Medical Policy Bulletin
Title:
Aprepitant (Cinvanti™), Fosaprepitant Dimeglumine (Emend®), Granisetron (Sustol®), and Rolapitant (Varubi®)
Policy #:
MA08.091c

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

MEDICALLY NECESSARY

Intravenous aprepitant (Cinvanti™) is considered medically necessary and, therefore, covered for individuals 18 years of age or older when all of the following criteria are met:

- The individual is prescribed intravenous aprepitant (Cinvanti™) for one of the following indications whose appropriate regimen is also listed in Attachment A of this Policy*:
    - Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin with or without olanzapine
    - Prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)
- Intravenous aprepitant (Cinvanti™) will be used in combination with dexamethasone and a 5-HT_3 antagonist (e.g., granisetron [Kytril®], ondansetron [Zofran®], palonosetron [Aloxi®]), unless the individual is intolerant of, or has a contraindication to, those drugs

Intravenous fosaprepitant dimeglumine (Emend®) is considered medically necessary and, therefore, covered for individuals six months of age or older when all of the following criteria are met:

- The individual is taking fosaprepitant dimeglumine (Emend®) for one of the following indications whose appropriate regimen is also listed in Attachment A of this Policy*:
    - Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin, with or without olanzapine
    - Prevention of nausea and vomiting associated with concurrent radiotherapy and cisplatin-based chemotherapy
    - Prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

- Intravenous fosaprepitant dimeglumine (Emend®) will be used in combination with dexamethasone and a 5-HT_3 antagonist (e.g., granisetron [Kytril®], ondansetron [Zofran®], palonosetron [Aloxi®]) in adult individuals, and with or without a corticosteroid on chemotherapy day one for pediatric individuals, unless the individual is intolerant of, or has a contraindication to, those drugs

Granisetron (Sustol®) is considered medically necessary and, therefore, covered in individuals 18 years of age or older for the prevention of acute and delayed nausea and vomiting when all of the following criteria are met:

- Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of high or moderately emetogenic chemotherapy or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens, whose appropriate regimen is also listed in Attachment A of this Policy*
- Granisetron (Sustol®) will be used in combination with other antiemetics (e.g., dexamethasone, fosaprepitant dimeglumine [Emend®]), unless the individual is intolerant of, or has a contraindication to those drugs

Intravenous rolapitant (Varubi®) is considered medically necessary and, therefore, covered for individuals 18 years of age or older when all of the following criteria are met:

- The individual is taking rolapitant (Varubi®) for one of the following indications whose appropriate regimen is also listed in Attachment A of this Policy*:
    - Prevention of delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy with or without olanzapine
    - Prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy
- Intravenous rolapitant (Varubi®) will be used in combination with dexamethasone and a 5-HT_3 antagonist (e.g., granisetron [Kytril®], ondansetron [Zofran®], palonosetron [Aloxi®]), unless the individual is intolerant of, or has a contraindication to, those drugs

* To define emetogenicity risk of chemotherapy agents/regimens, see Attachment A, Risk of Emesis Without Prophylaxis

EXPERIMENTAL/INVESTIGATIONAL

All other uses for aprepitant (Cinvanti™), fosaprepitant dimeglumine (Emend®), granisetron (Sustol®) and rolapitant (Varubi®) including use for the treatment of established nausea and vomiting, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

BENEFIT APPLICATION

Subject to the applicable Evidence of Coverage, aprepitant (Cinvanti™), fosaprepitant dimeglumine (Emend®), granisetron (Sustol®), and rolapitant (Varubi®) are covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

There is no Medicare coverage determination addressing intravenous aprepitant (Cinvanti™), fosaprepitant dimeglumine (Emend®), granisetron (Sustol®), and rolapitant (Varubi®); therefore, the Company policy is applicable.

For Medicare Advantage members, certain drugs are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered.

This medical policy only addresses instances when intravenous aprepitant (Cinvanti™), fosaprepitant dimeglumine (Emend®), granisetron (Sustol®), and rolapitant (Varubi®) are covered under a member's medical benefit (Part B benefit). It does not address instances when intravenous aprepitant (Cinvanti™), fosaprepitant dimeglumine (Emend®), granisetron (Sustol®), and rolapitant (Varubi®) are covered under a member's pharmacy benefit (Part D benefit).

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Aprepitant (Cinvanti™) was approved by the FDA on November 9, 2017 for use 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 (HEC) including high-dose cisplatin
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

Fosaprepitant dimeglumine (Emend®) was approved by the FDA on January 25, 2008 for use in adults, and pediatric individuals six months of age and older, on April 3, 2018 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 (HEC) including high-dose cisplatin
- delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

Granisetron (Sustol®) was approved by the FDA on August 9, 2016 for use in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens. The safety and effectiveness of granisetron (Sustol®) have not been established in pediatric patients.

Rolapitant (Varubi®) was approved by the FDA on October 25, 2017 for use in combination with other antiemetic agents in adults for 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. The safety and effectiveness of rolapitant (Varubi®) have not been established in pediatric patients.

Description

Chemotherapy-induced nausea and vomiting may be a serious adverse effect of chemotherapy. There are three types of chemotherapy-induced nausea and vomiting:

- Acute emesis: occurs within one to two hours of chemotherapy and usually peaks in four to six hours
- Delayed emesis: occurs more than 24 hours after chemotherapy
- Anticipatory emesis: occurs prior to chemotherapy as a conditioned response in individuals who had previously experienced significant nausea and vomiting during previous cycles.

The risk of emesis without prophylaxis has been defined by The National Comprehensive Cancer Network (NCCN) for chemotherapy agents and their regimens. Based on this data, decisions regarding antiemetic prophylaxis (e.g., when to initiate, which antiemetic agents to use) can be made:

- Highly emetic: more than 90 percent risk of emesis
- Moderately emetic: 30 to 90 percent risk of emesis
- Low emetogenicity: 10 to 30 percent risk of emesis
- Minimally emetic: less than 10 percent risk of emesis

Examples of options for chemotherapy-induced antiemetic prophylaxis include oral, injectable, transdermal, or intravenous infusions of:

- 5-hydroxytryptamine ($5\text{-}HT_3$) receptor antagonists (e.g., granisetron [Kytril®, Sustol®], ondansetron [Zofran®], palonosetron [Aloxi®])
- neurokinin-1 receptor (NK1R) antagonists (e.g., aprepitant [Cinvanti™], aprepitant or fosaprepitant dimeglumine [Emend®], rolapitant [Varubi®])
- dexamethasone

- olanzapine (Zyprexa®)

APREPITANT (CINVANTI™)

Aprepitant (Cinvanti™) was approved by the US Food and Drug Administration (FDA) on November 9, 2017 for use 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 (HEC) including high-dose cisplatin
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

Aprepitant (Cinvanti™) is a substance P/neurokinin-1 (NK1) receptor antagonist. Aprepitant (Cinvanti™) has been shown to augment the antiemetic activity of dexamethasone and a 5-HT_3-receptor antagonist. Aprepitant (Cinvanti™) is an intravenous infusion that is administered on Day 1 of chemotherapy over a period of 30 minutes, approximately 30 minutes prior to chemotherapy. Aprepitant (Cinvanti™) is administered in a regimen with dexamethasone and a 5-HT_3 antagonist.

FOSAPREPITANT DIMEGLUMINE (EMEND®)

Fosaprepitant dimeglumine (Emend®) was approved by the FDA on January 25, 2008 for use in adults, and pediatric individuals six months of age and older, on April 3, 2018 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 (HEC) including high-dose cisplatin
- delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

Fosaprepitant dimeglumine (Emend®) is a prodrug of aprepitant, which is a substance P/neurokinin-1 (NK1) receptor antagonist. Aprepitant has been shown to augment the antiemetic activity of dexamethasone and a 5-HT_3-receptor antagonist. Fosaprepitant dimeglumine (Emend®) is an intravenous infusion that is administered on Day 1 of chemotherapy over a period of 20 to 30 minutes, approximately 30 minutes prior to chemotherapy. Fosaprepitant dimeglumine (Emend®) is administered in a regimen with dexamethasone and a 5-HT_3 antagonist.

GRANISETRON (SUSTOL®)

Granisetron (Sustol®) was approved by the FDA on August 9, 2016 for use 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 moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.

Granisetron (Sustol®) is a selective serotonin-3 (5-hydroxytryptamine$_3$ or 5-HT_3) receptor antagonist. When binding to 5-HT_3 receptors, granisetron (Sustol®) inhibits the release of serotonin from its receptors and stops the process of vomiting.

Granisetron (Sustol®) is administered as a slow subcutanous injection in combination with dexamethasone at least 30 minutes before the initiation of MEC or AC combination chemotherapy. It is administered on Day one of chemotherapy and not more frequently than once every seven days because of the extended-release properties of the formulation.

ROLAPITANT (VARUBI®)

Rolapitant (Varubi®) was approved by the FDA on October 25, 2017 for use in combination with other antiemetic agents in adults for 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.

Rolapitant (Varubi®) is a substance P/neurokinin-1 (NK1) receptor antagonist. Rolapitant (Varubi®) has been shown to augment the antiemetic activity of dexamethasone and a 5-HT_3-receptor antagonist. Rolapitant (Varubi®) is an intravenous infusion that is administered on Day one of chemotherapy over a period of 30 minutes, given two hours prior to the initiation of chemotherapy. Rolapitant (Varubi®) is administered in a regimen with dexamethasone and a 5-HT_3 antagonist.

OFF-LABEL INDICATION

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

R11.0 Nausea

R11.11 Vomiting without nausea

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

T66.XXXA Radiation sickness, unspecified, initial encounter

T66.XXXD Radiation sickness, unspecified, subsequent encounter

T66.XXXS Radiation sickness, unspecified, sequela

Z51.0 Encounter for antineoplastic radiation therapy

Z51.11 Encounter for antineoplastic chemotherapy

HCPCS Level II Code Number(s)

J0185 Injection, aprepitant, 1 mg

J1453 Injection, fosaprepitant, 1 mg

J1627 Injection, granisetron, extended-release, 0.1 mg

J2797 Injection, rolapitant, 0.5 mg

Revenue Code Number(s)

N/A

Cross Reference

Attachment A: Aprepitant (Cinvanti™), Fosaprepitant Dimeglumine (Emend®), Granisetron (Sustol®), and Rolapitant (Varubi®)
Description: Risk of Emesis Without Prophylaxis: Intravenous and Oral Antineoplastic Agents

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Policy History

Revisions from MA08.091c

07/28/2021	This policy has been reissued in accordance with the Company's annual review process.
04/08/2020	This policy has been reissued in accordance with the Company's annual review process.

03/11/2019	This version of the policy will become effective 03/11/2019. The following criteria have been **added** to this policy: • New FDA approval for pediatric individuals for fosaprepitant dimeglumine (Emend) • New age criteria added for all agents • Optional use of olanzapine based on NCCN recommendations.

Revisions from MA08.091b

03/11/2019	This policy has been identified for the HCPCS code update, effective 01/01/2019. The following HCPCS codes have been **added** to this policy: J0185 Injection, aprepitant, 1 mg J2797 Injection, rolapitant, 0.5 mg The following HCPCS codes have been **termed** from this policy: C9463 Injection, aprepitant, 1 mg C9464 Injection, rolapitant, 0.5 mg ---------- -- On 1/9/2019 the following HCPCS code and header have been removed from this policy because the more specific code of J0185 is in effect: **THE FOLLOWING CODE IS USED TO REPRESENT APREPITANT [CINVANTI™] AND ROLAPITANT [VARUBI®]:** J3490 Unclassified drugs

Revisions from MA08.091a

04/01/2018	This policy has been identified for the HCPCS code update, effective 04/01/2018. The following HCPCS codes have been **added** to this policy: C9463 Injection, aprepitant, 1 mg C9464 Injection, rolapitant, 0.5 mg The following HCPCS code has been **removed** from this policy: C9486 Injection, granisetron extended release, 0.1 mg

Revisions from MA08.091

01/01/2018	This version of the policy will become effective 01/01/2018. The following new policy has been developed to communicate the Company's coverage criteria for aprepitant (Cinvanti™), fosaprepitant

	dimeglumine (Emend), granisetron (Sustol), and rolapitant (Varubi®). On 11/07/2017, the following Medical Necessity language was removed from the Policy Section: • Note: This policy does not review or set policy standards for oral aprepitant (Emend®), a generic formulation that may be utilized instead of intravenous fosaprepitant dimeglumine (Emend®)

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