09-J2000-60

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Reviewed: 02/12/25

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Subject: Aprepitant (Cinvanti®) and fosaprepitant (Focinvez) injectable therapy

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Chemotherapy-induced nausea and vomiting (CINV) can significantly affect a patient's quality of life, leading to poor compliance with further chemotherapy. The severity and incidence of CINV are affected by factors such as the selected agent and dose of chemotherapy, schedule and route of administration, and patient specific factors (e.g., age, sex, prior chemotherapy, history of alcohol use).

Neurokinin-1(NK-1) receptor antagonists block the binding of substance P at the NK-1 receptor in the central nervous system to prevent emesis. Fosaprepitant (Emend) injection is a prodrug of aprepitant that was the first injectable NK-1 receptor antagonist approved by the U.S. Food and Drug Administration (FDA) in 2008. It is currently available as a generic fosaprepitant injection. A new brand of fosaprepitant injection was FDA approved in 2023 as Focinvez. Fosaprepitant is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic chemotherapy. An injectable emulsion of aprepitant (Cinvanti) was FDA-approved in 2017 for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly or moderate emetogenic chemotherapy. Aprepitant injectable emulsion demonstrated bioequivalence to fosaprepitant in healthy subjects in a cross-over study. National Comprehensive Cancer Network (NCCN) Guidelines for Antiemesis recommend NK1 receptor antagonist containing regimens (e.g., aprepitant, fosaprepitant, rolapitant PO, or netupitant) for acute and delayed emesis prevention in combination with dexamethasone and a serotonin antagonist with or without lorazepam, histamine-2 blockers, or proton pump inhibitors before intravenous antineoplastic therapy with high or moderate emetic risk. The use of NK1 receptor antagonist therapy is also recommended in combination with olanzapine, dexamethasone, and a serotonin antagonist for high risk antineoplastic therapy or if emesis occurred during a previous cycle of antineoplastic therapy with a 3-drug regimen.

NCCN specifically states that use of NK1 receptor antagonists are for the prevention of CINV, not treatment of CINV.

POSITION STATEMENT:

I. Aprepitant injection (Cinvanti®) and fosaprepitant (Focinvez) **meets the definition of medical necessity** when **ALL** of the following are met:

1. Use is for prevention of acute or delayed chemotherapy-induced nausea and vomiting associated with initial or repeat courses of chemotherapy
2. **ONE** of the following:
    a. Chemotherapy has a moderate or high emetogenic potential (Table 1)
    b. Chemotherapy has a low emetogenic potential (Table 1) and the member has an inadequate response or contraindication to use of a serotonin antagonist (i.e., ondansetron, granisetron, or palonosetron) to prevent chemotherapy-induced nausea and vomiting[a]
3. Use is in combination with a corticosteroid (i.e.,dexamethasone) and a serotonin antagonist (i.e., ondansetron, granisetron, or palonosetron)[b] **OR** the member has a contraindication to corticosteroids or serotonin antagonist therapy
4. The member is not receiving an additional NK1 receptor antagonist[c] (e.g., fosaprepitant, rolapitant, oral aprepitant, fosnetupitant/palonosetron, or netupitant/palonosetron)
5. **ONE** of the following:
    a. For Aprepitant, the member had an inadequate response or intolerance to fosaprepitant[a]
    b. For Focinvez, generic fosaprepitant (J1453) is **NOT** available for use due to a national drug shortage[d] – documentation must be provided
6. The dose does not exceed the following and is given prior to chemotherapy
    a. Aprepitant injection (Cinvanti): 130 mg
    b. Fosaprepitant injection (Focinvez): 150 mg

Duration of approval: 1 year

Notes:

[a] Step therapy requirement does not apply if the member was previously approved by Florida Blue or a prior health plan

[b] Given with or without olanzapine, lorazepam, histamine-2 receptor blocker or proton pump inhibitor

[c] Exception when aprepitant 100 mg IV is prescribed on day 1, followed by oral aprepitant on Day 2 and 3.

[d] To verify non-availability, the status of fosaprepitant injection must be listed as “Currently in Shortage” on the ASHP Current Shortages webpage (Drug Shortages List (ashp.org)) **AND** all listed manufacturers must have all strengths unavailable

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Cinvanti

Aprepitant injectable emulsion is indicated in adults, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin. It is also indicated in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy. It has not been studied for the treatment of established nausea and vomiting.

The recommended dosing of aprepitant injectable emulsion is the following:

- Highly emetogenic chemotherapy and moderately emetogenic chemotherapy (single dose regimen): 130 mg intravenously either by injection over 2 minutes or as an infusion (mixed with 100 ml of 0.9% sodium chloride) over 30 minutes on Day 1, completing the injection or infusion approximately 30 minutes prior to chemotherapy in combination with dexamethasone and a 5HT3 antagonist.
- Moderately emetogenic chemotherapy 3 day regimen: 100 mg intravenously either by injection over 2 minutes or as an infusion (mixed with 100 ml of 0.9% sodium chloride) over 30 minutes on Day 1, completing the injection or infusion approximately 30 minutes prior to chemotherapy in combination with dexamethasone and a 5HT3 antagonist. Aprepitant capsules (80 mg) are given on day 2 and 3.

Focinvez

Fosaprepitant injection is indicated in adults, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin. It is also indicated in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy. Fosaprepitant has not been studied for the treatment of established nausea and vomiting.

The recommended dosing of fosaprepitant injection is 150 mg intravenously over 20 to 30 minutes approximately 30 minutes prior to chemotherapy in combination with dexamethasone and a 5HT3 antagonist.

Dose Adjustments

- There were no studies conducted in patients with severe hepatic impairment (Child-Pugh score greater than 9) thus additional monitoring for adverse reactions is recommended. No dose adjustment is necessary in patients with mild to moderate hepatic impairment.

Drug Availability

- Cinvanti: 130 mg single dose vial. See product label for dilution instructions.
- Focinvez: 150 mg single dose vial for reconstitution

PRECAUTIONS:

Cinvanti and Focinvez

Contraindications

- Should not be administered to patients with known hypersensitivity to any component of the product. Anaphylactic reactions, flushing, erythema and dypsnea have been reported.
- Should not be administered concurrently with pimozide due to a drug interaction that may result in increased plasma concentrations of pimozide and potentially life-threatening reactions, including QT prolongation.

Precautions/Warnings

- **Clinically Significant CYP3A4 Drug Interactions**— Fosaprepitant, a prodrug of aprepitant, is a weak inhibitor of CYP3A4, and aprepitant is a substrate, inhibitor, and inducer of CYP3A4. Use with other drugs that are CYP3A4 substrates, may result in increased plasma concentration of the concomitant drug. Use with strong or moderate CYP3A4 inhibitors (e.g., ketoconazole, diltiazem) or strong CYP3A4 inducers (e.g., rifampin) may alter the plasma concentrations of aprepitant.
- **Hypersensitivity Reactions** – reactions including flushing, erythema, dyspnea, and anaphylaxis have been reported. Discontinue and do not reinitiate the infusion in patients who experience these symptoms.
- **Decrease in INR with Concomitant Warfarin** –Monitor the INR in patients on chronic warfarin therapy in the 2-week period, particularly at 7 to 10 days, following initiation of fosaprepitant injection with each chemotherapy cycle
- **Risk of Reduced Efficacy of Hormonal Contraceptives –**the efficacy of hormonal contraceptives may be altered.
- **Infusion site reactions (Focinvez only)** – infusion site reactions have been reported with the use of intravenous fosaprepitant. The majority of severe infusion site reactions include thrombophlebitis and vasculitis. Necrosis was reported in some patients with concomitant vesicant chemotherapy.

BILLING/CODING INFORMATION:

HCPCS Coding

J0185	Injection, aprepitant, 1 mg
J1434	Injection, fosaprepitant (focinvez), 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

R11.0	Nausea
R11.10 – R11.12	Vomiting, unspecified

R11.2	Nausea with vomiting, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs, sequela
T45.95XA	Adverse effect of unspecified primarily systemic and hematological agent, initial encounter
T50.905A	Adverse effect of unspecified drugs, medicaments and biological substances
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the guideline creation.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Acute chemotherapy-induced nausea and vomiting – nausea and/or vomiting that occurs within a few minutes to several hours after drug administration and commonly resolves within the first 24 hours.

Delayed chemotherapy-induced nausea and vomiting – nausea and/or vomiting that occurs 24 hours after drug administration.

RELATED GUIDELINES:

Fosnetupitant-palonosetron (Akynzeo), 09-J3000-01

Granisetron (Sustol), 09-J0000-97

OTHER:

Table 1

Emetogenic Potential of Antineoplatic Agents		
	High emetic risk (>90% frequency of emesis)	**Moderate emetic risk (30-90% frequency of emesis)**
IV	AC combination (doxorubicin or epirubicin with cyclophosphamide) Carboplatin AUC ≥ 4 Carmustine (>250 mg/m2) Cisplatin Cyclophosphamide (> 1500 mg/m2) Dacarbazine Doxorubicin (≥60 mg/m2) Epirubicin (>90 mg/ m2) Fam-trastuzumab deruxtecan-nxki Ifosfamide (≥2 g/ m2) Mechlorethamine Melphalan (≥ 140 mg/m2) Sacituzumab govitecan-hziy Streptozocin	Aldesleukin (>12-15 million IU/m2) Amifostine (>300 mg/m2) Bendamustine Busulfan Carboplatin AUC < 4 Carmustine (≤250 mg/m2) Clofarabine Cyclophosphamide (≤1500 mg/m2) Cytarabine (>200 mg/m2) Dactinomycin Daunorubicin Dinutuximab Doxorubicin (<60 mg/m2) Dual-drug liposomal encapsulation of cytarabine and daunorubicin Epirubicin (≤90 mg/m2) Idarubicin Ifosfamide (< 2g/m2) Irinotecan Irinotecan (liposomal) Lurbinectedin Melphalan (< 140 mg/m2) Methotrexate (≥250 mg/m2) Mirvetuximab soravtansine-gynx Naxitamab-gqgk Oxaliplatin Romidepsin Temozolomide Trabectedin
IV	**Low emetic risk (10 – 30% frequency of emesis)**	
	Ado-trastuzumab emtansine Aldesleukin ≤12 million international units/m2 Amifostine ≤300 mg/m2 Amivantamab-vmjw Arsenic trioxide Axicabtagene ciloleucel Azacitidine Belinostat	

	Brexucabtagene autoleucel Brentuximab vedotin Cabazitaxel Carfilzomib Ciltacabtagene autoleucel Copanlisib Cytarabine (low dose) 100 – 200 mg/m2 Docetaxel Doxorubicin (liposomal) Enfortumab vedotin-ejfv Eribulin Etoposide 5-FU Floxuridine Gemcitabine Gemtuzumab ozogamicin Idecabtagene vicleucel Inotuzumab ozogamicin Isatuximab-irfc Ixabepilone Lisocabtagene maraleucel Loncastuximab tesirine-lpyl Methotrexate > 50 mg/m^2 - <250 mg/m^2 Mitomycin Mitomycin pyelocalyceal solution Mitoxantrone Mogamulizumab-kpkc Mosunetuzumab-axgb Necitumumab Omacetaxine Paclitaxel Paclitaxel-albumin Pemetrexed Pentostatin Polatuzumab vedotin-piig Pralatrexate Tafasitamab-cxix Tagraxofusp-erzs Talimogene laherparepvec Tebentafusp-tebn Thiotepa Tisagenlecleucel Tisotumab vedotin-tftv Topotecan

	Ziv-aflibercept

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 02/12/25.

GUIDELINE UPDATE INFORMATION:

06/15/16	New Medical Coverage Guideline.
06/15/17	Review and revision to guideline consisting of updating position statement and references.
03/15/18	Review and revision to guideline consisting of updating position statement, description, dosing, coding and references.
04/01/18	Addition of HCPCS codes C9463 and C9464
05/15/18	Review and revision to guideline consisting of updating position statement and references.
01/01/19	Revision: HCPCS code updates. Added J0185 and J2797, and removed C9463, C9464, and J3490.
05/15/19	Review and revision to guideline consisting of updating Table 1 and references.
01/01/20	Revision to guideline; consisting of updating the position statement.
05/15/20	Review and revision to guideline; consisting of updating Table 1, dosing and references.
12/15/20	Review and revision to guideline; consisting of updating the position statement, description, dosing and references.

05/15/21	Review and revision to guideline; consisting of updating Table 1 and references.
07/01/21	Revision to guideline; consisting of removing Emend from the policy.
05/15/22	Review and revision to guideline; consisting of updating Table 1, description, and references.
04/15/23	Review and revision to guideline; consisting of updating Table 1 (Emetic potential of neoplastic agents) and references.
04/15/24	Review and revision to guideline; consisting of updating Table 1 (Emetic potential of neoplastic agents) and references.
03/15/25	Review and revision to guideline; consisting of including Focinvez, and updating dosing, precautions, coding, and references.