasone daily on days 2, 3, 4 (PO/IV)
Treatment option B, use the following combination: • Olanzapine orally once • Palonosetron once (IV) • Dexamethasone once (PO/IV)	Treatment option B: • Olanzapine orally daily (bedtime) on days 2, 3, 4
Treatment option C, use the following combination: • NK1 RA once (PO or IV)	Treatment option C: • Aprepitant orally on days 2, 3 (if aprepitant PO was used on day 1)

• 5-HT3 RA once (PO, SQ or IV) • Dexamethasone once (PO/IV)	• Dexamethasone daily on days 2, 3, 4 (PO/IV)
Abbreviations: 5-HT3 RA – serotonin receptor antagonist; IV – intravenous; NK1 RA – neurokinin-1 receptor antagonist; PO – by mouth; SQ – subcutaneous Key: * All treatments should be started before chemotherapy	

Table 6. NCCN Recommendations for Acute and Delayed Emesis Prevention for Moderate Emetic Risk Parenteral Anticancer Agents*[6]

Day 1 (Select option D, E, or F)	Days 2, 3
Treatment option D (preferred) use the following combination: • 5-HT3 RA (PO, SQ, IV) • Dexamethasone once (PO or IV)	Treatment option D: • Dexamethasone daily on days 2, 3 (PO/IV) **OR** • 5-HT3 RA monotherapy daily on days 2, 3
Treatment option E, use the following combination: • Olanzapine orally once • Palonosetron IV once • Dexamethasone once (PO/IV)	Treatment option E: • Olanzapine orally daily on days 2, 3
Treatment option F, use the following combination: • NK1 RA once (PO or IV) • 5-HT3 RA once (PO, SQ or IV) • Dexamethasone once (PO/IV)	Treatment option F: • Aprepitant orally on days 2, 3 (if aprepitant orally was used on day 1) +/- Dexamethasone days 2,3 (PO/IV)
Abbreviations: 5-HT3 RA – serotonin receptor antagonist; IV – intravenous; NK1 RA – neurokinin-1 receptor antagonist; PO – by mouth; SQ – subcutaneous Key: * All treatments should be started before chemotherapy	

Table 7. NCCN Recommendations for Acute and Delayed Emesis Prevention for Low Emetic Risk Parenteral Anticancer Agents*†[6]

• Dexamethasone once (PO or IV) once OR • Prochlorperazine (PO/IV) once OR • 5-HT3 RA (PO) once
Abbreviations: 5-HT3 RA – serotonin receptor antagonist; IV – intravenous; PO – by mouth; SQ – subcutaneous Key: * All treatments should be started before chemotherapy; † Order does not imply preference

Parenteral therapy with minimal emetic risk requires no routine prophylaxis.[6]

Oral chemotherapy can have a risk of emesis, and recommendations for antiemetics are separated into high to moderate emetic risk and low to minimal emetic risk (**Table 8**).

Table 8. NCCN Recommendations for Oral Chemotherapy Emesis Prevention*[6]

Moderate to high emetic Risk	• Start before chemotherapy and continue daily while receiving chemotherapy Choose one: • 5-HT3 RA recommended (PO or transdermal) • Ondansetron orally • Olanzapine orally (bedtime)
Low to Minimal Emetic Risk	• As-needed antiemetic use is recommended • If nausea or vomiting occurs, start treatment before chemotherapy in future cycles and continue daily • Use metoclopramide orally *OR* • Prochlorperazine orally *OR* • 5-HT3 RA orally
Breakthrough therapy for moderate to high emetic risk	• As-needed dosing appropriate initially • Prophylactic dosing if needed: • 5-HT3 RA *OR* • Olanzapine orally (bedtime)
Breakthrough therapy for minimal to low emetic risk	• As-needed dosing appropriate initially • Prophylactic dosing if needed: • 5-HT3 RA *OR* • Olanzapine orally (bedtime)
Abbreviations: 5-HT3 RA – serotonin receptor antagonist; PO - orally Key: *With or without oral lorazepam given IV or sublingual every 6 hours as needed	

In addition to scheduled emesis prevention, breakthrough treatment for chemotherapy-induced nausea and vomiting may be needed.[6] In general, breakthrough treatment should be from a different drug class than currently used therapy and should be added to current regimen (see options below).[6] If nausea and vomiting is controlled, the medication should be continued on a schedule. If breakthrough nausea/vomiting remains uncontrolled then a dose adjustment should be considered and/or one therapy from another drug class should be added.[6] Re-evaluation of antiemetic therapy should be considered to prevent need for breakthrough therapy and a higher level of primary antiemetic treatment should be used for the next cycle.

Antiemetic choices for breakthrough chemotherapy-induced nausea/vomiting are the following:[6]

- Olanzapine orally (preferred category 1)
- Benzodiazepine (e.g., lorazepam) orally/sublingual/IV
- Cannabinoid (e.g., cannabinoid) orally
- Haloperidol orally/IV
- Metoclopramide orally/IV
- Scopolamine transdermal patch
- Phenothiazine (prochlorperazine or promethazine)
- 5-HT3 RA orally/transdermal

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- Dexamethasone orally/IV

Antiemetic therapy for radiation is based on amount of the body that is being irradiated, location on the body and the total dose delivered.[6] The use of granisetron orally or ondansetron (+/- dexamethasone orally) should be given to patients as pretreatment for each day patients receive radiation therapy to the upper abdomen/localized sites.[6] For patients receiving total body irradiation, pretreatment for each day of radiation therapy should be with granisetron or ondansetron orally (+/- dexamethasone orally).[6] If the patients is receiving chemotherapy and radiation therapy then recommendations should be based on emetogenicity of chemotherapy regimen.

In patients who experience anticipatory nausea/vomiting, preventative therapy is most important.[6] Recommendations include using optimal antiemetic therapy during every cycle of treatment, avoidance of smells that precipitate treatment, behavioral therapy, acupuncture/acupressure, and consideration of anxiolytic therapy.

If patients are receiving multiday emetogenic chemotherapy they may need antiemetic therapy for acute and delayed nausea/vomiting.[6] General therapies include dexamethasone (unless regimen already includes a steroid, or olanzapine if the patient cannot tolerate dexamethasone), 5-HT3 RAs, and NK1 RAs.[6]

ASCO Guideline – Cannabis and Cannabinoids in Adults with Cancer

A 2024 guideline from the ASCO was published to offer guidance on the medical use of cannabis and cannabinoids in individuals with cancer.[7] A systematic review of the literature ranging from database inception to January 27, 2023. Eighteen publications were included and graded by authors as having a low or very low certainty of evidence.[7] The recommendations pertaining to the use of cannabinoid as antiemetics will be presented.

For adults with cancer that experience refractory nausea or vomiting on guideline directed antiemetic prophylaxis due to moderate or highly emetogenic antineoplastic agents may augment their antiemetic regimen with dronabinol, nabilone or quality-controlled oral 1:1 THC:CBD extract (Moderate quality of evidence for dronabinol and nabilone, Low for THC/CBD extract; Strength of recommendation for all is Weak).[7] Other pharmacological options for refractory nausea or vomiting include olanzapine, or antiemetic from another class not already being administered (e.g., NK1 RA, dopamine RA, benzodiazepine or synthetic THC). There was low quality of evidence that dronabinol and nabilone was effective for promoting weight gain or improving appetite and quality of life.

AGA Clinical Practice Guideline on Management of Gastroparesis

In 2025 the AGA updated guidance on the treatment of gastroparesis. A systematic review was used to identify and assess evidence based on the Grading of Recommendations, Assessment Development and Evaluation (GRADE) framework. The guideline is comprised of 12 recommendations for management and treatment. Drug therapy will be presented.

The use of metoclopramide is conditionally recommended for use in patients with gastroparesis (conditional; low-quality evidence).[10] Adverse effects of metoclopramide should be considered, including boxed warning for the risk of tardive dyskinesia (TD). Recommended dosing is 5 mg before meals increased up to 10 mg before meals if needed and 15 mg before meals and at bedtime for intranasal metoclopramide.[10] Use for 1-4 weeks with drug holidays every 8-12 weeks is advised. The use of aprepitant is recommended against as a first-line treatment option (conditional; low-quality evidence).[10]

Karrento - Guidelines for Management of Cyclic Vomiting Syndrome in Children

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A 2025 guideline from North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition provides recommendations for the pharmacological and non-pharmacological management of cyclic vomiting in children.[9] Cyclic vomiting is characterized by repeated vomiting attacks with considerable overlap with migraine. A systematic review of the evidence was performed. Recommendations were made based on the GRADE approach. The guidance provides 16 recommendations divided into acute treatment and preventative interventions.[9] Pharmacological recommendations regarding the use of antiemetics will be presented.

Recommendations:[9]

- The use of NK1 RAs (e.g., aprepitant) is suggested for the treatment of acute cyclic vomiting episodes in children and adolescents (conditional recommendation; very-low quality of evidence)
- The use of 5-HT3 RAs (e.g., ondansetron) is suggested for the treatment of acute cyclic vomiting episodes in children and adolescents (conditional recommendation; very-low quality of evidence)
- The use of IV NK1 RAs (e.g., fosaprepitant) is suggested for the treatment of acute cyclic vomiting episodes in children and adolescents not responding to outpatient abortive therapies (conditional recommendation; very-low quality of evidence)
- The use of IV 5-HT3 RAs (e.g., ondansetron) is suggested for the treatment of acute cyclic vomiting episodes in children and adolescents not responding to outpatient abortive therapies (conditional recommendation; very-low quality of evidence)
- The use of NK1 RAs (e.g., aprepitant) for prevention of cyclic vomiting episodes in children and adolescents (conditional recommendation; very-low quality of evidence)

Gan - Postoperative Nausea and Vomiting Guidelines

Guidance on the management of PONV was updated in 2026.[11] The guidelines provided updates on topics of PONV risk factors, risk reduction interventions, single antiemetic and combination options, PONV in children, and pharmacoeconomic considerations. Literature was searched from January 2019 to September 2024 and graded as one of the following: Category A (supportive literature of difference), Category B (suggestive literature of difference), Category C (equivocal literature – difference in benefits or harms cannot be determined), or Category D (insufficient evidence).[11] Antiemetic therapy will be presented.

Antiemetics from several classes are used for PONV (**Table 9**). Combination therapy is recommended as it has found to be more effective than monotherapy.[11] Combinations commonly recommended are 5-HT3 RAs + dexamethasone, 5-HT3 RAs + NK1 RAs, NK1 RAs + dexamethasone, 5-HT3 RAs + droperidol (all based on level A evidence).[11]

Table 9. Drugs Used for the Management of PONV[11]

Drug	Dose	Evidence Category	Timing
NK1 RAs			
Aprepitant	40- 80 mg PO 32 mg IV	A1	At induction
5-HT3 RAs			
Ondansetron	4 mg IV 16 mg ODT	A1	End of surgery
Granisetron	0.1-3 mg IV	A1	End of surgery

Palonosetron	0.075 mg IV	A1	
Corticosteroids			
Dexamethasone	4-8 mg IV	A1	At induction
Anticholinergics			
Dimenhydrinate	25-50 mg IV Dose of 62.5 mg can be considered	A1	
Scopolamine	Transdermal patch	A1	Prior evening or 2 hrs. before surgery
Dopamine receptor antagonists			
Metoclopramide*	10 mg	A1	
Droperidol	0.625mg IV	A1	End of surgery
Miscellaneous			
Ephedrine	0.5 mg/kg IM	A2	
Haloperidol	0.5-<2 mg IM/IV	A1	
Promethazine	6.25mg	A2	
Key: * Not recommended for PONV unless other dopamine antagonists are not available. Abbreviations: IM = intramuscular; IV = intravenous			

If rescue treatment is needed an antiemetic from a different class than the prophylactic drug should be chosen.[11] Transdermal scopolamine is not recommended due to its slow onset. Re-dosing of long-acting antiemetics (e.g., palonosetron, aprepitant, and fosaprepitant) should be avoided.[11]

Medications used for prophylactic antiemetic therapy in pediatric patients is presented in **Table 10**. First-line recommendations are 5-HT3 RAs or dexamethasone.[11] Monotherapy is recommended unless pediatric patient has one or more risk factors for nausea and vomiting.

Table 10. Prophylactic Antiemetics for PONV for use in Pediatrics[11]

Drug	Dose	Evidence Level
Ondansetron	0.1 mg/kg up to 4 mg	A1
Dolasetron	0.35 mg/kg up to 12.5 mg	A2
Granisetron	0.04 mg/kg up to 0.6 mg	A2
Palonosetron	0.5-1.5 mcg/kg	A2
Droperidol	10-15 mcg/kg up to 1.25 mg	A1
Dimenhydrinate	0.5 mg/kg up to 25 mg	A1
Dexamethasone	0.15 mg/kg up to 4 mg	A1
Aprepitant	3 mg/kg up to 125 mg	A3
Ondansetron + Dexamethasone	See above	A1

After review, four guidelines were excluded due to poor quality or not applicable to the review.[23–26]

New Formulations or Indications:

New formulations:

GIMOTI (metoclopramide nasal spray): In June of 2020 metoclopramide nasal spray was approved for relief of symptoms in adults with acute and recurrent diabetic gastroparesis.[27] Metoclopramide nasal spray is a dopamine-2 (D_2) antagonist with each spray containing 15 mg of metoclopramide. In adult patients less than 65 years, the nasal spray is given as one spray (15 mg) in one nostril, 30 minutes before each meal and at bedtime for 2 to 8 weeks depending upon symptoms (not more than 4 sprays daily). In adults 65 years of age and older on established metoclopramide therapy of 10 mg four times daily can be switched to metoclopramide nasal spray up to four times daily for 2-8 weeks, depending on response.[27] Metoclopramide nasal spray is not recommended for initial therapy in geriatric patients. See additional boxed warning of the risk of tardive dyskinesia in **Table 11**. Use longer than 12 weeks is not recommended.

APONVIE (aprepitant): In September of 2022 aprepitant was formulated as an injectable emulsion for the prevention of PONV use in adults.[28] Aprepitant is a NK1 RA to be give as a 32 mg dose intravenous (IV) injection prior to anesthesia induction. Approval was based off studies of single-dose oral aprepitant in adults.[28] This is the only formulation specifically approved for PONV prophylaxis.

FOCINVEZ (fosaprepitant): Fosaprepitant was approved in August 2023 for 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 including high-dose cisplatin and for delayed nausea and vomiting associated with repeat courses of moderately emetogenic cancer chemotherapy.[29] Fosaprepitant is a NK1 RA given as an IV infusion in adults approximately 30 minutes prior to chemotherapy. The package insert should be consulted for dosing instructions for use in pediatrics. FOCINVEZ does not need to be reconstituted or diluted and does not contain polysorbate 80 which has been associated with infusion-site reactions. Safety and efficacy has been established based on other forms of IV fosaprepitant.[29]

NAVITRUX (fosaprepitant): A formulation of fosaprepitant IV was approved in June of 2026.[30] Fosaprepitant works by being a NK1 RA. It is indicated for 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 including high-dose cisplatin and for delayed nausea and vomiting associated with repeat courses of moderately emetogenic cancer chemotherapy.[30] In adults fosaprepitant is given as a 150 mg dose approximately 30 minutes prior to chemotherapy. The package insert should be consulted for dosing instructions for use in pediatrics. There are no clinical differences from EMEND (fosaprepitant) IV formulation. Approval was based on study data from other IV fosaprepitant formulations.[30]

New Indications:

POSFREA (palonosetron injection): An additional indication for the use of palonosetron injection was approved in April of 2025 for the use in pediatric patients aged 1 month to less than 17 years old for prevention of acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including highly emetogenic cancer chemotherapy.[31] Evidence comes from a 2 trials in children 2 months to 17 years.[31]

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New FDA Safety Alerts:

Table 11. Description of New FDA Safety Alerts

Generic Name	Brand Name	Month / Year of Change	Location of Change (Boxed Warning, Warnings, CI)	Addition or Change and Mitigation Principles
Granisetron[32] (subcutaneous injection)	SUSTOL	February 2026	Warnings and Precautions	Risk of severe injection site reactions including infection, prolonged bleeding, bruising, hematomas, nodules, pain and tenderness have been reported. Patients who are neutropenic or receiving anticoagulants or antiplatelets are at greater risk. Consider an alternate site or discontinuing use.
Metoclopramide[33]	GIMOTI	February 2026	Boxed Warning	May cause TD. The risk of developing TD increases with duration of treatment and total cumulative dose. Use is contraindicated in patients with a history of TD. Use for the shortest duration and reassess need for continued treatment. Avoid use longer than 12 weeks, including in diabetic gastroparesis and GI reflux.
Ondansetron[34]	ZOFRAN	October 2021	Warnings and Precautions	Myocardial ischemia has been reported with ondansetron, most commonly during IV administration. The most common underlying cause is coronary artery spasm. Monitor patients for signs or symptoms of myocardial ischemia after IV and oral ondansetron.
		April 2025	Warnings and Precautions	Hyperthermia has been reported in postmarketing reports. Advise patients if body temperature increases to remove the transdermal system and contact their healthcare provider.
Scopolamine[35]	TRANSDERM-SCOP	March 2019	Warning and Precautions	Several updates to this section were updated: - Use in acute angle closure glaucoma due to increase in intraocular pressure due to the mydriatic effect of scopolamine. Remove patch if they experience symptoms of acute angle closure glaucoma. - Exacerbation of psychosis. Monitor patients of worsening psychiatric symptoms. - Seizure and seizure-like activity have been reported and risk benefit of use should be done before prescribing. - Cognitive adverse reactions, such as drowsiness and confusion, have been reported especially in elderly patients. Monitor more frequently. - Scopolamine may interfere with hazardous tasks and patients should not operate vehicles or participate in underwater sports until they know scopolamine will not adversely affect them. - Eclamptic seizures have been reported in pregnant women with severe preeclampsia after IV or IM scopolamine. Avoid use in this population.

				- Scopolamine may decrease GI motility and cause urinary retention. Discontinue use if this occurs. - Discontinuation after several days of use may result in withdrawal symptoms and medical attention should be sought if they experience these symptoms. - Blurred vision may occur if scopolamine comes in contact with the eyes. - Skin burns may occur if the patch is worn during an MRI and should be removed before testing.
Abbreviations: GI = gastrointestinal; IM = intramuscular; IV = intravenous; MRI = magnetic resonance imaging; TD = tardive dyskinesia				

Randomized Controlled Trials:
A total of 433 citations were manually reviewed from the initial literature search. After further review, all citations were excluded because of wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).

NEW DRUG EVALUATION:

See **Appendix 4** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations. Pharmacology and pharmacokinetic properties are listed in **Appendix 5**.

Clinical Efficacy:
Tradipitant is a substance P/NK1 receptor antagonist approved for the prevention of vomiting induced by motion in adults.[12] Tradipitant is given approximately 60 minutes before an event expected to cause vomiting due to motion. Tradipitant is available as a single dose as 85 mg or 170 mg (2 capsules) and should be taken on an empty stomach, at least 1 hour prior to event or 2 hours after a full meal. A single dose of 85 mg or 170 mg should not be exceeded in 24 hours. The use of tradipitant for more than 90 doses has not been studied.[12]

Evidence from 2 RCTs provide evidence for the effectiveness of tradipitant. In the Motion Syros study patients were randomized to tradipitant 85 mg, tradipitant 170 mg or placebo.[13] Patients were given their randomized treatment 60 minutes prior to entering the boat for travel assessment and each participant only took one boat trip. Every 30 minutes participants were asked about motion sickness symptoms by completing a Vomiting Assessment (VA) and nausea assessment (NA). The VA assessment was a yes/no question and the NA was a 5-point scale rating nausea 0-4.[13] At trip completion the participants were asked to fill out the Motion Sickness Assessment Questionnaire (MSAQ) and Patient Global Impression Severity Questionnaire (PGI-S).[13] The MSAQ measures motion sickness via a 16-item questionnaire. The PGI-S is a 5-item scale where participants rank the severity of their motion sickness symptoms from none to very severe. Participants, in groups of 1 to 35, were taken on a boat trip lasting 125 to 265 minutes. Sea conditions varied with peak wave heights ranging from 0.5 to 2.5 meters.[13] Participants were asked to return within 7 days of trip to be assessed for safety. The primary endpoint was the percentage of patients who vomited during travel, one more instance of vomiting, and vomiting in rough seas.[13] Subgroup analysis of the incidence of vomiting incidence was divided into calm seas (wave height < 1 m) or rough seas (wave height $\geq$ 1 m).[13]

Participants had similar baseline characteristics. There were more females (66.7%) compared to males.[13] The mean age was 48.6 years and a mean body mass index (BMI) of 27.3 kg/m^2. Eighty-three percent of participants were White.

Both doses of tradipitant were superior to placebo for the 3 primary endpoints (**Table 13**). The percentage of participants with vomiting during boat travel was less with tradipitant 170 mg compared to placebo RR 0.42 (95% CI; 0.272 to 0.638; P<0.0001) and less for the tradipitant 85 mg dose compared to placebo RR 0.44 (L95% CI; 0.293 to 0.655; P<0.0001).[13] Fewer participants had more than one instance of vomiting with an absolute risk reduction (ARR) of 20/nNNT 5 for the tradipitant 170 mg and of ARR 17/NNT 6 for the tradipitant 85 mg dose.[13] The number of participants with vomiting in rough seas was lower with tradipitant 85 mg and 170 mg doses compared to placebo, 22.0%, 20.5% and 49.5%, respectively.[13] Changes in the secondary endpoints of MSAQ and PGI-S were not statistically different from placebo for both doses of tradipitant. There was no significant difference in results based on sex, age or BMI.

In a second trial, Motion Sifnos, tradipitant was studied in a double-blind, multi-center, randomized, placebo-controlled study (n=126).[14] Participants were between the ages of 18-75 years (mean age of 39 years) and had a history of motion sickness, and 23% were male. Participants were randomized to tradipitant 170 mg or placebo. Each participant was given a single dose 60 minutes prior to a single boat trip for assessment. Groups ranged from 10-26 individuals. Participants were asked to fill out the Motion Sickness Severity Scale (MSSS) to assess motion sickness symptoms. [14]The MSSS measures severity of main symptoms of motion sickness, with a score of 6 indicating vomiting. The primary outcomes were incidence of vomiting and the severity of motion sickness as measured by the highest score recorded on the MSSS.

The percentage of participants with vomiting was reduced with tradipitant 170 mg compared to placebo for the primary endpoint of percentage of vomiting during boat travel, 17.5% versus 39.7% (absolute difference [AD] -0.22; 95% CI, -0.380 to -0.07; P=0.0039).[14] The MSSS Worst Score was less with tradipitant 170 mg compared to placebo, 3.40 versus 3.75 (AD -0.35; 95% CI, -0.99 to -0.30; P=0.2936); however, results were not significantly different. For the secondary endpoint of vomiting incidence on rough seas was reduced with tradipitant compared to placebo, 15.79% versus 72.22% (p=0.0009).[14]

There is limited evidence of efficacy provided by 2 small studies. Participants went out for motion sickness assessment on different days with different weather and small numbers in each group so differences in treatment may be hard to detect. Motion sickness is more common in women which is reflected in the study populations.

Clinical Safety:
The most common adverse events associated with tradipitant are somnolence, headache and fatigue (**Table 12**).[12] Since tradipitant may impair mental or physical abilities caution should be taken when driving a motor vehicle or operating heavy machinery. No contraindications or severe adverse events have been identified.

Table 12. Adverse Reactions for Tradipitant compared to Placebo[12]

Adverse Reaction	Studies 1 and 2		Studies 1, 2, and 3*	
	Tradipitant 85 mg N = 227	Placebo N = 228	Tradipitant 170 mg N = 289	Placebo N = 291
Somnolence	14 (6%)	9 (4%)	36 (12%)	17 (6%)
Headache	16 (7%)	12 (5%)	28 (10%)	17 (6%)
Fatigue	14 (6%)	6 (3%)	24 (8%)	6 (2%)

Key: * Study 3 was used for safety data only.

Tradipitant is metabolized by the CYP3A4 enzyme system and strong CYP3A4 inhibitors may increase tradipitant levels and AE.[12] There is insufficient evidence for the use of tradipitant in repeated doses or for multiple bouts of motion sickness within a certain timeframe. Tradipitant use exceeding 90 doses in 12 months has not been studied. Long-term safety is unknown and use in pediatrics has not been studied.

Look-alike / Sound-alike Error Risk Potential: None identified

Comparative Endpoints:

Clinically Meaningful Endpoints:
1) Incidence of vomiting
2) Complete prevention of vomiting
3) Absence of nausea
4) Serious adverse events
5) Study withdrawal due to an adverse event

Primary Study Endpoint:
1) Percentage of patients with vomiting during travel.
2) More than one instance of vomiting
3) Vomiting in rough seas

Table 13. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
1. Polymeropoulos, et al[13] (Motion Syros) DB, Phase 3, RCT	1. Tradipitant 170 mg as one dose 60 minutes prior to boat travel assessment 2. Tradipitant 85 mg as one dose 60 minutes prior to boat travel assessment 3. Placebo as one dose 60 minutes prior to boat travel assessment	Demographics: Male: 33.3% Mean Age: 48.6 years White: 84.7% Asian: 7.4% Baseline BMI: 27.38 kg/m^2 Key Inclusion Criteria: - 18-75 years - Significant history of motion sickness verified by a Motion Sickness Eligibility Questionnaire (MSEQ) - Good health - No condition known to cause nausea	ITT: 1. 120 2. 123 3. 122 PP: 1. 120 2. 123 3. 122 Attrition: 1. 0 2. 0 3. 0	Primary Endpoint: Percentage of participants with vomiting during one instance of boat travel*: Tradipitant 170 mg: 22 (18.3%) Tradipitant 85 mg: 24 (19.5%) Placebo: 54 (44.3%) Tradipitant 170 mg vs. Placebo: RR 0.42 (95% CI, 0.272 to 0.638) P<0.0001 Tradipitant 85 mg vs. Placebo: RR 0.44 (95% CI, 0.293 to 0.655) P<0.0001 More than one instance of vomiting: Tradipitant 170 mg: 13 (10.8%) Tradipitant 85 mg: 17 (13.8%) Placebo: 38 (31.1%)	ARR 26 / NNT4 ARR 24 / NNT 4	Treatment Emergent Adverse Events: Tradipitant 170 mg: 34 (28.3%) Tradipitant 85 mg: 33 (26.8%) Placebo: 11 (9.0%) Headache: Tradipitant 170 mg: 10 (8.3%) Tradipitant 85 mg: 7 (5.7%) Placebo: 3 (2.5%) Somnolence: Tradipitant 170 mg: 10 (8.3%) Tradipitant 85 mg: 8 (6.5%) Placebo: 0 (0%)	NA for all	**Risk of Bias (low/high/unclear)**: Selection Bias: (Low) Assigned in a ratio 1:1:1 by an Interactive Web Response System. Performance Bias: (Unclear) Stated as double-blind but not described. Detection Bias: (Unclear) Somnolence associated with tradipitant may lead to unblinding in small number of patients. Attrition Bias: (Low) There was no attrition as only one dose was given. Reporting Bias: (High) Only one primary outcome was described; however, there were 3 given in the table. Secondary outcomes were not clearly stated in the text but were provided in a table. The outcome of severe nausea and vomiting was a *post hoc* analysis. Other Bias: (Unclear) Funded by manufacturer and role in study was not described.

		Key Exclusion Criteria: - Use of any other anti-nausea medication during the study		Tradipitant 170 mg vs. Placebo: RR 0.35 (95% CI, 0.196 to 0.623) P<0.0001 Tradipitant 85 mg vs. Placebo: RR 0.44 (95% CI, 0.264 to 0.736) P<0.0001 Vomiting in Rough Seas (wave height > 1 m): Tradipitant 170 mg: 21 (20.4%) Tradipitant 85 mg: 22 (22%) Placebo: 50 (49.5%) Tradipitant 170 mg vs. Placebo: RR 0.41 (95% CI, 0.269 to 0.638) P<0.0001 Tradipitant 85 mg vs. Placebo: RR 0.43 (95% CI, 0.289 to 0.655) P<0.0001 Secondary Endpoints: Overall MSAQ Score (0-100): Tradipitant 170 mg: 46.0 Tradipitant 85 mg: 49.2 Placebo: 45.1 Tradipitant 170 mg vs. Placebo: LSM 0.9 (95% CI, -5.34 to 7.17) P=0.7746 Tradipitant 85 mg vs. Placebo: LSM 4.1 (95% CI, -2.06 to 10.33) P=0.1899 PGI-S Score (0-4): Tradipitant 170 mg: 2.1 Tradipitant 85 mg: 2.0 Placebo: 2.2 Tradipitant 170 mg vs. Placebo: LSM -0.1 (95% CI, -0.42 to 0.23) P=0.5542	ARR 20 / NNT 5 ARR 17 / NNT 6 ARR 30 / NNT 3 ARR 28 / NNT 4 NA NA NA			**Applicability**: Patient: Results are most applicable to female, overweight individuals who are otherwise healthy and middle-aged. Intervention: The tradipitant dose of 170 mg had been previously studied and shown efficacy. Comparator: An active comparator, such as meclizine or scopolamine, would inform comparative efficacy. Outcomes: Outcomes are appropriate for motion sickness. Setting: The Atlantic Ocean, the Gulf of Mexico, and Pacific Ocean.

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				Tradipitant 85 mg vs. Placebo: LSM -0.2 (95% CI, -0.49 to 0.15) P=0.3025	NA			
2. Polymeropoulos, et al[14] (Motion Sifnos) DB, Phase 3, RCT	1. Tradipitant 170 mg as one dose 60 minutes prior to boat travel assessment 2. Placebo as one dose 60 minutes prior to boat travel assessment	Demographics: Male: 23% Mean Age: 39.1 years White: 73.8% Asian: 11.1% Baseline BMI: 27.22 kg/m^2 Key Inclusion Criteria: - 18-75 years - Significant history of motion sickness verified by a MSEQ - Good health - No known condition to cause nausea Key Exclusion Criteria: - Irritable bowel syndrome - Gastroparesis - Cyclic vomiting syndrome	ITT: 1. 63 2. 63 PP: 1. 63 2. 63 Attrition: 1. 0 2. 0	Primary Endpoint: Percentage of vomiting during boat travel*: Tradipitant 170 mg: 11 (17.5%) Placebo: 25 (39.7%) AD -0.22 (95% CI, -0.380 to -0.07) P=0.0039 MSSS Worst Score (LSM): Tradipitant 170 mg: 3.40 Placebo: 3.75 AD -0.35 (95% CI, -0.99 to -0.30) P=0.2936	ARR 22 / NNT 5 NA	Headache: Tradipitant 170 mg: 8 (12.7%) Placebo: 5 (7.9%) Somnolence: Tradipitant 170 mg: 17 (27%) Placebo: 8 (12.7%)		**Risk of Bias (low/high/unclear)**: Selection Bias: (Low) Assigned in a ratio 1:1:1 by an Interactive Web Response System. Performance Bias: (Unclear) Stated as double-blind but not described. Detection Bias: (Unclear) Somnolence associated with tradipitant may lead to unblinding. Attrition Bias: (Low) There was no attrition as only one dose was given. Reporting Bias: (Low) The trial was conducted as stated. Other Bias: (Unclear) Funded by manufacturer and role in study was not described. **Applicability**: Patient: Results are most applicable to female participants who are otherwise healthy and middle aged. Intervention: The tradipitant had been previously shown to have efficacy in nausea and vomiting at study doses. Comparator: An active comparator, such as meclizine or scopolamine, would inform comparative efficacy. Outcomes: Outcomes are appropriate for motion sickness. Setting: Pacific Ocean near Los Angeles, California.

Key: *Measured every 30 minutes during 4-hour trips.

Abbreviations: AD = absolute difference; ARR = absolute risk reduction; BMI = body mass index; CI = confidence interval; DB = double-blind; ITT = intention to treat; LSM = least square mean; m = meter; mITT = modified intention to treat; MSAQ = Motion Sickness Assessment Questionnaire; MSEQ = Motion Sickness Eligibility Questionnaire; MSSS = Motion Sickness Severity Scale; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; PGI-S = Patient Global Impression Severity Questionnaire; PP = per protocol; RCT = randomized controlled trial.

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30. Navitrux (fosaprepitant IV)[prescribing information]. New Jersey; Avyxa Pharma, LLC. June 2026.

31. Posfrea (palonosetron injection) [prescribing information]. New Jersey; Avyxa Pharma, LLC. April 2025.

32. Sustol (granistetron injection) [prescring information]. Cary, NC; Heron Therapeutics, Inc. February 2026.

33. Reglan (metoclopramide) [prescribing information]. Baudette, MN; ANI Pharmaceuticals. February 2026.

34. Zofran (ondansetron) [prescribing information]. Research Triangle Park, NC. October 2016.

35. Transderm Scop (scopolamine trandermal system)[prescribing information]. Warren, NJ; GSK Consumer Healthcare. March 2019.

Appendix 1: Current Preferred Drug List

Conventional Antiemetics

Generic	Brand	Form	PDL
metoclopramide HCl	METOCLOPRAMIDE HCL INTENSOL	ORAL CONC	Y
metoclopramide HCl	METOCLOPRAMIDE HCL	SOLUTION	Y
metoclopramide HCl	METOCLOPRAMIDE HCL	TABLET	Y
metoclopramide HCl	REGLAN	TABLET	Y
phosphorated carbo(dext-fruct)	ANTI-NAUSEA	SOLUTION	Y
phosphorated carbo(dext-fruct)	NAUSEA RELIEF	SOLUTION	Y
prochlorperazine	COMPRO	SUPP.RECT	Y
prochlorperazine edisylate	COMPAZINE	SYRUP	Y
prochlorperazine maleate	PROCHLORPERAZINE	TABLET	Y
prochlorperazine maleate	PROCHLORPERAZINE MALEATE	TABLET	Y
promethazine HCl	PROMETHAZINE HCL	SUPP.RECT	Y
promethazine HCl	PROMETHAZINE HCL	SYRUP	Y

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promethazine HCl	PROMETHAZINE HCL	TABLET	Y
dimenhydrinate	DRIMINATE	TABLET	N
dimenhydrinate	MOTION SICKNESS	TABLET	N
dimenhydrinate	MOTION SICKNESS RELIEF	TABLET	N
dronabinol	DRONABINOL	CAPSULE	N
dronabinol	MARINOL	CAPSULE	N
dronabinol	DRONABINOL	SOLUTION	N
meclizine HCl	ANTIVERT	TAB CHEW	N
meclizine HCl	MECLIZINE HCL	TAB CHEW	N
meclizine HCl	MECLIZINE HCL	TAB CHEW	N
meclizine HCl	MOTION SICKNESS	TAB CHEW	N
meclizine HCl	MOTION SICKNESS RELIEF	TAB CHEW	N
meclizine HCl	MOTION-TIME	TAB CHEW	N
meclizine HCl	TRAVEL EASE	TAB CHEW	N
meclizine HCl	MECLIZINE HCL	TABLET	N
meclizine HCl	MECLIZINE HCL	TABLET	N
meclizine HCl	MOTION SICKNESS	TABLET	N
meclizine HCl	MOTION SICKNESS RELIEF	TABLET	N
metoclopramide HCl	GIMOTI	SPRAY/PUMP	N
scopolamine	SCOPOLAMINE	PATCH TD 3	N
scopolamine	TRANSDERM-SCOP	PATCH TD 3	N
trimethobenzamide HCl	TRIMETHOBENZAMIDE HCL	CAPSULE	N
dimenhydrinate	DIMENHYDRINATE	VIAL	
meclizine HCl	ANTIVERT	TABLET	
meclizine HCl	MECLIZINE HCL	TABLET	
metoclopramide HCl	METOCLOPRAMIDE HCL	SYRINGE	
metoclopramide HCl	METOCLOPRAMIDE HCL	VIAL	
prochlorperazine edisylate	COMPAZINE	VIAL	
prochlorperazine edisylate	PROCHLORPERAZINE EDISYLATE	VIAL	
promethazine HCl	PHENERGAN	AMPUL	
promethazine HCl	PROMETHAZINE HCL	AMPUL	
promethazine HCl	ANERGAN 50	VIAL	
promethazine HCl	PHENERGAN	VIAL	
promethazine HCl	PROMETHAZINE HCL	VIAL	
trimethobenzamide HCl	TIGAN	VIAL	

Newer Antiemetics

Generic	Brand	Form	PDL
ondansetron	ONDANSETRON ODT	TAB RAPDIS	Y
ondansetron HCl	ONDANSETRON HCL	SOLUTION	Y

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ondansetron HCl	ONDANSETRON HCL	TABLET	Y
aprepitant	APREPITANT	CAP DS PK	N
aprepitant	EMEND	CAP DS PK	N
aprepitant	APREPITANT	CAPSULE	N
aprepitant	EMEND	CAPSULE	N
aprepitant	EMEND	SUSP RECON	N
dolasetron mesylate	ANZEMET	TABLET	N
doxylamine succinate/vit B6	BONJESTA	TAB IR DR	N
doxylamine succinate/vit B6	DICLEGIS	TABLET DR	N
doxylamine succinate/vit B6	DOXYLAMINE SUCC-PYRIDOXINE HCL	TABLET DR	N
granisetron	SUSTOL	LIQ ER SYR	N
granisetron	SANCUSO	PATCH TDWK	N
granisetron HCl	GRANISOL	SOLUTION	N
granisetron HCl	GRANISETRON HCL	TABLET	N
netupitant/palonosetron HCl	AKYNZEO	CAPSULE	N
ondansetron	ONDANSETRON ODT	TAB RAPDIS	N
tradipitant	NEREUS	CAPSULE	N
amisulpride	BARHEMSYS	VIAL	
aprepitant	APONVIE	VIAL	
aprepitant	CINVANTI	VIAL	
fosaprepitant dimeglumine	EMEND	VIAL	
fosaprepitant dimeglumine	FOCINVEZ	VIAL	
fosaprepitant dimeglumine	FOSAPREPITANT DIMEGLUMINE	VIAL	
fosaprepitant dimeglumine	NAVITRUX	VIAL	
fosnetupitant/palonosetron	AKYNZEO	VIAL	
granisetron HCl	GRANISETRON HCL	VIAL	
granisetron HCl/PF	GRANISETRON HCL	VIAL	
ondansetron HCl	ONDANSETRON HCL	VIAL	
ondansetron HCl/PF	ONDANSETRON HCL	SYRINGE	
ondansetron HCl/PF	ONDANSETRON HCL	VIAL	
palonosetron HCl	PALONOSETRON HCL	SYRINGE	
palonosetron HCl	PALONOSETRON HCL	VIAL	
palonosetron HCl	POSFREA	VIAL	

Appendix 2: Abstracts of Comparative Clinical Trials
Not applicable

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Appendix 3: Medline Search Strategy

Conventional Antiemetics

Database(s): **Ovid MEDLINE(R) ALL** 1946 to August 25, 2026
Search Strategy:

#	Searches	Results
1	metoclopramide.mp. or Metoclopramide/	7708
2	phosphorated carbohydrate solution.mp.	4
3	Prochlorperazine/ or prochlorperazine.mp.	1520
4	Promethazine/ or promethazine.mp.	4288
5	Dimenhydrinate/ or dimenhydrinate.mp.	679
6	dronabinol.mp. or Dronabinol/	9657
7	Meclizine/ or meclizine.mp.	411
8	scopolamine.mp. or Scopolamine/	13548
9	trimethobenzamide.mp.	114
10	Meclizine/ or meclizine.mp.	411
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	36898
12	limit 11 to (english language and humans and yr="2017 -Current")	3804
13	limit 12 to (clinical trial, phase iii or guideline or meta analysis or practice guideline or "systematic review")	263

Newer Antiemetics

Database(s): **Ovid MEDLINE(R) ALL** 1946 to August 26, 2026
Search Strategy:

#	Searches	Results
1	ondansetron.mp. or Ondansetron/	5935
2	Aprepitant/ or aprepitant.mp.	1475

3	dolasetron.mp.	314
4	doxylamine.mp. or Doxylamine/	588
5	granisetron.mp. or Granisetron/	1909
6	netupitant.mp.	226
7	tradipitant.mp.	21
8	Amisulpride/ or amisulpride.mp.	1629
9	fosaprepitant.mp.	270
10	fosnetupitant.mp.	42
11	palonosetron.mp. or Palonosetron/	968
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	11305
13	limit 12 to (english language and humans and yr="2020 -Current")	1408
14	limit 13 to (clinical trial, phase iii or guideline or meta analysis or practice guideline or "systematic review")	170

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Appendix 4: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NEREUS safely and effectively. See full prescribing information for NEREUS.

NEREUS™ (tradipitant) capsules, for oral use
Initial U.S. Approval: 2025

INDICATIONS AND USAGE

NEREUS is a substance P/neurokinin-1 (NK-1) receptor antagonist indicated for the prevention of vomiting induced by motion in adults. (1)

DOSAGE AND ADMINISTRATION

- The recommended dosage of NEREUS is 85 mg or 170 mg as a single oral dose approximately 60 minutes before an event expected to cause vomiting induced by motion. The safety of NEREUS for the prevention of vomiting induced by motion in adults for more than 90 doses has not been established in clinical trials. (2.1)
- The maximum dosage in a 24-hour period is a single dose of 85 mg or 170 mg. (2.1)
- Administer on an empty stomach, at least 1 hour prior to or 2 hours after a full meal. (2.1)

DOSAGE FORMS AND STRENGTHS

Capsules: 85 mg (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

Effects on the Ability to Drive or Operate Machinery: May impair mental and/or physical abilities required for driving a motor vehicle or operating heavy machinery. Concomitant use of other drugs that cause central nervous system depression and strong CYP3A4 inhibitors may increase this effect. If concomitant use is unavoidable, warn patients against driving and other activities requiring complete mental alertness. (5.1, 7.1)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5%) are: somnolence, headache, and fatigue. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Vanda Pharmaceuticals Inc. at 1-844-438-5469 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

Strong CYP3A4 Inhibitors: May increase tradipitant exposure and the risk of adverse reactions. (7.1)

USE IN SPECIFIC POPULATIONS

Lactation: Monitor breastfed infants for somnolence. (8.2)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2025

Appendix 5. Pharmacology and Pharmacokinetic Properties.

Parameter	
Mechanism of Action	P/neurokinin-1 (NK1) antagonist
Oral Bioavailability	Not studied
Distribution and Protein Binding	1956 Liters 96-99% protein bound
Elimination	80% feces and 7% in the urine
Half-Life	34 hours
Metabolism	Non-CYP450-mediated processes and CYP enzymes (CYP3A4, CYP2C19, and to a lesser extent by CYP2C8) are involved in the metabolism of tradipitant. Tradipitant is also glucuronidated by UGT1A4 and UGT2B7.

Abbreviations: CYP = cytochrome; UGT = glucuronosyltransferase

Appendix 6: Key Inclusion Criteria

Population	Patients with CINV, PONV, cyclic vomiting syndrome and pregnancy related nausea and vomiting
Intervention	Antiemetics
Comparator	Active treatment comparison or placebo
Outcomes	Complete response, proportion of patients with no nausea, proportion of patients with no vomiting
Setting	Outpatient and short-term hospitalization
Abbreviations: CINV = chemotherapy induced nausea and vomiting, PONV = post-operative nausea and vomiting	

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Antiemetics

Goal(s):

- Promote use of preferred antiemetics.
- Restrict use of costly antiemetic agents for appropriate indications.

Length of Authorization:

- Up to 6 months

Requires PA:

- Non-preferred drugs (oral and topical) will be subject to PA criteria.

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What is the diagnosis being treated?	Record ICD10 Code.	
2. Will the prescriber consider a change to the preferred product? Message: • Preferred products do not require a PA. • Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of covered alternatives in class.	**No:** Go to #3

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3. Is the request for doxylamine/pyridoxine (Diclegis® or Bonjesta) for pregnancy-related nausea or vomiting?	**Yes:** Go to #4	**No:** Go to #5
4. Has the patient failed a trial of pyridoxine? Message: • Preferred vitamin B products do not require a PA. • Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Approve for up to 9~~3~~ months	**No:** Pass to RPh; deny and recommend a trial of pyridoxine.
5. Is the request for dronabinol (Marinol®)?	**Yes:** Go to #6	**No:** Go to #7
6. Does the patient have anorexia associated with HIV/AIDS?	**Yes:** Approve for up to 6 months.*	**No:** Go to #7
7. Does the patient have a cancer diagnosis AND receiving chemotherapy or radiation?	**Yes:** Approve for up to 6 months.	**No:** Go to #8
8. Does patient have refractory nausea/vomiting that has resulted in hospitalizations or ED visits?	**Yes:** Approve for up to 6 months.*	**No:** Go to #9
9. Has the patient tried and failed, or have contraindications, to at least 2 preferred antiemetics?	**Yes:** Approve for up to 6 months.*	**No:** Pass to RPh. Deny; medical appropriateness. Must trial at least 2 preferred antiemetics
* If the request is for dronabinol (Marinol®) do not exceed 3 doses/day for 2.5 mg and 5 mg strengths and 2 doses/day for the 10 mg strength.		