

<b>CMS Manual System</b>	<b>Department of Health &amp; Human Services (DHHS)</b>
<b>Pub 100-03 Medicare National Coverage Determinations</b>	<b>Centers for Medicare &amp; Medicaid Services (CMS)</b>
<b>Transmittal 165</b>	<b>Date: April 15, 2014</b>
	<b>Change Request 8418</b>

**Transmittal 163, dated February 21, 2014, is being rescinded and replaced by Transmittal 165, dated April 15, 2014, to correct the language for the title to the NCD Manual. All other information remains the same.**

**SUBJECT: Aprepitant for Chemotherapy-Induced Emesis**

**I. SUMMARY OF CHANGES:** Effective for claims with dates of service May 29, 2013, and later, CMS extends coverage of the oral antiemetic three-drug regimen of oral aprepitant, an oral 5HT3 antagonist and oral dexamethasone to beneficiaries who are receiving one or more of the following anti-cancer chemotherapeutic agents.

This revision to the Medicare National Coverage Determinations Manual is a national coverage determination (NCD). NCDs are binding on all carriers, fiscal intermediaries, contractors with the Federal government that review and/or adjudicate claims, determinations, and/or decisions, quality improvement organizations, qualified independent contractors, the Medicare appeals council, and administrative law judges (ALJs) (see 42 CFR section 405.1060(a)(4) (2005)). An NCD that expands coverage is also binding on a Medicare advantage organization. In addition, an ALJ may not review an NCD. (See section 1869(f)(1)(A)(i) of the Social Security Act.)

**EFFECTIVE DATE: May 29, 2013**

**IMPLEMENTATION DATE: July 7, 2014**

*Disclaimer for manual changes only: The revision date and transmittal number apply only to red italicized material. Any other material was previously published and remains unchanged. However, if this revision contains a table of contents, you will receive the new/revised information only, and not the entire table of contents.*

**II. CHANGES IN MANUAL INSTRUCTIONS:** (N/A if manual is not updated)

R=REVISED, N=NEW, D=DELETED-*Only One Per Row.*

<b>R/N/D</b>	<b>CHAPTER / SECTION / SUBSECTION / TITLE</b>
R	1/110.18/Aprepitant for Chemotherapy-Induced Emesis

**III. FUNDING:**

**For Medicare Administrative Contractors (MACs):**

The Medicare Administrative Contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as a change to the MAC statement of Work. The contractor is not obliged to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the Contracting Officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the Contracting Officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

#### **IV. ATTACHMENTS:**

**Business Requirements**

**Manual Instruction**

*\*Unless otherwise specified, the effective date is the date of service.*

# Attachment - Business Requirements

Pub. 100-03	Transmittal: 165	Date: April 15, 2014	Change Request: 8418
-------------	------------------	----------------------	----------------------

**Transmittal 163, dated February 21, 2014, is being rescinded and replaced by Transmittal 165, dated April 15, 2014, to correct the language for the title to the NCD Manual. All other information remains the same.**

**SUBJECT: Aprepitant for Chemotherapy-Induced Emesis**

**EFFECTIVE DATE: May 29, 2013**

**IMPLEMENTATION DATE: July 7, 2014**

## **I. GENERAL INFORMATION**

**A. Background:** Chemotherapy induced emesis is the occurrence of nausea and vomiting (N&V) during or after anticancer treatment with chemotherapy agents. The Social Security Act permits oral drugs to be paid under part B in very limited circumstances, one of which is antiemetic therapy administered immediately before and within 48 hours after anticancer chemotherapy as described in §1861(s)(2) of the Act. These drugs must fully replace the non-self-administered drug that would otherwise be covered.

On April 4, 2005, the Centers for Medicare & Medicaid Services (CMS) announced a National Coverage Determination (NCD) for the use of the oral three-drug regimen of aprepitant, a 5HT3 antagonist and dexamethasone for patients who are receiving certain highly emetogenic chemotherapeutic agents.

CMS recently received a formal written request to reconsider this NCD and to expand coverage for the use of aprepitant, a 5HT3 antagonist and dexamethasone in the patients receiving anticancer therapeutic agents currently considered moderately emetogenic.

On May 29, 2013 CMS announced an updated NCD, section 110.18, to cover the use of the oral antiemetic three-drug combination of oral aprepitant, an oral 5HT3 antagonist, and oral dexamethasone for patients receiving highly and moderately emetogenic chemotherapy.

## **B. Policy:**

Effective for services on or after May 29, 2013, the following anti-cancer chemotherapeutic agents have been added to the list of anticancer chemotherapeutic agents for which the use of the oral antiemetic 3-drug combination of oral aprepitant, an oral 5HT3 antagonist and oral dexamethasone is deemed reasonable and necessary:

Alemtuzumab

Azacitidine

Bendamustine

Carboplatin

Clofarabine

Cytarabine

Daunorubicin

Idarubicin

Ifosfamide

Irinotecan

Oxaliplatin

Please note the entire list includes also the existing 9 anticancer chemotherapeutic agents that are listed below: Carmustine, Cisplatin, Cyclophosphamide, Dacarbazine, Mechlorethamine, Streptozocin, Doxorubicin, Epirubicin, Lomustine. Claims for oral aprepitant must also be accompanied with a diagnosis code of an encounter for antineoplastic chemotherapy.

CMS also permits the Medicare Administrative Contractors (MACs) to 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, or any other anticancer chemotherapeutic agents that are FDA approved and may in future be defined as highly or moderately emetogenic. 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.

This coverage policy applies only to the oral forms of the three drug regimen as full replacement for their intravenous equivalents. All other indications or combinations for the use of oral aprepitant are non-covered under Medicare Part B, but may be considered under Medicare Part D.

## II. BUSINESS REQUIREMENTS TABLE

"Shall" denotes a mandatory requirement, and "should" denotes an optional requirement.

Number	Requirement	Responsibility									
		A/B MAC			D M E M A C S	Shared- System Maintainers				Other	
		A	B	H H H		F I S S	M C S	V M S	C W F		
8418.1	Contractors shall be advised that effective for claims with dates of service on or after May 29, 2013, the following list of anti-cancer chemotherapeutic agents has been added for which the oral antiemetic drug aprepitant used in combination with an oral 5HT3 antagonist and oral dexamethasone is eligible for coverage: <ul style="list-style-type: none"> <li>Alemtuzumab</li> <li>Azacitidine</li> <li>Bendamustine</li> <li>Carboplatin</li> </ul>	X			X						

Number	Requirement	Responsibility								
		A/B MAC			D M E M A C	Shared- System Maintainers				Other
		A	B	H H H		F I S S	M C S	V M S	C W F	
	<ul style="list-style-type: none"> <li>• Clofarabine</li> <li>• Cytarabine</li> <li>• Daunorubicin</li> <li>• Idarubicin</li> <li>• Ifosfamide</li> <li>• Irinotecan</li> <li>• Oxaliplatin</li> </ul> <p>See NCD Manual Pub.100-03 chapter 1, section 110.18 for more information on coverage, and CPM Manual Pub. 100-04, Chapter 17, section 80.2.4 for payment.</p> <p>Please also note that the entire list includes the eleven new drugs listed above and the nine existing anticancer chemotherapeutic agents listed below:</p> <ul style="list-style-type: none"> <li>• Carmustine</li> <li>• Cisplatin</li> <li>• Cyclophosphamide</li> <li>• Dacarbazine</li> <li>• Mechlorethamine</li> <li>• Streptozocin</li> <li>• Doxorubicin</li> <li>• Epirubicin</li> <li>• Lomustine</li> </ul>									

### III. PROVIDER EDUCATION TABLE

Number	Requirement	Responsibility
--------	-------------	----------------

		A/B MAC			D M E M A C	C E D I
		A	B	H H H		
8418.2	MLN Article : A provider education article related to this instruction will be available at <a href="http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/">http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/</a> shortly after the CR is released. You will receive notification of the article release via the established "MLN Matters" listserv. Contractors shall post this article, or a direct link to this article, on their Web sites and include information about it in a listserv message within one week of the availability of the provider education article. In addition, the provider education article shall be included in the contractor's next regularly scheduled bulletin. Contractors are free to supplement MLN Matters articles with localized information that would benefit their provider community in billing and administering the Medicare program correctly.	X			X	

#### IV. SUPPORTING INFORMATION

**Section A: Recommendations and supporting information associated with listed requirements: N/A**

*"Should" denotes a recommendation.*

X-Ref Requirement Number	Recommendations or other supporting information: N/A

**Section B: All other recommendations and supporting information: N/A**

#### V. CONTACTS

**Pre-Implementation Contact(s):** Cheryl Gilbreath, 410-786-4919 or [cheryl.gilbreath@cms.hhs.gov](mailto:cheryl.gilbreath@cms.hhs.gov) (Coverage) , Wanda Belle, 410-786-7491 or [wanda.belle@cms.hhs.gov](mailto:wanda.belle@cms.hhs.gov) (Coverage) , Patricia Brocato-Simons, 410-786-0261 or [patricia.brocato-simons@cms.hhs.gov](mailto:patricia.brocato-simons@cms.hhs.gov) (Coverage) , Wendy Knarr, 410-786-0843 or [Wendy.Knarr@cms.hhs.gov](mailto:Wendy.Knarr@cms.hhs.gov) ((DME) Call relay #711 Then have agent contact phone number) , Bridgitte Davis-Hawkins, 410-786-4573 or [Bridgitte.Davis-hawkins@cms.hhs.gov](mailto:Bridgitte.Davis-hawkins@cms.hhs.gov) (Part B) , Cami DiGiacomo, 410-786-5888 or [Cami.DiGiacomo@cms.hhs.gov](mailto:Cami.DiGiacomo@cms.hhs.gov) (Institutional Claims)

**Post-Implementation Contact(s):** Contact your Contracting Officer's Representative (COR) or Contractor Manager, as applicable.

#### VI. FUNDING

##### **Section A: For Medicare Administrative Contractors (MACs):**

The Medicare Administrative Contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS do not construe this as a change to the MAC Statement of Work. The contractor is not obligated to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the Contracting Officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the Contracting Officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

# **Medicare National Coverage Determinations Manual**

## **Chapter 1, Part 2 (Sections 90 – 160.26)**

### **Coverage Determinations**

**Table of Contents**  
*(Rev. 165, 04-15-14)*

**110.18 – Aprepitant for Chemotherapy-Induced Emesis**

## 110.18 – Aprepitant for Chemotherapy-Induced Emesis

*(Rev. 165, Issued: 04-15-14, Effective: 05-29-13, Implementation: 07-07-14)*

### A. General

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 Medicare 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.*

### B. Nationally Covered Indications

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 5HT<sub>3</sub>* antagonist, and *oral* dexamethasone is reasonable and necessary for a specified patient population. CMS has defined the patient population for which the use of the oral antiemetic *three*-drug combination of *oral* aprepitant (Emend®), *an oral 5HT<sub>3</sub>* 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
- Lomustine

*Effective for services performed on or after May 29, 2013, the oral three-drug regimen of oral aprepitant, an oral 5HT<sub>3</sub> 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.*

### **C. 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 drugs in 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.*

### **D. Other**

*Medicare Administrative Contractors 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 5HT<sub>3</sub> 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.*

*(Last reviewed May 2013.)*