

Clinical Policy: Aprepitant (Emend, Cinvanti), Fosaprepitant (Emend for injection)

Reference Number: CP.PMN.19

Effective Date: 11.01.06

Last Review Date: 02.21

Line of Business: HIM*, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Aprepitant (Emend®, Cinvanti®) and Fosaprepitant (Emend® for injection) are substance P/neurokinin 1 (NK₁) receptor antagonists.

**For Health Insurance Marketplace (HIM), if request is through the pharmacy benefit, aprepitant oral suspension, aprepitant capsule therapy pack, fosaprepitant (Emend for injection), and Cinvanti are non-formulary and should not be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)

Emend and Cinvanti are indicated:

- In combination with other antiemetic agents for patients 6 months of age and older (*Emend oral suspension and injection*), 12 years of age and older (*Emend capsules*), or 18 years of age and older (*Cinvanti*), for 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)
- For prevention of postoperative nausea and vomiting (PONV) in adults (*Emend capsules only*)
- For prevention of delayed nausea and vomiting associated with initial and repeat courses of MEC as a single-dose regimen (*Cinvanti only*)

Limitation(s) of use:

- Emend and Cinvanti have not been studied for treatment of established nausea and vomiting.
- Chronic continuous administration of Emend is not recommended.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Emend and Cinvanti are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

- A. **Prevention of Nausea and Vomiting Associated with Cancer Chemotherapy** (must meet all):

1. Prescribed for the prevention of chemotherapy-induced nausea/vomiting;
2. Member meets one of the following (a, b, or c):
 - a. Emend oral suspension or injection: age \geq 6 months;
 - b. Emend capsules: age \geq 12 years;
 - c. Cinvanti: age \geq 18 years;
3. Member is scheduled to receive moderately to highly emetogenic cancer chemotherapy (*see Appendix D*);
4. Prescribed in combination with a serotonin (5-HT₃) receptor antagonist (*ondansetron is preferred*) and dexamethasone;
5. Dose does not exceed:
 - a. Emend oral suspension or capsules: 125 mg on Day 1, followed by 80 mg on Days 2 and 3 per chemotherapy cycle;
 - b. Emend for injection: 150 mg on Day 1;
 - c. Cinvanti: 130 mg on Day 1 for HEC and MEC (single-dose regimen), or 100 mg on Day 1 for MEC (3-day regimen).

Approval duration:

Medicaid – Projected duration of chemotherapy

HIM – Projected duration of chemotherapy for capsules (*refer to HIM.PA.103 for aprepitant oral suspension, aprepitant capsule therapy pack, fosaprepitant (Emend for injection), and Cinvanti if pharmacy benefit*)

B. Prevention of Postoperative Nausea and Vomiting (must meet all):

1. Request is for Emend capsules;
2. Prescribed for the prevention of PONV;
3. Age \geq 18 years;
4. Member is scheduled to receive surgery;
5. Failure of a 5-HT₃ receptor antagonist (*ondansetron is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 40 mg (1 capsule) once.

Approval duration: 3 days (one time dose)

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Prevention of Nausea and Vomiting Associated with Cancer Chemotherapy (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member continues to receive moderately to highly emetogenic cancer chemotherapy (*see Appendix D*);

4. Prescribed in combination with a 5-HT₃ receptor antagonist (*ondansetron is preferred*) and dexamethasone;
5. If request is for a dose increase, new dose does not exceed:
 - a. Emend oral suspension or capsules: 125 mg on Day 1, followed by 80 mg on Days 2 and 3 per chemotherapy cycle;
 - b. Emend for injection: 150 mg on Day 1;
 - c. Cinvanti: 130 mg on Day 1 for HEC and MEC (single-dose regimen), or 100 mg on Day 1 for MEC (3-day regimen).

Approval duration:

Medicaid – Projected duration of chemotherapy

HIM – Projected duration of chemotherapy for capsules (*refer to HIM.PA.103 for aprepitant oral suspension, aprepitant capsule therapy pack, fosaprepitant (Emend for injection), and Cinvanti if pharmacy benefit*)

B. Prevention of Postoperative Nausea and Vomiting

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

5-HT₃: serotonin 5-hydroxytryptamine, type 3

ASCO: American Society of Clinical Oncology

FDA: Food and Drug Administration

HEC: highly emetogenic cancer chemotherapy

MEC: moderately emetogenic cancer chemotherapy

NCCN: National Comprehensive Cancer Network

NK₁: neurokinin 1

PONV: postoperative nausea and vomiting

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|--|---|---------------------------------|
| 5-HT₃ Serotonin Antagonists | | |
| granisetron (Kytril [®]) | Prevention of PONV* 0.35 to 3 mg (5 to 20 mcg/kg) IV at the end of surgery | 20 mcg/kg/dose |
| ondansetron (Zofran [®] , Zofran [®] ODT) | Prevention of PONV 16 mg PO given 1 hr prior to anesthesia or 4 mg IM/IV as a single dose given 30 min before end of anesthesia | PO: 16 mg/dose IV: 4 mg/dose |

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity, concurrent use with pimozide
- Boxed warning(s): none reported

Appendix D: American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) Recommendations in Oncology

- Minimal emetic risk chemotherapy: No routine prophylaxis is recommended.
- Low emetic risk chemotherapy: Recommended options include dexamethasone (recommended by both ASCO and NCCN) or metoclopramide, prochlorperazine, or a 5-HT₃ receptor antagonist (recommended by NCCN only). NK₁ receptor antagonists are not included in low risk antiemetic recommendations.
- Moderate emetic risk chemotherapy: 5-HT₃ receptor antagonists and dexamethasone may be used in combination and with or without NK₁ receptor antagonists. Olanzapine may also be used in combination with palonosetron and dexamethasone.
 - Examples of moderate emetic risk chemotherapy: azacitidine, alemtuzumab, bendamustine, carboplatin, clofarabine, cyclophosphamide < 1,500 mg/m², cytarabine < 1,000 mg/m², daunorubicin, doxorubicin, epirubicin, idarubicin, ifosfamide, irinotecan, oxaliplatin
- High emetic risk chemotherapy: NK₁ receptor antagonists are recommended for use in combination with 5-HT₃ receptor antagonists and dexamethasone. Olanzapine may also be used in combination with 5-HT₃ receptor antagonists, dexamethasone, and/or NK₁ receptor antagonists.
 - Examples of high emetic risk chemotherapy: carmustine, cisplatin, cyclophosphamide ≥ 1,500 mg/m², dacarbazine, dactinomycin, mechlorethamine, streptozocin
- Breakthrough emesis: Per NCCN, an agent from a different drug class is recommended to be added to the current antiemetic regimen. Drug classes include atypical antipsychotics (olanzapine), benzodiazepines (lorazepam), cannabinoids (dronabinol, nabilone), phenothiazines (prochlorperazine, promethazine), 5-HT₃ receptor antagonists (dolasetron,

ondansetron, granisetron), steroids (dexamethasone), or (haloperidol, metoclopramide, scopolamine). An NK₁ receptor antagonist may be added to the prophylaxis regimen of the next chemotherapy cycle if not previously included.

V. Dosage and Administration

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---------------------------------------|--|---|---|
| Cinvanti [®] (aprepitant) | Prevention of chemotherapy-induced nausea and vomiting | <i>HEC or MEC (single-dose regimen):</i> 130 mg IV on Day 1 <i>MEC (3-day regimen):</i> 100 mg IV on Day 1 | Single-dose: 130 mg/dose 3-day regimen: 100 mg/dose |
| Emend [®] (aprepitant) | Prevention of chemotherapy-induced nausea and vomiting | <i>Capsules:</i> 125 mg PO on Day 1, then 80 mg PO on Days 2 and 3 of each chemotherapy cycle <i>Oral suspension:</i> 3 mg/kg PO on Day 1, then 2 mg/kg PO on Days 2 and 3 | Per chemotherapy cycle: Day 1: 125 mg Days 2 and 3: 80 mg |
| Emend [®] (aprepitant) | Prevention of postoperative nausea and vomiting | <i>Capsules:</i> 40 mg PO within 3 hours prior to induction of anesthesia | 40 mg/dose |

VI. Product Availability

- Emend capsules: 40 mg, 80 mg, 125 mg
- Emend capsule therapy pack: 80 mg/125 mg
- Emend powder for oral suspension: 125 mg
- Emend for injection single-dose vial, powder for reconstitution: 150 mg
- Cinvanti single-dose vial, injectable emulsion: 130 mg/18 mL

VII. References

1. Emend Prescribing Information. Whitehouse Station, NJ: Merck & Company, Inc.: October 2020. Available at: <http://www.emend.com>. Accessed November 13, 2020.
2. Cinvanti Prescribing Information. San Diego, CA: Heron Therapeutics, Inc.; October 2019. Available at: <http://www.cinvanti.com>. Accessed November 13, 2020.
3. Hesketh, PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2017: JCO2017744789.
4. National Comprehensive Cancer Network. Antiemesis Version 2.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed November 13, 2020.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: <http://www.clinicalpharmacology-ip.com/>.
6. Micromedex[®] Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 13, 2020.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPSC Codes | Description |
|-------------|--------------------------------|
| J1453 | Injection, fosaprepitant, 1 mg |
| J0185 | Injection, aprepitant, 1 mg |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|--|----------|-------------------|
| Converted into new policy template; Added age limits (≥ 12 years or ≤ 12 years and weight at least 30kg per labeling) for initial approval; Added tables 1 & 2 to show degree of emetogenicity for different chemotherapy regimen; Divided diagnosis with separate criteria, I, II, III; Updated Moderately Emetogenic Cancer Chemotherapy criteria per 2011 ASCO guideline;; Added criteria for continuity of care Updated references | 12.15 | 02.16 |
| Updated criteria to allow the use of oral suspension in patients 6 months to 11 years or those unable to swallow pills; For prevention of post-operative nausea/vomiting, added that member must have contraindication or intolerance to PDL ondansetron; Added criteria not to exceed FDA approved maximum recommended dose and health plan approved daily quantity limit. | 07.16 | 08.16 |
| Removed age restriction for oral suspension as its use is not limited to patients between 6 months-11 years per FDA labeling Removed age restriction for capsules as it is not an absolute contraindication per FDA labeling | 03.17 | 08.17 |
| 3Q 2018 annual review: policies combined for HIM and Medicaid lines of business; HIM and Medicaid: added age requirement, added requirement that Emend is prescribed for the prevention of chemo-induced N/V, specialist requirements were removed, therapy pack dosage form was added; HIM: added requirement for trial and failure of a 5-HT ₃ antagonist for postop N/V, added requirement for positive response to therapy for continued therapy approval of chemo-induced N/V per template, added confirmation that member is receiving chemo, added requirement that Emend is prescribed in combination with a 5-HT ₃ antagonist and dexamethasone; For Medicaid: generalized trial of ondansetron to a 5-HT ₃ antagonist (ondansetron is | 05.15.18 | 08.18 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|--|----------|-------------------|
| preferred) for PONV, requirement that member has a scheduled surgery was added; references reviewed and updated. | | |
| 1Q 2019 annual review: added age requirement for postoperative N/V; no significant changes; references reviewed and updated. | 10.30.18 | 02.19 |
| RT4: Cinvanti added to policy. | 04.04.19 | |
| 1Q 2020 annual review: no significant changes; RT4 Cinvanti new FDA indication added for prevention of delayed nausea and vomiting associated with initial and repeat courses of MEC as a single-dose regimen, dosage/administration updated; references reviewed and updated. | 11.01.19 | 02.20 |
| 1Q 2021 annual review: no significant changes; removed HIM-Medical Benefit; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated. | 11.13.20 | 02.21 |

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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