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.

<table>
<thead>
<tr>
<th>R/N/D</th>
<th>CHAPTER / SECTION / SUBSECTION / TITLE</th>
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</thead>
<tbody>
<tr>
<td>R</td>
<td>1/110.18/Aprepitant for Chemotherapy-Induced Emesis</td>
</tr>
</tbody>
</table>

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.
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.

<table>
<thead>
<tr>
<th>Number</th>
<th>Requirement</th>
<th>Responsibility</th>
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<tbody>
<tr>
<td></td>
<td>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:</td>
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<tr>
<td>8418.1</td>
<td>• Alemtuzumab</td>
<td>X</td>
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<td></td>
<td>• Azacitidine</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>• Bendamustine</td>
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<td></td>
<td>• Carboplatin</td>
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### III. PROVIDER EDUCATION TABLE

<table>
<thead>
<tr>
<th>Number</th>
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<tr>
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<td>A/B MAC</td>
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<td>CMS</td>
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<tr>
<td></td>
<td></td>
<td>Other</td>
</tr>
</tbody>
</table>

- Clofarabine
- Cytarabine
- Daunorubicin
- Idarubicin
- Ifosfamide
- Irinotecan
- Oxaliplatin

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.

Please also note that the entire list includes the eleven new drugs listed above and the nine existing anticancer chemotherapeutic agents listed below:

- Carmustine
- Cisplatin
- Cyclophosphamide
- Dacarbazine
- Mechlorethamine
- Streptozocin
- Doxorubicin
- Epirubicin
- Lomustine
IV. SUPPORTING INFORMATION

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

"Should" denotes a recommendation.

<table>
<thead>
<tr>
<th>Requirement Number</th>
<th>Recommendations or other supporting information: N/A</th>
</tr>
</thead>
</table>

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 (Coverage), Wanda Belle, 410-786-7491 or wanda.belle@cms.hhs.gov (Coverage), Patricia Brocato-Simons, 410-786-0261 or patricia.brocatosimons@cms.hhs.gov (Coverage), Wendy Knarr, 410-786-0843 or 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 (Part B), Cami DiGiacomo, 410-786-5888 or 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.
110.18 – Aprepitant for Chemotherapy-Induced Emesis
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 5HT3 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 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
- 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.

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_3 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.)