POLICY NUMBER UM_1038	**SUBJECT** Emend™ (Aprepitant oral or Fosaprepitant), Cinvanti (aprepitant injection) and Varubi™ (rolapitant oral/injection)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 3**
DATE REVIEWED 01/12/11, 03/08/12, 10/16/13, 11/12/14, 12/17/15, 5/23/16, 03/04/17, 05/10/17, 01/19/18, 02/06/19	**APPROVAL DATE** February 13, 2019	**EFFECTIVE DATE** February 13, 2019	**REVISION DATES** (latest version listed last) 01/12/11, 03/08/12, 10/16/13, 11/12/14, 12/17/15, 05/24/16, 05/10/17, 02/14/18, 02/13/19	
PRIMARY BUSINESS OWNER: **APPROVED BY:** Dr. Andrew Hertler		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Oncology	

I. PURPOSE

To define and describe the accepted indications for Emend (aprepitant oral or fosaprepitant), Cinvanti (aprepitant injection), and Varubi (rolapitant oral/injection) usage in cancer supportive care.

II. DEFINITIONS

Emend (aprepitant oral or fosaprepitant) and Cinvanti (aprepitant injection): is a highly selective substance P neurokinin 1 (NK1) receptor antagonist. Emend inhibits emesis via central actions; it crosses the blood brain barrier and occupies brain NK_1 receptors. Fosaprepitant is a prodrug that is converted to aprepitant.

Varubi (rolapitant oral/injection): prevents delayed nausea and vomiting associated with emetogenic chemotherapy. It does this as competitive and selective antagonist inhibiting the substance P/neurokinin 1(NK1) receptor.

Emend (aprepitant oral or fosaprepitant) or Cinvanti (aprepitant injection) has FDA approved indication as an adjunct in combination with other antiemetic agents to help prevent acute and delayed nausea and vomiting due to highly and moderately emetogenic chemotherapy. Emend (aprepitant) is FDA approved in adults for the prevention of postoperative nausea and vomiting.

Varubi (rolapitant oral/injection) is FDA approved to prevent delayed phase chemotherapy-induced nausea and vomiting (emesis). It was approved in combination with other antiemetic agents (Dexamethasone and 5-HT3 antagonists) to prevent nausea and vomiting with initial and repeated courses of emetogenic chemotherapy.

Varubi (rolapitant oral/injection) is available in 90 mg oral tablets and 165 mg intravenous emulsion.

Emend is available as Aprepitant in 40 mg, 80 mg, and 125 mg capsules and oral suspension.

Emend is available as Fosaprepitant 150 mg vial.

Cinvanti (aprepitant injection) is available as 130 mg intravenous emulsion.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Emend (aprepitant or fosaprepitant) may be considered medically necessary when ALL of the following selection criteria is met:

1. Antiemesis

a. Emend (aprepitant oral or fosaprepitant), Cinvanti (aprepitant injection), or Varubi (rolapitant oral/injection) is being used in combination with dexamethasone and a serotonin antagonist before chemotherapy:

i. Before moderately/highly emetic risk chemotherapy based on the antiemetic practice guideline from NCCN **OR**

ii. Before low or minimal emetic risk chemotherapy in members who failed, intolerant, or has a contraindication to Zofran (ondansetron) **OR** Kytril (granisetron).

Exclusion Criteria: Emend is not considered medically necessary if:

1. Emend, Cinvanti, or Varubi is not to be used for the treatment of established nausea and vomiting.
2. Emend, Cinvanti, or Varubi is not used in conjunction with a $5HT_3$ antagonists (i.e. ondansetron) and dexamethasone.
3. Fosaprepitant (IV aprepitant) is being used in combination or failure with oral/injectable aprepitant.
4. Varubi (rolapitant oral/injection) is being used in patients with severe hepatic impairment (Child-Pugh class C).
5. Dosing exceeds the single dose limit of aprepitant oral 125 mg and fosaprepitant 150 mg or rolapitant 180 mg and aprepitant injection 130 mg .
6. Emend or Cinvanti is being used concomitantly with pimozide, terfenadine, astemizole, or cisapride.
7. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Emend shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. Dosing and Administration

a. Fosaprepitant (IV aprepitant):

i. Single dose regimen: 150 mg IV over 20 to 30 min given 30 min prior to chemotherapy on day 1 only (with no aprepitant capsules given on days 2 or 3).

b. Oral aprepitant (three day dosing regimen): 125 mg on day 1 and 80 mg on days 2 and 3

c. Varubi (rolapitant oral/injection): 180 mg by mouth 1 to 2 hours prior to starting chemotherapy treatment.

d. Fosaprepitant, aprepitant, or rolapitant is used concurrently with a $5HT_3$ antagonists (i.e. Ondansetron) and Dexamethasone.

e. Cinvanti (aprepitant injection): 130 mg IV over 30 min given 30 min prior to highly emetic chemotherapy on day 1 only. 100 mg is given prior to moderately emetic chemotherapy.

2. **Dosage Adjustments**:

a. Varubi (rolapitant oral/injection)-Hepatic, severe impairment (Child-Pugh class C): Avoid use

3. **Monitoring**

a. Fluid and electrolyte status in member with significant diarrhea.

b. Monitor vital signs and hepatic enzymes in symptomatic member.

c. Emend is a dose-dependent inhibitor of cytochrome P450 isoenzyme 3A4 (CYP3A4). Emend should not be used concurrently with pimozide, terfenadine, astemizole, or cisapride. Inhibition of CYP3A4 by aprepitant could result in elevated plasma concentrations of these drugs, potentially causing serious or life-threatening reactions.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

VII. REFERENCES

1. Cinvanti prescribing information. Heron Therapeutics, Inc., San Diego, CA. 2018.
2. Emend prescribing information. Merck & Co, Inc. Whitehouse Station, NJ. 2018.
3. Rolapitant prescribing information. TESARO, Inc. 1000 Winter St., Waltham, MA. 2018.
4. Hesketh PJ, et al. Antiemetics: American Society of Clinical Oncology Focused Guideline Update. J Clin Oncol. 2015 Nov 2. pii: JCO.2015.64.3635.
5. Clinical Pharmacology Elsevier Gold Standard. 2019.
6. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
7. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
8. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.