**APREPITANT FOR CHEMOTHERAPY-INDUCED EMESIS**

**(NCD 110.18)**

**Guideline Number:** MPG017.06  
**Approval Date:** October 9, 2019

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**Overview**

Chemotherapy-induced nausea and vomiting (CINV) can range from mild to severe, with the most severe cases resulting in dehydration, malnutrition, metabolic imbalances, and potential withdrawal from future chemotherapy treatments. The incidence and severity of CINV are influenced by the specific chemotherapeutic agent(s) used; dosage, schedule and route of administration; and drug combinations. Patient specific risk factors such as gender, age, history of motion sickness, and prior exposure to chemotherapeutic agents can also have an effect on CINV incidence and severity. Progress has been made in reducing CINV, although it can still be hard to control symptoms that occur more than a day after chemotherapy, during repeat cycles of chemotherapy, and when chemotherapy is given on more than one day or in very high doses. No single antiemetic agent is completely effective in all patients. As noted above, many factors influence the incidence and severity of CINV, with the specific chemotherapeutic agent as the primary factor to consider when deciding which antiemetic to administer. Aprepitant (Emend®) is the first Food and Drug Administration-approved drug of its type. Aprepitant has been proposed to function in combination with other oral antiemetics for a specified population of patients receiving highly emetogenic chemotherapy and/or moderately emetogenic chemotherapy.

CMS is defining highly emetogenic chemotherapy and moderately emetogenic chemotherapy as those anticancer agents so designated in at least two of three guidelines published by the National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and European Society of Medical Oncology (ESMO)/Multinational Association of Supportive Care in Cancer (MASCC). The inclusive examples are: NCCN plus ASCO, NCCN plus ESMO/MASCC, or ASCO plus ESMO/MASCC.

**Guidelines**

Effective for services performed between April 4, 2005, and May 28, 2013, the Centers for Medicare & Medicaid Services makes the following determinations regarding the use of aprepitant in the treatment of reducing chemotherapy-induced emesis: The evidence is adequate to conclude that the use of the oral antiemetic three-drug combination of oral aprepitant (Emend®), an oral 5HT3 antagonist, and oral dexamethasone is reasonable and necessary for a specified patient population. We have defined the patient population for which the use of the oral antiemetic three-drug combination of oral aprepitant (Emend®), an oral 5HT3 antagonist, and oral dexamethasone is reasonable and necessary as only those patients who are receiving one or more of the following anti-cancer chemotherapeutic agents:

- Carmustine
- Cisplatin
- Cyclophosphamide
- Dacarbazine
- Mechlorethamine
- Streptozocin
- Doxorubicin
- Epirubicin

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Related Medicare Advantage Policy Guideline

- Anzemet for Chemotherapy Induced Nausea

Related Medicare Advantage Coverage Summary

- Chemotherapy, and Associated Drugs and Treatments

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**Related Medicare Advantage Policy Guideline**

- Anzemet for Chemotherapy Induced Nausea

**Related Medicare Advantage Coverage Summary**

- Chemotherapy, and Associated Drugs and Treatments
• Lomustine

Effective for services performed on or after May 29, 2013, the oral three-drug regimen of oral aprepitant, an oral 5HT3 antagonist and oral dexamethasone is reasonable and necessary for beneficiaries receiving, either singularly or in combination with other drugs the following anticancer chemotherapeutic agents:

• Alemtuzumab
• Azacitidine
• Bendamustine
• Carboplatin
• Carmustine
• Cisplatin
• Clofarabine
• Cyclophosphamide
• Cytarabine
• Dacarbazine
• Daunorubicin
• Doxorubicin
• Epirubicin
• Idarubicin
• Ifosfamide
• Irinotecan
• Lomustine
• Mechlorethamine
• Oxaliplatin
• Streptozocin

The oral three drug regimen must be administered immediately before and within 48 hours after the administration of these chemotherapeutic agents.

Nationally Noncovered Indications
The evidence is adequate to conclude that aprepitant cannot function alone as a full replacement for intravenously administered antiemetic agents for patients who are receiving highly emetogenic chemotherapy and/or moderately emetogenic chemotherapy. Medicare does not cover under Part B for oral antiemetic drug combination regimens that are administered in part, via an oral route and in part, via an intravenous route. Medicare does not cover under Part B aprepitant when it is used alone for anticancer chemotherapy related nausea and vomiting.

Other
UnitedHealthcare may determine coverage for other all-oral three-drug antiemesis regimens of aprepitant or any other FDA approved oral NK-1 antagonist in combination with an oral 5HT3 antagonist and oral dexamethasone with the chemotherapeutic agents listed above, or any other anticancer chemotherapeutic agents that are FDA approved and are defined as highly or moderately emetogenic.

Documentation Requirements
The supplier must enter a diagnosis code corresponding to the beneficiary's cancer diagnosis on each claim. The billing of an oral antiemetic 3-drug combination is accomplished by one of the following methods:

• Aprepitant (J8501) or rolapitant (J8670) used with a separate 5HT3 antagonist (Q0162, Q0166 or Q0180) and dexamethasone (J8540) must be billed on the same claim.
• Netupitant with its fixed combination of palonosetron (J8655) and dexamethasone (J8540) must be billed on the same claim.

If the NK-1 antagonist and/or dexamethasone is given as an oral anti-emetic outside of the 3-drug regimen, claims will be denied as statutorily non-covered, no benefit.

In addition to the diagnosis code corresponding to the beneficiary’s cancer diagnosis, claims for oral aprepitant (J8501), rolapitant (J8670) 300mg netupitant/0.5mg palonosetron (J8655), or Q0181 must also be accompanied with a diagnosis code of an encounter for antineoplastic chemotherapy.

If dexamethasone (J8540) and either aprepitant (J8501), rolapitant (J8670) or 300mg netupitant/0.5mg palonosetron (J8655) are used in conjunction with one of the anticancer chemotherapeutic agents listed in this policy, a KX modifier must be added to each code.
APPLICABLE CODES

The following list(s) of codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>J8501</td>
<td>Aprepitant, oral, 5 mg</td>
</tr>
<tr>
<td>J8540</td>
<td>Dexamethasone, oral, 0.25 mg</td>
</tr>
<tr>
<td>J8655</td>
<td>Netupitant 300 mg and palonosetron 0.5 mg, oral</td>
</tr>
<tr>
<td>J8670</td>
<td>Rolapitant, oral, 1 mg</td>
</tr>
<tr>
<td>Q0162</td>
<td>Ondansetron 1 mg, oral, FDA approved prescription antiemetic, for use as a complete therapeutic substitute for an IV antiemetic at the time of chemotherapy treatment, not to exceed a 48 hour dosage regimen</td>
</tr>
<tr>
<td>Q0166</td>
<td>Granisetron HCl, 1 mg, oral, FDA approved prescription antiemetic, for use as a complete therapeutic substitute for an IV antiemetic at the time of chemotherapy treatment, not to exceed a 24-hour dosage regimen</td>
</tr>
<tr>
<td>Q0180</td>
<td>Dolasetron mesylate, 100 mg, oral, FDA approved prescription antiemetic, for use as a complete therapeutic substitute for an IV antiemetic at the time of chemotherapy treatment, not to exceed a 24-hour dosage regimen</td>
</tr>
<tr>
<td>Q0181</td>
<td>Unspecified oral dosage form, FDA approved prescription antiemetic, for use as a complete therapeutic substitute for an IV antiemetic at the time of chemotherapy treatment, not to exceed a 48-hour dosage regimen</td>
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<table>
<thead>
<tr>
<th>Modifier</th>
<th>Description</th>
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<tr>
<td>EY</td>
<td>No physician or other licensed health care provider order for this item or service</td>
</tr>
<tr>
<td>GZ</td>
<td>Item or service expected to be denied as not reasonable and necessary</td>
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<tr>
<td>KX</td>
<td>Requirements specified in the medical policy have been met</td>
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<tr>
<th>ICD-10 Diagnosis Code</th>
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<tr>
<td>Z51.11</td>
<td>Encounter for antineoplastic chemotherapy</td>
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PURPOSE

The Medicare Advantage Policy Guideline documents are generally used to support UnitedHealthcare Medicare Advantage claims processing activities and facilitate providers’ submission of accurate claims for the specified services. The document can be used as a guide to help determine applicable:

- Medicare coding or billing requirements, and/or
- Medical necessity coverage guidelines; including documentation requirements.

UnitedHealthcare follows Medicare guidelines such as LCDs, NCDs, and other Medicare manuals for the purposes of determining coverage. It is expected providers retain or have access to appropriate documentation when requested to support coverage. Please utilize the links in the References section below to view the Medicare source materials used to develop this resource document. This document is not a replacement for the Medicare source materials that outline Medicare coverage requirements. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

REFERENCES

CMS National Coverage Determination (NCD)
NCD 110.18 Aprepitant for Chemotherapy-Induced Emesis
Aprepitant for Chemotherapy-Induced Emesis (NCD 110.18)

CMS Local Coverage Determination (LCD)

<table>
<thead>
<tr>
<th>LCD</th>
<th>DME</th>
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<tr>
<td>L33827 (Oral Antiemetic Drugs (Replacement for Intravenous Antiemetics))</td>
<td>CGS: AL, AR, CO, FL, GA, IL, IN, KY, LA, MI, MN, MS, NC, NM, OH, OK, PR, SC, TN, TX, VA, VT, WI, WV&lt;br&gt;Noridian: AK, AS, AZ, CA, CT, DC, DE, GU, HI, IA, ID, KS, MA, MD, ME, MO, MP, MT, ND, NE, NH, NJ, NV, NY, OR, PA, RI, SD, UT, VT, WA, WV</td>
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CMS Articles

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<th>Article</th>
<th>DME</th>
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<tr>
<td>A52480 (Oral Antiemetic Drugs (Replacement for Intravenous Antiemetics) - Policy Article)</td>
<td>CGS: AL, AR, CO, FL, GA, IL, IN, KY, LA, MI, MN, MS, NC, NM, OH, OK, PR, SC, TN, TX, VA, VT, WI, WV&lt;br&gt;Noridian: AK, AS, AZ, CA, CT, DC, DE, GU, HI, IA, ID, KS, MA, MD, ME, MO, MP, MT, ND, NE, NH, NJ, NV, NY, OR, PA, RI, SD, UT, VT, WA, WV</td>
</tr>
<tr>
<td>A55426 (Standard Documentation Requirements for All Claims Submitted to DME MACs)</td>
<td>CGS: AL, AR, CO, FL, GA, IL, IN, KY, LA, MI, MN, MS, NC, NM, OH, OK, PR, SC, TN, TX, VA, VT, WI, WV&lt;br&gt;Noridian: AK, AS, AZ, CA, CT, DC, DE, GU, HI, IA, ID, KS, MA, MD, ME, MO, MP, MT, ND, NE, NH, NJ, NV, NY, OR, PA, RI, SD, UT, VT, WA, WV</td>
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CMS Benefit Policy Manual
Chapter 15; § 50.5.4 Oral Anti-Nausea (Anti-Emetic) Drugs

CMS Claims Processing Manual
Chapter 17; § 80.2 Oral Anti-Emetic Drugs Used as Full Replacement for Intravenous Anti-Emetic Drugs as Part of a Cancer Chemotherapeutic Regimen, § 80.2.1 HCPCS Codes for Oral Anti-Emetic Drugs, § 80.2.4 Billing and Payment Instructions for Part A MACs

CMS Transmittal
Transmittal 2362, Change Request 11392, Dated 09/19/2019 (International Classification of Diseases, 10th Revision (ICD-10) and Other Coding Revisions to National Coverage Determination (NCDs)--January 2020 Update)

GUIDELINE HISTORY/REVISION INFORMATION

Revisions to this summary document do not in any way modify the requirement that services be provided and documented in accordance with the Medicare guidelines in effect on the date of service in question.

<table>
<thead>
<tr>
<th>Date</th>
<th>Action/Description</th>
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<tr>
<td>10/09/2019</td>
<td>• Annual review&lt;br&gt;• Removed HCPCS code J8650 from this policy as it is not applicable to this NCD per CMS</td>
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TERMS AND CONDITIONS

The Medicare Advantage Policy Guidelines are applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

These Policy Guidelines are provided for informational purposes, and do not constitute medical advice. Treating physicians and healthcare providers are solely responsible for determining what care to provide to their patients. Members should always consult their physician before making any decisions about medical care.

Benefit coverage for health services is determined by the member specific benefit plan document* and applicable laws that may require coverage for a specific service. The member specific benefit plan document identifies which services are covered, which are excluded, and which are subject to limitations. In the event of a conflict, the member specific benefit plan document supersedes the Medicare Advantage Policy Guidelines.

Medicare Advantage Policy Guidelines are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support UnitedHealthcare coverage decision making. UnitedHealthcare may modify these Policy Guidelines at any time by publishing a new version of the policy on this website. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the Medicare Advantage Policy Guidelines is believed to be accurate and current as of the date of
publication, and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

You are responsible for submission of accurate claims. Medicare Advantage Policy Guidelines are intended to ensure that coverage decisions are made accurately based on the code or codes that correctly describe the health care services provided. UnitedHealthcare Medicare Advantage Policy Guidelines use Current Procedural Terminology (CPT®), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT® or other sources are for definitional purposes only and do not imply any right to reimbursement or guarantee claims payment.

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*For more information on a specific member's benefit coverage, please call the customer service number on the back of the member ID card or refer to the Administrative Guide.