



**Texas Medicaid/CHIP Vendor Drug Program**  
**Drug Utilization Criteria For Outpatient Use Guidelines**  
**Aprepitant (Emend®)**

**About**

Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with an asterisk [\*]. The information contained is for the convenience of the public. The Texas Health and Human Services Commission is not responsible for any errors in transmission or any errors or omissions in the document.

**Publication History**

Revised September 2016; May 2015; August 2013; June 2013; September 2011; October 2009; February 2006; January 2006. Developed December 2003.

**1. Dosage [\*]**

**Current therapies for chemotherapy-induced nausea/vomiting (CINV) and post-operative nausea and vomiting (PONV) target corticosteroid, dopamine, and serotonin (5-HT<sub>3</sub>) receptors. In the central nervous system, tachykinins and neurokinins play a role in some autonomic reflexes and behaviors. Aprepitant is a selective human substance P/neurokinin 1 (NK<sub>1</sub>) antagonist with a high affinity for NK<sub>1</sub> receptors and little, if any, attraction for corticosteroid, dopamine, or 5-HT<sub>3</sub> receptors. A new aprepitant suspension formulation was recently FDA-approved for prevention of CINV.**

*Adults*

Aprepitant is FDA-approved for prevention of CINV due to high and moderate emetogenic agents including high dose cisplatin, as well as prevention for PONV. *When used to prevent CINV with highly emetogenic chemotherapy, aprepitant is prescribed as triple therapy in combination with a 5-HT<sub>3</sub> receptor antagonist and corticosteroids based on clinical trial data as well as data from available published anti-emetic guidelines showing more significant reductions in acute emesis on day 1 of chemotherapy and decreased incidence of delayed emesis with the addition of aprepitant.* Maximum recommended **adult** dosages for aprepitant are summarized in Table 1. Dosages exceeding those listed in Table 1 will be reviewed.

<b>Table 1: Maximum Recommended Oral Aprepitant Dosages in Adults</b>		
<b>Indication</b>	<b>Dosage Form</b>	<b>Maximum Recommended Dosage</b>
CINV: <i>highly emetogenic chemotherapy:</i> <ul style="list-style-type: none"> <li>day 1 (one hour before chemotherapy)</li> <li>days 2 and 3</li> </ul> <i>moderately emetogenic chemotherapy:</i> <ul style="list-style-type: none"> <li>day 1 (one hour before chemotherapy)</li> <li>days 2 and 3</li> </ul>	<b>40 mg, 80 mg, 125 mg capsules (Emend®)</b>  <b>125 mg/5 ml oral suspension (Emend®)</b>	<ul style="list-style-type: none"> <li>125 mg/day (as capsule or suspension)*</li> <li>80 mg/day (as capsule or suspension)+</li> </ul> <ul style="list-style-type: none"> <li>125 mg/day (as capsule or suspension)*</li> <li>80 mg/day (as capsule or suspension)+</li> </ul>
PONV: <ul style="list-style-type: none"> <li>within 3 hours of anesthesia induction</li> </ul>		<ul style="list-style-type: none"> <li>40 mg as a single dose (as capsule)</li> </ul>

*\*in conjunction with a 5-HT<sub>3</sub> receptor antagonist plus dexamethasone  
 +in conjunction with dexamethasone on days 2-3; dexamethasone also given on day 4*



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**Pediatrics**

Aprepitant capsules are FDA-approved for use in children and adolescents 12 years of age and older to prevent nausea and vomiting associated with initial and repeat courses of moderately to highly emetogenic chemotherapy (includes high-dose cisplatin). Aprepitant oral suspension is FDA-approved to prevent acute and delayed nausea and vomiting seen with initial and repeat courses of highly emetogenic chemotherapy (includes high-dose cisplatin) as well as nausea and vomiting associated with moderately emetogenic chemotherapy in pediatric patients 6 months of age and to 11 years of age weighing at least 6 kg or pediatric patients of any age weighing at least 6 kg who cannot swallow capsules. Pediatric aprepitant dosages are summarized in Table 2. Aprepitant dosages exceeding these recommendations in pediatric patients will be reviewed.

Table 2: Maximum Recommended Oral Aprepitant Dosages in Pediatric Patients		
Indication/Patient Age	Usual Dosage/Dosage Form	Maximum Recommended Dosage
<b>CINV:</b> <i>moderately emetogenic chemotherapy:</i> <ul style="list-style-type: none"> <li>6 months to &lt; 12 years (at least 6 kg):</li> <li>pediatric patients any age (at least 6 kg) unable to swallow capsules:</li> <li>&gt; 12 years of age:</li> </ul>	<ul style="list-style-type: none"> <li>3 mg/kg on day 1, followed by 2 mg/kg on days 2 and 3 (as suspension)*+</li> </ul>	125 mg on day 1, 80 mg on days 2 and 3
	<ul style="list-style-type: none"> <li>3 mg/kg on day 1, followed by 2 mg/kg on days 2 and 3 (as suspension)*+</li> </ul>	125 mg on day 1, 80 mg on days 2 and 3
	<ul style="list-style-type: none"> <li>125 mg on day 1 (one hour before chemotherapy), followed by 80 mg on days 2 and 3 (as capsule)*+</li> </ul>	125 mg on day 1, 80 mg on days 2 and 3

*\*in conjunction with a 5-HT3 receptor antagonist plus dexamethasone on day 1  
+in conjunction with dexamethasone on days 2-3; dexamethasone also given on day 4*

**2. Duration of Therapy**

The maximum treatment duration for aprepitant is three days per chemotherapy cycle for moderately or highly emetogenic chemotherapy regimens. Chemotherapy regimens are administered for one to several days within a 30-day time period and repeated in cycles. The number of cycles varies based on the type of cancer being treated. Unless otherwise specified, aprepitant treatment regimens continuing for greater than three days per chemotherapy cycle will be reviewed for appropriateness of use.

**3. Duplicative Therapy [\*]**

Aprepitant is the first medication in the class of selective human substance P/NK<sub>1</sub> antagonists. Fosaprepitant, the injectable aprepitant formulation, was indicated for use on day 1 of the chemotherapy cycle as the 115 mg dose with oral aprepitant administered on days 2 and 3; however, the 115 mg vial is no longer commercially available. Fosaprepitant 150 mg injection is not administered with oral aprepitant on any treatment days. Dosage regimens incorporating concurrent use of fosaprepitant 150 mg and aprepitant will be reviewed.



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**4. Drug-Drug Interactions [\*]**

Patient profiles will be monitored to identify regimens that may have clinically significant drug-drug interactions. Drug-drug interactions considered clinically relevant for aprepitant are summarized in Table 3. Only those interactions classified as clinical significance level 1, contraindicated, or life threatening which have not been classified will be reviewed:

<b>Table 3: Aprepitant Drug-Drug Interactions</b>				
<b>Target Drug</b>	<b>Interacting Drug</b>	<b>Interaction</b>	<b>Recommendation</b>	<b>Clinical Significance*</b>
aprepitant	CYP3A4 inducers (e.g., carbamazepine, rifampin)	adjunctive use may induce aprepitant metabolism and potential for reduced aprepitant serum levels and decreased aprepitant efficacy; CYP3A4 inducer activity may also be reduced, as aprepitant is also a CYP3A4 inducer	monitor patients for aprepitant efficacy; if needed, modify aprepitant dose or choose alternative anti-emetic without CYP3A4 inducer interaction; monitor CYP3A4 inducer activity and adjust dose as necessary	moderate (DrugReax) 3-moderate (CP)
aprepitant	CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, nefazodone, clarithromycin, ritonavir)	combined use may result in reduced aprepitant metabolism, increased serum aprepitant levels, and the potential for adverse effects; however, aprepitant appears to be tolerated over a wide dosage range and is prescribed for short time periods	clinical significance of interaction not well defined; observe patients for increased aprepitant adverse effects and adjust dose if necessary	major (DrugReax) 3-moderate (CP)
aprepitant	CYP3A4 substrates (e.g., aripiprazole, <b>colchicine</b> , diltiazem, <b>phenytoin</b> , ranolazine, ziprasidone)	combined use may result in elevated substrate plasma levels and potential for toxicity or loss of efficacy, as aprepitant is known CYP3A4 inhibitor and inducer and may interfere with metabolism of medications metabolized by CYP3A4	use aprepitant cautiously with compounds metabolized by CYP3A4; monitor patients carefully for signs/ symptoms of substrate toxicity or loss of efficacy and adjust substrate dose as necessary	major (DrugReax) 2-major, 3-moderate (CP)
aprepitant	oral contraceptives (OC)	adjunctive use may result in reduced OC efficacy as AUC for both estrogen and progestin components may be reduced	alternative or back-up methods of contraception recommended during time that aprepitant is prescribed and for one month following last aprepitant dose	moderate (DrugReax) 2-major (CP)



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**Table 3: Aprepitant Drug-Drug Interactions (continued)**

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance*
aprepitant	pimozide (Orap®)	co-use may result in elevated plasma pimozide levels and increased risk for cardiac arrhythmias, QT interval prolongation, as aprepitant inhibits CYP3A4 (enzyme for pimozide metabolism)	adjunctive use contraindicated	contraindicated (DrugReax) 1-severe (CP)
aprepitant	phenytoin	combined use may result in reduced phenytoin levels and potential loss of seizure control as aprepitant induces CYP2C9, the enzyme that metabolizes phenytoin	administer cautiously together; observe for loss of seizure control	moderate (DrugReax) 3-moderate (CP)
aprepitant	warfarin	co-administration may result in significant decreases in warfarin serum levels, INR and warfarin efficacy, as aprepitant induces CYP2C9, the enzyme involved in warfarin metabolism	monitor clotting status closely within 2-week period (especially 7 to 10 days) after each 3-day chemotherapy regimen or following single-dose therapy for PONV	major (DrugReax) 2-major (CP)

\*CP = Clinical Pharmacology

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