

DRUG QUANTITY MANAGEMENT POLICY – PER RX

POLICY: netupitant and palonosetron capsules (Akynzeo® – Eisai)
aprepitant capsules and powder packet (Emend® – Merck, generics-
capsules only)
rolapitant tablets (Varubi™ – Tesaro)
Dispensing limit

DATE REVIEWED: 07/27/2020

DESCRIPTION

As substance P/neurokinin 1 (NK1) receptor antagonists, Akynzeo and Emend are indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy.^{1,5} Varubi is also a substance P/NK1 receptor antagonist and is indicated for the prevention of delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy.⁶ Nausea and vomiting can have an acute onset (within a few minutes to several hours after drug administration) or delayed onset (developing more than 24 hours after chemotherapy administration).²

Once nausea and vomiting occur, it is very difficult to treat and therefore, prevention is the goal. Patients receiving high emetic risk chemotherapy are at risk for three days following each dose, and guidelines recommend protection for the duration of the risk period. Likewise, for moderate emetic risk chemotherapy, protection is recommended for two days following the last dose of chemotherapy.²

Decisions about the combinations of medications within an antiemetic regimen are individualized for each patient. A prescriber accounts for the emetic risk of the chemotherapy/radiation, pharmacology of each medication, and patient-specific factors, such as, prior experience, labs, disease states, concomitant medications, and psychological factors.²

NATIONAL COMPREHENSIVE CANCER NETWORK (NCCN) GUIDELINES²

The preferred treatment option for **high emetic risk intravenous (IV) chemotherapy**, a serotonin receptor antagonist (5-HT3 antagonist), a neurokinin-1 receptor antagonist (NK1), plus dexamethasone and olanzapine, are given on day one, and another drug is also given to cover delayed nausea and vomiting over the next two through four days. **For moderate emetic risk IV chemotherapy**, the patient receives a 5-HT3 antagonist (and other agents in the regimen, such as a steroid) for three days (if an extended duration product such as Aloxi IV or Sancuso was not given on day 1). The use of a NK1 antagonist can also be used in combination with 5-HT3 antagonists and steroids. **High to moderate emetic risk oral chemotherapy** regimens consist solely of oral 5-HT3 antagonists. Therapy is given once daily starting prior to chemotherapy administration and continuing daily to cover the delayed emesis protection period.

QUANTITY LIMIT

The per Rx Drug Quantity Management program is intended to provide coverage for NK1 receptor antagonists in accord with labeling and NCCN dosing recommendations for high to moderate emetic risk **IV** chemotherapy. For example, coverage for oral Emend capsules is provided for a total of three days of therapy. This provides coverage for one day of chemotherapy, followed by two days of protection after the last dose of chemotherapy. Exceptions are generally made for patients receiving multiple courses or more than one day of chemotherapy in any one month (30 day) period. Akynzeo, Emend, and Varubi have not been studied for the treatment of established nausea and vomiting. Chronic continuous use for

prevention of nausea and vomiting is not recommended because there are no data and because the drug interaction profile may change during chronic continuous use.¹

Akynzeo 300 mg/0.5 mg	Maximum quantity per RX = 1 capsule
Emend 40 mg	Maximum quantity per RX = 1 capsule
Emend 80 mg, Emend 80 mg BiPack	Maximum quantity per RX = 2 capsules (1 BiPack)
Emend 125 mg	Maximum quantity per RX = 1 capsule
Emend 125 mg oral suspension single-dose kit	Maximum quantity per RX – 3 kits
Emend TriPack	Maximum quantity per RX = 1 pack
Varubi 90 mg	Maximum quantity per RX = 2 tablets (1 package)

Akynzeo is available in a blister pack containing one capsule. Akynzeo is a fixed combination capsule with palonosetron and is given as a single dose one hour before chemotherapy. For highly-emetogenic chemotherapy, dexamethasone is also recommended to be given on days 1 through 4; dexamethasone is only recommended on day one for regimens that are not considered highly emetogenic. The safety and effectiveness of Akynzeo has been established for up to 8 cycles highly and moderately emetogenic chemotherapy per month. One capsule per dispensing is sufficient per one-day course of chemotherapy.

Emend 40 mg is available in a unit-of-use package of one. The recommended dose of Emend for the prevention of postoperative nausea and vomiting is 40 mg within 3 hours prior to induction of anesthesia. One capsule per dispensing will accommodate one surgery and additional surgeries will require additional copayments.

Emend 125 mg and 80 mg capsules are available as individual capsules or in a unit-of-use TriPack containing one 125 mg capsule and two 80 mg capsules. The 80 mg capsules are also available as a BiPack containing two 80 mg capsules. Emend 125 mg powder for oral suspension is available in a single-use pouch. These strengths of Emend are given as part of a 3-day regimen for prevention of chemotherapy-induced nausea and vomiting (CINV) that also includes administering a corticosteroid and a serotonin (5-HT₃) receptor antagonist. The recommended dose of Emend for the prevention of CINV is 125 mg oral capsule or suspension given 1 hour before chemotherapy (day 1) and 80 mg oral capsule or suspension once daily in the morning on days 2 and 3. ASCO and NCCN guidelines suggest that aprepitant may have a role in preventing nausea and vomiting for patients receiving multiday emetogenic chemotherapy regimens by extending oral Emend to days 4 and 5.² Further data suggest that Emend may be effective for delayed effects of multiday chemotherapy when started on day 3 and continued through day 7.³ The safety and effectiveness of Emend has been established for up to 6 cycles highly emetogenic chemotherapy per month. One of the Emend 125 mg and two of the 80 mg capsules (or one tri-fold pack) or three Emend 125 mg single-use powder for oral suspension packets are sufficient per course of chemotherapy.

Varubi 90 mg tablets are available as a unit-of-use blister package containing two 90 mg tablets. These tablets are both taken on Day 1 as part of a three to four day regimen for prevention of delayed CINV that also includes administering a corticosteroid and a serotonin (5-HT₃) receptor antagonist. The recommended dose of Varubi for the prevention of CINV is 180 mg given 1 to 2 hours before chemotherapy (day 1). The safety and effectiveness of Varubi has been established for up to 6 cycles highly and moderately emetogenic chemotherapy per month.

CRITERIA

All approvals are provided for 12 months in duration unless otherwise noted below.

Akynzeo 300 mg/0.5 mg

1. Patient is receiving Akynzeo for the prevention of nausea and vomiting associated with multiple courses of cancer chemotherapy within one month. Approve the quantity requested, not to exceed a total of 8 capsules per dispensing.
2. An override is not recommended for other indications (e.g., prevention of radiation-induced nausea and vomiting, prevention or treatment of postoperative nausea and vomiting, as needed for nausea and vomiting after chemotherapy, vertigo or motion-induced nausea and vomiting, opioid-induced nausea and vomiting, pregnancy-induced nausea and vomiting).

Emend 40 mg

Recommended **no** overrides to this quantity limit.

Emend 80 mg, Emend 80 mg BiPack

Emend 125 mg

1. Patient is receiving Emend for the prevention of nausea and vomiting associated with multiple courses or multiple days of cancer chemotherapy within one month. Approve the quantity requested, not to exceed a total of 6 of the 125 mg capsules per dispensing or 12 of the 80 mg capsules per dispensing (or 6 BiPacks, each BiPack consists of two 80 mg capsules).
2. An override is not recommended for other indications (e.g., prevention of radiation-induced nausea and vomiting, prevention or treatment of postoperative nausea and vomiting, as needed for nausea and vomiting after chemotherapy, vertigo or motion-induced nausea and vomiting, opioid-induced nausea and vomiting, pregnancy-induced nausea and vomiting).

Emend 125 mg for oral suspension single-dose kit

3. Patient is receiving Emend for the prevention of nausea and vomiting associated with multiple courses or multiple days of cancer chemotherapy within one month. Approve the quantity requested, not to exceed a total of 18 of the 125 mg packets per dispensing..
4. An override is not recommended for other indications (e.g., prevention of radiation-induced nausea and vomiting, prevention or treatment of postoperative nausea and vomiting, as needed for nausea and vomiting after chemotherapy, vertigo or motion-induced nausea and vomiting, opioid-induced nausea and vomiting, pregnancy-induced nausea and vomiting).

Emend TriPack

1. Patient is receiving Emend for the prevention of nausea and vomiting associated with multiple courses of cancer chemotherapy within one month. Approve the quantity requested, not to exceed a total of 6 TriPacks per dispensing (18 tablets; each pack consists of one 125 mg capsule and two 80 mg capsules). **NOTE:** for multiday regimens, refer to the individual 80 mg capsules or BiPacks.
2. An override is not recommended for other indications (e.g., prevention of radiation-induced nausea and vomiting, prevention or treatment of postoperative nausea and vomiting, as needed for nausea and vomiting after chemotherapy, vertigo or motion-induced nausea and vomiting, opioid-induced nausea and vomiting, pregnancy-induced nausea and vomiting).
3. An override is not recommended for additional days of therapy for delayed nausea and vomiting for non-FDA approved indications (note: chemotherapy is an FDA approved indication).

Varubi 90 mg

1. Patient is receiving Varubi for the prevention of nausea and vomiting associated with multiple courses of cancer chemotherapy within one month. Approve the quantity requested, not to exceed a total of 12 tablets (6 packages) per dispensing.
2. An override is not recommended for other indications (e.g., prevention of radiation-induced nausea and vomiting, prevention or treatment of postoperative nausea and vomiting, as needed for nausea and vomiting after chemotherapy, vertigo or motion-induced nausea and vomiting, opioid-induced nausea and vomiting, pregnancy-induced nausea and vomiting).

REFERENCES

1. Emend[®] capsules, oral suspension powder [prescribing information]. Whitehouse Station, NJ: Merck & Co., Inc.; November 2019.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 2.2020. Antiemesis. Accessed on 07/27/2020 at http://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf.
3. Roila F, Molassiotis A, Herrstedt J, et al. 2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. *Annals of Oncology* 27 (Supplement 5): v119-v133, 2016.
4. Hesketh PJ, Bohlke K, Lyman GH, et al. Antiemetics: American Society of Clinical Oncology (ASCO) Clinical Practice Guideline Update. *J Clin Oncol* 34:381-386. . Accessed July 27, 2020. Available from URL: <http://ascopubs.org/doi/pdfdirect/10.1200/JCO.2015.64.3635>.
5. Akynzeo[®] capsules [prescribing information]. Iselin, NJ: Helsinn Therapeutics (U.S.), Inc.; May 2020.
6. Varubi[™] tablets [prescribing information]. Waltham, MA: Tesaro, Inc.; September 2018.