Drug and Biologic Coverage Policy

Effective Date **05/30/2025**
Coverage Policy Number **1705**

Antiemetic Therapy

Table of Contents

Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

Antiemetic Therapy includes the following products:

- **Akynzeo®** (palonosetron/netupitant) capsule
- **Anzemet®** (dolasetron) tablets
- **Emend®** (aprepitant) suspension
- **Sancuso®** (granisetron) transdermal
- **Varubi®** (rolapitant) tablet

This policy addresses the use of Antiemetic Therapy. Coverage for Antiemetic Therapy products may require the use of preferred or generic products according to the customer's benefit plan. Refer to the customer's benefit plan document for coverage details.

Antiemetic Therapy is considered medically necessary when the following criteria are met:

Drug	Criteria for Use
Akynzeo (palonosetron/ netupitant) capsule	**Considered as medically necessary for an adult in combination with dexamethasone for the prevention of nausea and vomiting for intravenous antineoplastic therapy meeting either of the following:** • High emetic risk • Moderate emetic risk *When criteria are met, a maximum of 4 capsules will be allowed per 28 days.*
Anzemet (dolasetron) tablet	Considered as medically necessary for the prevention of nausea and vomiting and treatment of breakthrough nausea and vomiting associated with low, moderate, and highly emetogenic cancer therapy

Emend (aprepitant) suspension	**Considered as medically necessary in an adult when both of the following are met:**
	• **ONE** of the following:
	  ○ Prevention of nausea and vomiting in combination with dexamethasone and a serotonin (5-HT_3) receptor antagonist for intravenous antineoplastic therapy that has high or moderate emetic risk
	  ○ Prevention of post-operative nausea and vomiting (PONV) in an adult
	• Documented intolerance or inability to use generic aprepitant capsules
	
	Considered as medically necessary in a pediatric individual when both of the following are met:
	• Prevention of nausea and vomiting associated with cancer chemotherapy in combination with a serotonin (5-HT_3) receptor antagonist
	• For individuals 12 years of age and older: Documented intolerance or inability to use generic aprepitant capsules
	
	When criteria are met, the following maximum quantities will be allowed:
	• *Suspension: 12 packets per 28 days (3 packets per week)*

Sancuso (granisetron) transdermal	**Considered as medically necessary for an adult for either of the following:**
	• Prevention of nausea and vomiting for either of the following:
	  ○ High or moderate emetic risk intravenous antineoplastic therapy in combination with dexamethasone
	  ○ High or moderate emetic risk oral antineoplastic therapy
	• Breakthrough treatment of chemotherapy-induced nausea/vomiting
	
	When criteria are met, a maximum of 4 patches will be allowed per 30 days.

Varubi (rolapitant) tablet	**Considered as medically necessary for an adult in combination with dexamethasone and a serotonin (5-HT_3) receptor antagonist for the prevention of nausea and vomiting for intravenous antineoplastic therapy meeting either of the following:** • High emetic risk • Moderate emetic risk *When criteria are met, a maximum of 4 tablets (2 doses) will be allowed per 28 days.*

Initial and reauthorization is up to 12 months.

Antiemetic Therapy is considered experimental, investigational or unproven for ANY other use.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

FDA Approved Indications

FDA Approved Indication

Product	FDA Approved Indication

Akynzeo (palonosetron/ fosnetupitant) capsule	Akynzeo capsules is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Akynzeo capsules is a combination of palonosetron and netupitant: palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.
Anzemet (dolasetron) tablet	Anzemet tablets are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses in adults and children 2 years and older.
Emend (aprepitant) suspension	**Prevention of Chemotherapy Induced Nausea and Vomiting (CINV)** Emend for oral suspension, in combination with other antiemetic agents, is indicated in patients 6 months of age and older 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. • nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). Emend capsules, in combination with other antiemetic agents, is indicated in patients 12 years of age and older 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. • nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). **Prevention of Postoperative Nausea and Vomiting (PONV)** Emend capsules are indicated in adults for the prevention of postoperative nausea and vomiting. **Limitations of Use** • Emend has not been studied for the treatment of established nausea and vomiting. • Chronic continuous administration of Emend is not recommended because it has not been studied, and because the drug interaction profile may change during chronic continuous use.
Sancuso (granisetron) transdermal	Sancuso (Granisetron Transdermal System) is indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration.
Varubi (rolapitant) tablet	Varubi is indicated in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

Recommended Dosing

FDA Recommended Dosing

Product	FDA Recommended Dosing

Akynzeo (palonosetron/ fosnetupitant) capsule

The recommended dosages of Akynzeo and dexamethasone in adults for the prevention of nausea and vomiting associated with administration of emetogenic chemotherapy are shown in Table 1.

Akynzeo capsules can be taken with or without food.

Table 1: Antiemetic Treatment Regimen

Treatment Regimen	Day 1		Days 2 to 4
Highly Emetogenic Chemotherapy, including Cisplatin-Based Chemotherapy			
Akynzeo capsules	1 capsule of Akynzeo	1 hour before chemotherapy	Dexamethasone 8 mg once a day
	Dexamethasone 12 mg	30 minutes before chemotherapy	
Anthracyclines and Cyclophosphamide-Based Chemotherapy and Chemotherapy Not Considered Highly Emetogenic			
Akynzeo capsules	1 capsule of Akynzeo	1 hour before chemotherapy	None
	Dexamethasone 12 mg	30 minutes before chemotherapy	

Anzemet (dolasetron) tablet

The recommended doses of Anzemet tablets should not be exceeded.

Adults
The recommended oral dosage of Anzemet (dolasetron mesylate) is 100 mg given within one hour before chemotherapy.

Pediatric Patients
The recommended oral dosage in pediatric patients 2 to 16 years of age is 1.8 mg/kg given within one hour before chemotherapy, up to a maximum of 100 mg. Safety and effectiveness in pediatric patients under 2 years of age have not been established.

In children for whom 100 mg is not appropriate based on their weight or ability to swallow tablets, the Anzemet injection solution may be mixed into apple or apple-grape juice for oral dosing in pediatric patients. The diluted product may be kept up to 2 hours at room temperature before use. However, Anzemet injection solution when administered intravenously is contraindicated in adult and pediatric patients for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy due to dose dependent QT prolongation.

Use in the Elderly, Renal Failure Patients, or Hepatically Impaired Patients
No dosage adjustment is recommended, however; ECG monitoring is recommended for elderly and renally impaired patients.

Emend (aprepitant) suspension

Prevention of Chemotherapy Induced Nausea and Vomiting (CINV)
Adults and Pediatric Patients 12 Years of Age and Older
For patients who cannot swallow oral capsules, Emend for oral suspension can be used instead of Emend capsules as shown in Table 3.

Table 1: Recommended Dosing for the Prevention of Nausea and Vomiting Associated with HEC

	Population	Day 1	Day 2	Day 3	Day 4
Dexamethasone	Adults	12 mg orally	8 mg orally	8 mg orally	8 mg orally
	Pediatric Patients 12 Years and Older	If a corticosteroid, such as dexamethasone, is co-administered, administer 50% of the recommended corticosteroid dose on Days 1 through 4. †			
5-HT_3 antagonist	Adults and Pediatric Patients 12 Years and Older	See selected 5-HT3 antagonist prescribing information for recommended dosage	None	None	None

†Administer dexamethasone 30 minutes prior to chemotherapy treatment on Day 1 and in the morning on Days 2 through 4. A 50% dosage reduction of dexamethasone is recommended to account for a drug interaction with Emend.

Table 2: Recommended Dosing for the Prevention of Nausea and Vomiting Associated with MEC

	Population	Day 1	Day 2	Day 3
Dexamethasone	Adults	12 mg orally	None	None
	Pediatric Patients 12 Years and Older	If a corticosteroid, such as dexamethasone, is coadministered, administer 50% of the recommended corticosteroid dose on Days 1 through 4.†		
5-HT_3 antagonist	Adults and Pediatric Patients 12 Years and Older	See selected 5-HT3 antagonist prescribing information for recommended dosage	None	None

†Administer dexamethasone 30 minutes prior to chemotherapy treatment on Day 1. A 50% dosage reduction of dexamethasone is recommended to account for a drug interaction with Emend.

Pediatric Patients 6 Months to less than 12 Years of Age or Pediatric and Adult Patients Unable to Swallow Capsules

The recommended dose of Emend for oral suspension to be administered with a 5-HT_3 antagonist, with or without a corticosteroid, for the prevention of nausea and vomiting associated with administration of HEC or MEC is specified in Table 3. Dosing of Emend for oral suspension is based on weight, to a maximum of 125 mg on Day 1 and 80 mg on Days 2 and 3. Dosing in pediatric patients less than 6 kg is not recommended.

Table 3: Recommended Dosing in Pediatric Patients 6 Months to Less than 12 Years of Age or Pediatric and Adult Patients Unable to Swallow Capsules

	Population	Day 1	Day 2	Day 3	Day 4
Emend for oral suspension*	Pediatric Patients 6 Months to Less than 12 Years or Pediatric and Adult Patients Unable to Swallow Capsules	3 mg/kg orally Maximum dose 125 mg	2 mg/kg orally Maximum dose 80 mg	2 mg/kg orally Maximum dose 80 mg	None
Dexamethasone	Adults Unable to Swallow Capsules	See Table 1 or 2	See Table 1 or 2	See Table 1 or 2	See Table 1 or 2
	Pediatric Patients 6 Months to Less than 12 Years or Pediatric Patients Unable to Swallow Capsules	If a corticosteroid, such as dexamethasone, is coadministered, administer 50% of the recommended corticosteroid dose on Days 1 through 4.†			
5-HT_3 antagonist	Pediatric Patients 6 Months to Less than 12 Years or	See selected 5-HT3 antagonist prescribing information for	None	None	None

		Pediatric Patients Unable to Swallow Capsules	recommended dosage			

*After preparation, the final concentration of Emend for oral suspension is 25 mg/mL. Administer Emend for oral suspension 1 hour prior to chemotherapy treatment on Days 1, 2, and 3. If no chemotherapy is given on Days 2 and 3, administer Emend for oral suspension in the morning.
†Administer dexamethasone 30 minutes prior to chemotherapy treatment on Day 1. A 50% dosage reduction of dexamethasone is recommended to account for a drug interaction with Emend.

Prevention of Postoperative Nausea and Vomiting (PONV)
The recommended oral dosage of Emend capsules in adults is 40 mg within 3 hours prior to induction of anesthesia.

Sancuso (granisetron) transdermal

The transdermal system (patch) should be applied to clean, dry, intact healthy skin on the upper outer arm. Sancuso should not be placed on skin that is red, irritated, or damaged.

Each patch is packed in a pouch and should be applied directly after the pouch has been opened.

The patch should not be cut into pieces.

Adults
Apply a single patch to the upper outer arm a minimum of 24 hours before chemotherapy. The patch may be applied up to a maximum of 48 hours before chemotherapy as appropriate. Remove the patch a minimum of 24 hours after completion of chemotherapy. The patch can be worn for up to 7 days depending on the duration of the chemotherapy regimen.

Varubi (rolapitant) tablet

The recommended dosage of Varubi tablets in adults in combination with a 5-HT3 receptor antagonist and dexamethasone for the prevention of nausea and vomiting with emetogenic cancer chemotherapy is shown in Table 1. There is no drug interaction between rolapitant and dexamethasone, so no dosage adjustment for dexamethasone is required. Administer a dexamethasone dose of 20 mg on Day 1.

Administer Varubi prior to the initiation of each chemotherapy cycle, but at no less than 2 week intervals.

Administer Varubi tablets without regards to meals.

Table 1: Recommended Dosing Regimen of Varubi Tablets

	Day 1	Day 2	Day 3	Day 4
Prevention of Nausea and Vomiting Associated with Cisplatin-Based Highly Emetogenic Cancer Chemotherapy				
Varubi	Administer orally within 2 hours prior to initiation of chemotherapy 180 mg orally as a single dose	None		
Dexamethasone	20 mg; 30 min prior to initiation of chemotherapy	8 mg twice daily	8 mg twice daily	8 mg twice daily
5-HT_3 receptor antagonist	See the prescribing information for the co-administered 5-HT3 receptor	None		

		antagonist for appropriate dosing information.	
	Prevention of Nausea and Vomiting Associated with Moderately Emetogenic Cancer Chemotherapy and Combinations of Anthracycline and Cyclophosphamide		
	Varubi	Administer orally within 2 hours prior to initiation of chemotherapy 180 mg orally as a single dose	None
	Dexamethasone	20 mg; 30 min prior to initiation of chemotherapy	None
	5-HT_3 receptor antagonist	See the prescribing information for the co-administered 5-HT3 receptor antagonist for appropriate dosing information.	See the prescribing information for the co-administered 5-HT3 receptor antagonist for appropriate dosing information.

Drug Availability

Product	Drug Availability
Akynzeo (palonosetron/ fosnetupitant) capsule	Supplied as capsules containing 300 mg netupitant/0.5 mg palonosetron.
Anzemet (dolasetron) tablet	Supplied as tablets containing 50 mg dolasetron.
Emend (aprepitant) suspension	Supplied as powder for oral suspension in a single-use pouch containing 125 mg aprepitant.
Sancuso (granisetron) transdermal	Supplied as a 52 cm^2 patch containing 34.3 mg of granisetron.
Varubi (rolapitant) tablet	Supplied as tablets containing 90 mg rolapitant.

General Background

Pharmacology

Aprepitant (Emend, Cinvanti), fosaprepitant (Emend), and rolapitant (Varubi) are a substance P/neurokinin 1 (NK1) receptor antagonists. Palonosetron (Aloxi), granisetron (Sustol) are selective serotonin-3 (5-HT3) receptor antagonists. Akynzeo is a combination product of a 5-HT3 receptor antagonist (palonosetron) and an NK1 receptor antagonist (netupitant).

Professional Societies/Organizations

National Comprehensive Cancer Network (NCCN) provides recommendations for antiemetic therapy regimens based on the emetogenic risk of the chemotherapy and if it is intravenous or oral. The emetogenic risk of intravenous antineoplastics is based on the frequency of emesis. High emetic risk agents have a greater than

90% frequency of emesis (an example includes combination regimens that contain an anthracycline and cyclophosphamide). Moderate emetic risk has a 30-90% frequency of emesis while low emetic risk and minimal emetic risk have a 10-30% and less than 10% frequency of emesis, respectively. For oral antineoplastic agents, the levels are divided into those with moderate to high emetic risk (greater than or equal to 30% frequency of emesis) and minimal to low emetic risk (less than 30% frequency of emesis). (NCCN, 2019)

For high emetic risk intravenous (IV) chemotherapy, NCCN recommends several options for acute and delayed emesis prevention without a preference given to one regimen over another. Regimens recommended include either aprepitant oral or IV, fosaprepitant IV, or rolapitant oral in combination with a 5-HT3 receptor antagonist (palonosetron IV; granisetron subcutaneous [SQ], oral, IV or transdermal; or ondansetron oral or IV) with dexamethasone. Other options include netupitant/palonosetron oral in combination with dexamethasone; olanzapine oral with palonosetron IV and dexamethasone; or aprepitant oral or fosaprepitant IV in combination with a 5-HT3 receptor antagonist, dexamethasone, and olanzapine. (NCCN, 2019)

For moderate emetic risk IV chemotherapy, several options are recommended without preference for acute and delayed emesis prevention. One option recommends a 5-HT3 receptor antagonist in combination with dexamethasone. NCCN notes a preference for palonosetron IV or granisetron SQ when a 5-HT3 receptor antagonist is not used in combination with an NK1 antagonist. Other options include use of aprepitant oral or IV, fosaprepitant IV, rolapitant oral in combination with a 5-HT3 receptor antagonist and dexamethasone; netupitant/palonosetron oral in combination with dexamethasone; or olanzapine oral with palonosetron IV and dexamethasone. (NCCN, 2019)

Emesis prevention for low emetic risk IV chemotherapy includes use of dexamethasone; metoclopramide; prochlorperazine; or an oral 5-HT3 receptor antagonist. There is not routine prophylaxis recommended for minimal emetic risk IV chemotherapy. (NCCN, 2019)

For emesis prevention with oral chemotherapy, NCCN recommends a 5-HT3 receptor antagonist granisetron oral or transdermal; or ondansetron oral) for high to moderate emetic risk therapy. As needed treatment is recommended initially for low to minimal emetic risk with recommendations provided when nausea/vomiting is experienced. (NCCN, 2019)

If breakthrough chemotherapy-induced nausea and vomiting occurs, recommendations for subsequent chemotherapy cycles include changing the antiemetic regimen to a higher level for primary treatment. (NCCN, 2019)

Off Label Uses

AHFS Drug Information 2019 Edition does not support any off-label uses of aprepitant, fosaprepitant, granisetron, palonosetron, palonosetron/fosnetupitant, or rolapitant.

References

1. Akynzeo (netupitant and palonosetron) [product information]. Iselin, NJ; Helsinn Therapeutics (U.S.), Inc. April 2018.
2. Centers for Medicare & Medicaid Services (CMS). National Coverage Determinations (NCD): Aprepitant for Chemotherapy-Induced Emesis. Available at URL address: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=309&ver=2. May 29, 2013. Accessed September 17, 2019.
3. McEvoy GK, ed. American Hospital Formulary Service 2017 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc. 2017.
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Antiemesis V1.2019; [available with free subscription] https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Updated February 28, 2019. Accessed September 16, 2019.
5. Sancuso (granisetron transdermal system) [product information]. Bedminster, NJ; Kyowa Kirin. January 2017.
6. Tesaro, Inc. Varubi (rolapitant) tablets, for oral use [product information]. Waltham, MA; Tesaro, Inc. March 2018.

Revision Details

Type of Revision	Summary of Changes	Date

Selected Revision	**Removed** Emend capsule medical necessity criteria from the policy.	01/01/2025
Selected Revision	**Removed** Akynzeo injection, Aloxi injection, Cinvanti, injection, Emend injection, Sustol injection, Zofran solution, Zofran tablets, Zofran ODT and Zuplenz film medical necessity criteria from the policy.	05/30/2025

The policy effective date is in force until updated or retired.