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Section:	Prescription Drugs	**Effective Date:**	July 1, 2023
Subsection:	Gastrointestinal Agents	**Original Policy Date:**	February 27, 2015
Subject:	NK1 Antagonists	**Page:**	1 of 8

Last Review Date: June 15, 2023

NK1 Antagonists

Description

Akynzeo capsules, (netupitant palonosetron), Akynzeo injection (fosnetupitant palonosetron), Cinvanti, Emend (aprepitant), Emend injection (fosaprepitant), Varubi (rolapitant)

Background
Cinvanti, Emend, Akynzeo, and Varubi are antiemetics which work by antagonizing the action of substance P at the neurokinin 1 (NK1) receptor. NK1 antagonists are used to help prevent the nausea and vomiting that happens acutely or which is delayed following the administration of certain anti-cancer medicines (chemotherapy) and can also be used in the prevention of postoperative nausea and vomiting (1).

Regulatory Status
FDA-approved indications:

Akynzeo capsules and injection (1)
Akynzeo is a fixed combination of netupitant, a substance P/ neurokinin 1 (NK1) receptor antagonist, and palonosetron, a serotonin-3 (5-HT3) receptor antagonist indicated for:

a. 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 for injection is a combination of fosnetupitant and palonosetron indicated for:

a. Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy.

Emend oral suspension (2)

1. In combination with other antiemetic agents, in patients 6 months of age and older for the:
    a. Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin
    b. Prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

Emend capsules (2)

1. In combination with other antiemetic agents, in patients 12 years of age and older for the:
    a. Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin
    b. Prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

2. For the prevention of postoperative nausea and vomiting (PONV)

Emend injection (3)

1. Indicated for adults and pediatric patients 6 months of age and older, in combination with other antiemetic agents for the:
    a. Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin
    b. Prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

Cinvanti injection (4)

2. Indicated for adults, in combination with other antiemetic agents for the:
    a. Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin

b. Prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

Varubi tablets and vials (5)

1. Varubi is indicated in combination with other antiemetic agents in adults for:
   a. 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

Limitations of Use:

1. Akynzeo for injection has not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy (1).
2. Emend is not used to treat nausea and vomiting that the patient already has and should not be used continuously for a long time (chronic use) (2-3).
3. Cinvanti has not been studied for treatment of established nausea and vomiting (4).

Related policies
5HT3 Antagonists, Barhemsys, Cannabinoids

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

NK1 Antagonists may be considered **medically necessary** if the conditions indicated below are met.

NK1 Antagonists may be considered **investigational** for all other indications.

Prior-Approval Requirements

Prior authorization is not required if prescribed by an oncologist and/or the member has paid pharmacy claims for an oncology medication(s) in the past 6 months

Akynzeo capsules and injection

Diagnosis

Patient must have the following:

1. Prevention of acute or delayed nausea and vomiting
    a. 18 years of age or older
    b. Undergoing chemotherapy for cancer
        i. **Akynzeo injection only**: chemotherapy is highly emetogenic
    c. Administered with dexamethasone
    d. Absence of severe renal impairment (eGFR less than 30 ml/min/1.73m^2) or end state renal disease (ESRD)
    e. Absence of severe hepatic impairment (Child-Pugh Class C)

Emend oral suspension and Emend Injection

Diagnosis

Patient must have the following:

1. Prevention of acute or delayed nausea and vomiting
    a. 6 months of age or older
    b. Undergoing chemotherapy for cancer
    c. Used in combination with other antiemetic

Emend capsules

Diagnoses

Patient must have **ONE** of the following:

1. Prevention of acute or delayed nausea and vomiting
    a. 12 years of age or older
    b. Undergoing chemotherapy for cancer
    c. Used in combination with other antiemetic

2. Postoperative nausea and vomiting (PONV)
    a. 18 years of age or older

Cinvanti Injection

Diagnosis

Patient must have the following:

1. Prevention of acute or delayed nausea and vomiting
    a. 18 years of age or older
    b. Undergoing chemotherapy for cancer
    c. Used in combination with other antiemetic

Varubi tablets and vials

Diagnosis

Patient must have the following:

1. Prevention of delayed nausea and vomiting
    a. 18 years of age or older
    b. Undergoing chemotherapy for cancer
    c. Administered with dexamethasone and a 5-HT3 receptor antagonist
    d. Absence of severe hepatic impairment (Child-Pugh Class C)

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

Quantity

Medication	Quantity Limit
Emend 40 mg	1 capsules per 90 days
Emend 80 mg	12 capsules per 90 days
Emend 125 mg	6 capsules per 90 days
Emend Bi-pack (contains two 80 mg caps)	6 packs per 90 days
Emend Tri-pack (contains one 125 mg and two 80 mg)	6 packs per 90 days
Emend 125 mg suspension	6 kits per 90 days
Emend 150 mg injection	6 vials per 90 days
Cinvanti 130 mg injection	6 vials per 90 days
Akynzeo 300 mg/0.5 mg capsules	6 capsules per 90 days
Akynzeo 235 mg/0.25 mg injection	6 vials per 90 days

Varubi 90 mg tablets	12 tablets per 90 days
Varubi 166.5 mg/92.5 mL (vial)	6 vials per 90 days

**Quantities are based 2 chemotherapy treatments per month

Prior - Approval Limits

Quantity

Postoperative nausea and vomiting

Medication	Quantity Limit
Emend 40 mg	5 capsules per 90 days

Acute or Delayed nausea and vomiting

Medication	Quantity Limit
Emend 80 mg	48 capsules per 90 days **OR**
Emend 125 mg	12 capsules per 90 days **OR**
Emend Bi-pack (contains two 80 mg caps)	24 packs per 90 days **OR**
Emend Tri-pack (contains one 125 mg and two 80 mg)	12 packs per 90 days **OR**
Emend 125 mg suspension	18 kits per 90 days **OR**
Emend 150 mg injection	12 vials per 90 days **OR**
Cinvanti 130 mg injection	12 vials per 90 days **OR**
Akynzeo 300 mg/0.5mg capsules	12 capsules per 90 days **OR**
Akynzeo 235 mg/0.25 mg injection	12 vials per 90 days **OR**
Varubi 90 mg tablets	24 tablets per 90 days **OR**
Varubi 166.5 mg/92.5 mL (vial)	12 vials per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

NK1 antagonists are indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy. Emend is also indicated for the prevention of postoperative nausea and vomiting in adults. Cinvanti and Emend are not

used to treat nausea and vomiting that the patient already has and should not be used continuously for a long time (chronic use) (1-5).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of NK1 antagonists while maintaining optimal therapeutic outcomes.

References

1. Akynzeo capsules and Akynzeo for Injection [package insert]. Iselin, NJ: Helsinn Therapeutics (U.S.), Inc.; June 2021.
2. Emend [package insert]. Whitehouse Station, NJ: Merck & CO, Inc.; February 2021.
3. Emend for Injection [package insert]. Whitehouse Station, NJ: Merck & CO, Inc.; May 2022.
4. Cinvanti [package insert]. San Diego, CA: Heron Therapeutics, Inc.; October 2019.
5. Varubi [package insert]. Deerfield, IL: TerSera Therapeutics LLC; August 2020.

Policy History

Date	Action
February 2015	New addition to PA
June 2015	Annual editorial review and reference update
September 2015	Annual review Update to qty limits
January 2016	Addition of Emend suspension and the ages for the different forms
March 2016	Annual editorial review Changed Emend suspension quantity limits from 12 to 18 per SME Policy number change from 5.09.05
June 2016	Annual editorial review Addition of Emend injection
September 2016	Annual editorial review and reference update.
March 2017	Annual editorial review
December 2017	Addition of Cinvanti and the no PA required if there has been pharmacy claims for an oncology medication(s) in the past 6 months
March 2018	Annual review
June 2018	Annual editorial review and reference update Addition of Akynzeo and Varubi to NK1 antagonist policy Akynzeo diagnosis verbiage updated to “prevention of” acute or delayed nausea or vomiting Updated quantities of Varubi tablets for pre- PA and PA amounts

September 2018	Annual editorial review and reference update Addition of Akynzeo for injection to PA per SME
March 2019	Annual editorial review and reference update. Decreased Emend Injection age to 6 months and older
March 2020	Annual review and reference update
December 2020	Annual review
June 2021	Annual review and reference update
September 2022	Annual review and reference update
June 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 15, 2023 and is effective on July 1, 2023.