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

Reference Number: CP.PMN.19
Effective Date: 11.06
Last Review Date: 02.20
Line of Business: HIM*, Medicaid, HIM-Medical Benefit

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 (NK_1) 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 cannot 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 ≥ 6 months;
   b. Emend capsules: age ≥ 12 years;
   c. Cinvanti: age ≥ 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-HT_3) 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 postoperative nausea/vomiting;
3. Age ≥ 18 years;
4. Member is scheduled to receive surgery;
5. Failure of a 5-HT_3 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.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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-HT_3 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.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid and HIM-Medical Benefit or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

5-HT_3: 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
NK_1: 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-HT$_3$ 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-HT$_3$ receptor antagonist (recommended by NCCN only). NK$_1$ receptor antagonists are not included in low risk antiemetic recommendations.
- Moderate emetic risk chemotherapy: 5-HT$_3$ receptor antagonists and dexamethasone may be used in combination and with or without NK$_1$ 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/m^2, cytarabine < 1,000 mg/m^2, daunorubicin, doxorubicin, epirubicin, idarubicin, ifosfamide, irinotecan, oxaliplatin
- High emetic risk chemotherapy: NK$_1$ receptor antagonists are recommended for use in combination with 5-HT$_3$ receptor antagonists and dexamethasone. Olanzapine may also be used in combination with 5-HT$_3$ receptor antagonists, dexamethasone, and/or NK$_1$ receptor antagonists.
  - Examples of high emetic risk chemotherapy: carmustine, cisplatin, cyclophosphamide ≥ 1,500 mg/m^2, 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-HT$_3$ receptor antagonists (dolasetron,

ondansetron, granisetron), steroids (dexamethasone), or (haloperidol, metoclopramide, scopolamine). An NK_1 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	*HEC or MEC (single-dose regimen):* 130 mg IV on Day 1 *MEC (3-day regimen):* 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	*Capsules*: 125 mg PO on Day 1, then 80 mg PO on Days 2 and 3 of each chemotherapy cycle *Oral suspension*: 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	*Capsules:* 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.: September 2019. Available at: http://www.emend.com. Accessed October 30, 2019.
2. Cinvanti Prescribing Information. San Diego, CA: Heron Therapeutics, Inc.; October 2019. Available at: http://www.cinvanti.com. Accessed November 1, 2019.
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 1.2019. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed October 30, 2019.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/.
6. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 15, 2018.

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.

HCPCS Codes	Description
J1453	Injection, fosaprepitant, 1 mg
J0185	Injection, aprepitant, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Updated reference section to reflect current literature search.	02.15	02.15
Updated to clarify use only for age 18 an older	05.15	05.15
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	05.15.18	08.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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 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

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy; HIM.PA.103.