



CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

**Subject Aprepitant , Fosaprepitant
 Dimeglumine (Emend®)**

**Effective Date 12/15/2010
Next Review Date.....12/15/2011
Coverage Policy Number 4018**

Table of Contents

Coverage Policy	1
General Background	3
Coding/Billing Information	6
References	6
Policy History.....	8

Related Coverage Policies

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

Coverage Policy

CIGNA covers aprepitant (Emend®) as medically necessary for EITHER of the following indications:

- prevention of nausea and vomiting associated with initial and repeat courses of highly emetogenic chemotherapy in conjunction with other antiemetic agents, such as dexamethasone and ondansetron
- prevention of postoperative nausea and vomiting

Quantity limits apply for aprepitant (Emend®) and are as follows:

- a **THREE** day supply consisting of **ONE** 125mg tablet and **TWO** 80 mg tablets per treatment cycle for prevention of nausea and vomiting associated with emetogenic chemotherapy
- one day of **ONE** 40 mg capsule for prevention of postoperative nausea and vomiting (given within three hours prior to induction of anesthesia)

CIGNA covers fosaprepitant dimeglumine (Emend®) injection as medically necessary for the prevention of nausea and vomiting associated with initial and repeat courses of highly emetogenic chemotherapy on Day 1 ONLY of the chemotherapy

CIGNA does not cover aprepitant (Emend®) or fosaprepitant dimeglumine (IV Emend®) for ANY of the following indications because it is considered experimental, investigational, or unproven (this list may not be all- inclusive):

- acute psychosis
 - anxiety
 - depression
 - established nausea and vomiting
 - pain
-

FDA Approved Indications

Emend Capsules

Emend, in combination with other antiemetic agents, is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin or prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy. Emend is indicated for the prevention of postoperative nausea and vomiting.

Emend for Injection

Emend for injection is a substance P/neurokinin-1 (NK₁) receptor antagonist indicated in adults for use 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 and prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). Emend for injection has not been studied for the treatment of established nausea and vomiting. Chronic continuous administration is not recommended.

FDA Recommended Dosing

Emend Capsules

Capsules of Emend are given for 3 days as part of a regimen that includes a corticosteroid and a 5-HT₃ antagonist. The recommended dose of Emend is 125 mg orally 1 hour prior to chemotherapy treatment (Day 1) and 80 mg orally once daily in the morning on Days 2 and 3. Emend for injection (115 mg) is a pro-drug of aprepitant and may be substituted for oral Emend (125 mg), 30 minutes prior to chemotherapy, on Day 1 only of the chemotherapy induced nausea and vomiting (CINV) regimen as an intravenous infusion administered over 15 minutes.

Emend for Injection

Emend for Injection 150 mg (Single Dose Regimen of Emend) is administered intravenously on Day 1 only as an infusion over 20-30 minutes initiated approximately 30 minutes prior to chemotherapy. No capsules of Emend are administered on Days 2 and 3. Emend for injection should be administered in conjunction with a corticosteroid and a 5-HT₃ antagonist. The recommended dosage of dexamethasone with Emend for injection 150 mg differs from the recommended dosage of dexamethasone with Emend for injection 115 mg on Days 3 and 4.

Emend for injection 115 mg (3-Day Dosing Regimen of Emend) is administered on Day 1 only as an infusion over 15 minutes initiated 30 minutes prior to chemotherapy. Capsules of Emend 80 mg should be administered on Days 2 and 3. Emend for injection 115 mg should be administered in conjunction with a corticosteroid and a 5-HT₃ antagonist. The recommended dosage of dexamethasone with Emend for injection 115 mg differs from the recommended dosage of dexamethasone with Emend for injection 150 mg on Days 3 and 4. Capsules of Emend 125 mg may be substituted for Emend for Injection 115 mg on Day 1.

Drug Availability

Emend Capsules

Available as 80 mg capsules - White, opaque, hard gelatin capsule with "461" and "80 mg" printed in black ink on the body supplied in unit-of-use BiPack of 2 and unit-dose package of 6; 125 mg capsules - Opaque, hard gelatin capsule with white body and pink cap with "462" and "125 mg" printed in black ink on the body supplied in unit-dose package of 6; one unit-of-use TriPack containing one 125 mg capsule and two 80 mg capsules; 40 mg capsules - Opaque, hard gelatin capsule with white body and mustard yellow cap with "464" and "40 mg" printed in black ink on the body supplied as unit-of-use package of 1 and unit-dose package of 5.

Emend for Injection

One 115 mg single dose glass vial: White to off-white lyophilized solid. Supplied as 1 vial per carton. One 150 mg single dose glass vial: White to off-white lyophilized solid. Supplied as 1 vial per carton.

General Background

Pharmacology

Aprepitant is a centrally-acting antiemetic. It works as a competitive antagonist of the neurokinin₁ (NK₁) receptor. Aprepitant is available as an oral agent. Substance P is a tachykinin found in neurons innervating the brainstem nucleus tractus solitarius and the area postrema. Exogenous Substance P applied to the cells in the nucleus tractus solitarius results in emesis. Substance P mediates its effects through the NK₁ receptor. The antiemetic mechanism of action of aprepitant is believed to be centrally mediated, in the vicinity of the nucleus tractus solitarius in the dorsal vagal complex. The dorsal vagal complex is composed of the nucleus tractus solitarius, area postrema, and dorsal motor nucleus of the vagus. At the nucleus tractus solitarius, vagal afferents from the gastrointestinal tract meet inputs from the area postrema and other regions involved in emesis. NK₁ receptor antagonists prevent emesis induced by the chemotherapeutic agent cisplatin, centrally acting emetogenic agents such as morphine and apomorphine, and gastric irritants. Aprepitant has a long duration of action due to its slow off rate from the NK₁ receptor (rate of dissociation $K_1=0.0054 \pm 0.003$ and half-life 154 ± 75 min).

Fosaprepitant is an intravenously administered prodrug of aprepitant, a neurokinin-1 receptor antagonist. Fosaprepitant is only labeled to replace oral aprepitant on the first day of a 3-day chemotherapy induced nausea and vomiting prophylaxis regimen. It is not labeled for prophylaxis or treatment of postoperative nausea and vomiting. Fosaprepitant is rapidly and nearly completely converted to aprepitant after intravenous infusion. The plasma concentration curve for aprepitant after intravenous administration of fosaprepitant 115 mg is almost identical to oral aprepitant 125 mg from 3-72 hours post-dose.

Guidelines

Several organizations, including the American Society of Health-System Pharmacists (ASHP), American Society of Clinical Oncology (ASCO), British Columbia Cancer Agency, the Antiemetic Subcommittee of the Multinational Association of Supportive Care in Cancer (MASCC), and the Systemic Treatment Disease Site Group (STDSG) of Ontario have published guidelines recommending antiemetic regimens for acute and delayed CINV .

According to the 2006 ASCO guideline, the combination of a 5-hydroxytryptamine-3 (5-HT₃) serotonin receptor antagonist, dexamethasone, and aprepitant is recommended before chemotherapy of high emetic risk. For persons receiving highly emetogenic chemotherapy, there is no group of patients for whom agents of lower therapeutic index are appropriate first-choice antiemetics. However, for the prevention of delayed emesis, the two-drug combination of dexamethasone and aprepitant is recommended in all patients receiving highly emetogenic chemotherapy. Per the 2006 guideline, the combination of a 5-HT₃ serotonin receptor antagonist and dexamethasone is no longer recommended for the prevention of delayed emesis after chemotherapeutic agents of high emetic risk. A detailed analysis of clinical trial data for these patients has failed to demonstrate that the combination of a 5-HT₃ serotonin receptor antagonist plus dexamethasone is superior to dexamethasone alone. In addition, results from a recent clinical trial reported in abstract form showed that a combination of aprepitant and dexamethasone was superior to ondansetron and dexamethasone in the prevention of cisplatin-induced delayed emesis. Based on this information and the demonstrated effectiveness of aprepitant and dexamethasone for this indication, both the MASCC Consensus Conference and the ASCO Update Committee no longer recommend that a 5-HT₃ antagonist plus dexamethasone be used to prevent delayed emesis after chemotherapy of high emetic risk.

Clinical Efficacy

The effects of aprepitant in the prevention of cisplatin-induced emesis were assessed in a multicenter, double-blind study enrolling 351 cisplatin-naïve patients scheduled to receive their first course of cisplatin-based chemotherapy with a cisplatin dose of 70 mg/m² or greater. Patients were randomized into one of the following groups: Group one - granisetron 10 mg/kg intravenously (IV) 30 minutes before cisplatin followed by placebo on days 2–5 (90 patients); Group two - granisetron 10 mcg/kg intravenously 30 minutes before cisplatin and aprepitant 400 mg orally two hours before cisplatin followed by aprepitant 300 mg orally on days 2–5 (86 patients); Group three - aprepitant 400 mg the evening before and two hours pre-cisplatin followed by aprepitant

300 mg orally on days 2–5 (89 patients); Group four - aprepitant 400 mg orally two hours before cisplatin, followed by aprepitant 300 mg orally on days 2–5 (86 patients).

All patients also received dexamethasone 20 mg orally 30 minutes before cisplatin. In the acute period (first 24 hours after the initiation of cisplatin), emesis did not occur in 57% of patients in group one, 80% in group two, 46% in group three, and 43% in group four ($p < 0.01$ for group two vs. group four). In the delayed period (days 2–5), emesis did not occur in 29% in group one, 63% in group two, 51% in group three, and 57% in group four ($p < 0.01$ for group two, three, and four vs. group one). The regimen of aprepitant plus dexamethasone was less effective than the regimen of granisetron plus dexamethasone for control of acute emesis and nausea. Acute emesis in the patients treated with aprepitant, but without granisetron, usually occurred in the first eight hours. Aprepitant plus dexamethasone was more effective than granisetron plus dexamethasone for the prevention of delayed emesis and nausea. A regimen of aprepitant plus granisetron and dexamethasone was highly effective at preventing acute and delayed emesis and nausea in patients receiving cisplatin chemotherapy.

In another double-blind study, aprepitant was compared to placebo when either was administered with granisetron and dexamethasone in 159 cisplatin-naïve patients receiving a cisplatin-containing chemotherapy regimen with a cisplatin dose of at least 70 mg/m^2 . All patients received granisetron 10 mcg/kg intravenously and dexamethasone 20 mg orally 30 minutes prior to the cisplatin dose. Patients were randomized to one of the following groups: Group one - aprepitant 400 mg before cisplatin and 300 mg on days 2–5 (54 patients); Group two - aprepitant 400 mg before cisplatin and placebo on days 2–5 (54 patients); Group three - placebo before cisplatin and on days 2–5 (51 patients).

The first aprepitant or placebo dose was given two hours prior to the cisplatin infusion. Rescue therapy, consisting of metoclopramide for day one and dexamethasone and metoclopramide for days 2–5, was available as needed. In the acute period (i.e., first 24 hours after cisplatin administration), emesis did not occur in 93% of patients in group one, 94% in group two, and 67% of patients in group three ($p < 0.001$ for group three vs. combined groups one and two). The percentage of patients with no emesis and no rescue therapy was 77% in group one, 83% in group two, and 57% in group three ($p < 0.001$ for group three vs. combined groups one and two). In the delayed period (days 2–5), emesis did not occur in 82% of patients in group one, 78% in group two, and 33% in group three ($p < 0.001$). The percentage of patients with no emesis in the delayed phase and no use of rescue medications was 52% in group one, 43% in group two, and 16% in group three ($p < 0.001$ group three vs. group one, $p = 0.003$ group three vs. group two). Median scores on the Visual Analog Scale for nausea were also reduced in group one and group two compared to group three.

Another randomized, double-blind, placebo-controlled trial assessed the efficacy ($n = 523$) and safety ($n = 568$) of aprepitant in cisplatin-naïve patients scheduled to receive their first course of cisplatin-based chemotherapy with a cisplatin dose of 70 mg/m^2 or greater. Patients were randomized into one of two groups: Standard therapy - ondansetron 32 mg IV and dexamethasone 20 mg on day one, followed by dexamethasone 8 mg twice daily on days 2–4; Aprepitant therapy - aprepitant 125 mg, ondansetron 32 mg IV and dexamethasone 12 mg on day one, followed by aprepitant 80 mg daily and dexamethasone 8 mg daily on days 2–3, followed by dexamethasone 8 mg on day four.

The primary endpoint of the study was complete response, defined as no emetic episodes and no use of rescue therapy in the overall study period (days 1–5). During the five days after chemotherapy, the percentages of patients who achieved a complete response were 62.7% in the aprepitant group versus 43.3% in the standard therapy group ($p < 0.001$). For day one, the complete response rates were 82.8% for the aprepitant group and 68.4% for the standard therapy group ($p < 0.001$); for days 2–5, the complete response rates were 67.7% in the aprepitant group and 46.8% in the standard therapy group ($p < 0.001$). The overall incidence of adverse events was similar in the two treatment groups, as were rates of serious adverse events, discontinuations due to adverse events, and deaths. Based on results from earlier studies, this study included aprepitant only for three days. In addition, the dexamethasone doses in the aprepitant group were reduced based on an earlier pharmacokinetic study which suggested that aprepitant increased dexamethasone levels by approximately two-fold.

In two multicenter, randomized, double-blind, active comparator-controlled, parallel-group studies, aprepitant was compared with ondansetron for the prevention of postoperative nausea and vomiting in 1658 patients undergoing open abdominal surgery. Patients randomly received aprepitant 40 mg one to three hours before anesthesia or ondansetron 4 mg given intravenously immediately before anesthesia. A single 125 mg dose of

aprepitant was also studied; however, no additional clinical benefit was seen as compared to the 40 mg dose. Of the patients receiving Emend 40 mg, 92% were women and 8% were men, and the age of patients in the group ranged from 19–84 years with a mean age of 46 years. Overall, the results showed that aprepitant 40 mg was superior to ondansetron 4 mg IV in preventing vomiting through 24 hours following surgery.

The first study (n=573) showed that aprepitant 40 mg was superior to ondansetron 4 mg IV for the prevention of emesis from 0 to 24 hours following surgery. Prevention of vomiting was defined as no emetic episodes and was one of two primary endpoints in the study. Of patients taking aprepitant 40 mg, 84% of patients (246 out of 293) did not experience vomiting through 24 hours compared to 71% of patients taking ondansetron 4 mg IV (200 out of 280, p<0.001).

In addition, in a prespecified non-inferiority analysis in this study, patients taking aprepitant 40 mg had a complete response in the 0 to 24 hours following surgery comparable to ondansetron 4 mg IV. Complete response was defined as no emetic episodes and no use of rescue therapy and was the other primary endpoint in the study. In this analysis, 64% of patients (187 out of 293) taking Emend 40 mg had a complete response compared to 55% of patients (154 out of 280) taking ondansetron 4 mg IV. Complete response in the 24 hours following surgery was also evaluated based on a prespecified superiority analysis in this study, which found that Emend was not superior to ondansetron on this endpoint. Also, in study one aprepitant 40 mg was superior to ondansetron 4 mg IV in the prevention of vomiting from 0 to 48 hours following surgery, a secondary endpoint. Of patients taking aprepitant 40 mg, 82% of patients did not experience vomiting through 48 hours compared to 66% of patients taking ondansetron 4 mg IV (p<0.001).

In the second study (n=494), the primary endpoint, superiority of aprepitant 40 mg is superior to ondansetron 4 mg IV in the prevention of postoperative nausea and vomiting as measured by the proportion of patients with a complete response in the 24 hours following the end of surgery, was not met. However, aprepitant 40 mg demonstrated a clinically meaningful effect with respect to the secondary endpoint of "no vomiting" during the first 24 hours after surgery. Aprepitant 40 mg was associated with a 16% improvement over ondansetron 4 mg IV in the prevention of vomiting. Aprepitant was generally well-tolerated. Clinical adverse experiences were reported in approximately 60% of patients treated with aprepitant compared to roughly 64% of people receiving ondansetron.

There are no published or unpublished clinical efficacy trials for fosaprepitant in any type of nausea and vomiting. Its approval was based on bioequivalence of intravenous fosaprepitant 115 mg to oral aprepitant 125 mg.

Adverse Reactions / Contraindications

Adverse effects observed during clinical trials with aprepitant have included headache, constipation, diarrhea, abdominal pain, dizziness, nausea, anorexia, somnolence, asthenia, irritability, and mild transaminase elevations.

In a bioequivalence study the most common adverse events with fosaprepitant were infusion site pain, headache, and infusion site induration. No comparative adverse event information is available for fosaprepitant. Lacking direct adverse event or drug interaction data for fosaprepitant, these qualities are presumed to be similar to oral aprepitant.

Aprepitant is a moderate CYP3A4 inhibitor. It should not be used concurrently with pimozone, terfenadine, astemizole, or cisapride. Inhibition of cytochrome P450 isoenzyme 3A4 by aprepitant could result in elevated plasma concentrations of these drugs, potentially causing serious or life-threatening reactions. Due to the small number of patients in clinical studies who received the CYP3A4 substrates vinblastine, vincristine, or ifosfamide, particular caution and careful monitoring are advised in patients receiving these agents or other chemotherapy agents metabolized primarily by CYP3A4 that were not studied. However, in a pharmacokinetic study, aprepitant did not influence the pharmacokinetics of docetaxel. Administration of EMEND may reduce the efficacy of hormonal contraceptives. Patients should be advised to use alternative or back-up methods of contraception during treatment with aprepitant and for one month following the last dose of aprepitant.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

HCPCS Codes	Description
J1453	Injection, fosaprepitant, 1 mg

ICD-9-CM Diagnosis Codes	Description
	No specific codes

Experimental/Investigational/Unproven/Not Covered:

ICD-9-CM Diagnosis Codes	Description
296.00-296.96	Episodic mod disorders
300.00	Anxiety state, unspecified
311	Depressive disorder, not elsewhere classified
787.01	Nausea with vomiting
	Multiple/varied

References

1. Aapro MS, Schmoll HJ, Poli-Bigelli S, et al. Comparison of aprepitant combination regimen with 4-day ondansetron _ 4-day dexamethasone for prevention of acute and delayed nausea/vomiting after cisplatin chemotherapy. *J Clin Oncol* 23:730s, 2005.
2. Ballard TM, Sanger S, Higgins GA. Inhibition of shock-induced foot tapping behaviour in the gerbil by a tachykinin NK₁ receptor antagonist. *Eur J Pharmacol.* 2001;412:255-64.
3. Campos D, Pereira JR, Reinhardt RR, et al. Prevention of cisplatin-induced emesis by the oral neurokinin-1 antagonist, MK-869, in combination with granisetron and dexamethasone or with dexamethasone alone. *J Clin Oncol.* 2001;19:1759-67.
4. Chawla SP, Grunberg SM, Gralla RJ, et al. Establishing the dose of oral NK-1 antagonist MK-869 for chemotherapy induced nausea and vomiting [abstract]. *Proceedings of the 2001 Annual Meeting of the American Society of Clinical Oncology.* 2001;abstract 1527.
5. Cocquyt V, Van Belle S, Reinhardt RR, et al. Comparison of L-758,298, a prodrug for the selective neurokinin-1 antagonist, L-754,030, with ondansetron for the prevention of cisplatin-induced emesis. *Eur J Cancer.* 2001;37:835-42.
6. de Wit R, de Boer AC, vd Linden GH, et al. Maintenance of protection against chemotherapy induced nausea and vomiting in multiple cycles with the oral NK₁ antagonist MK-0869 [abstract]. *Proceedings of*

the 2002 Annual Meeting of the American Society of Clinical Oncology. 2002;abstract 1467. Available at URL address: <http://www.asco.org>

7. DeVane CL. Substance P: A new era, a new role. *Pharmacotherapy*. 2001;21:1061-9.
8. Duffy RA, Varty GB, Morgan CA, Lachowicz JE. Correlation of neurokinin (NK) 1 receptor occupancy in gerbil striatum with behavioral effects of NK1 antagonists. *J Pharmacol Exp Ther*. 2002;301:536-42.
9. Hesketh PJ, Grunberg SM, Gralla RJ, et al. Differential time course of cisplatin induced emesis with a 5HT3 antagonist or an NK1 antagonist: Rationale for combination therapy [abstract]. Proceedings of the 2002 Annual Meeting of the American Society of Clinical Oncology. 2002;abstract 1476. Accessed December 6, 2002. Available at URL address: <http://www.asco.org>.
10. Hesketh PJ, Grunberg SM, Gralla RJ, et al. The oral neurokinin-1 antagonist aprepitant for the prevention of chemotherapy-induced nausea and vomiting: A multinational, randomized, double-blind, placebo-controlled trial in patients receiving highdose cisplatin—The Aprepitant Protocol 052 Study Group. *J Clin Oncol* 21:4112-4119, 2003.
11. Huskey SW, Luffer-Atlas D, Dean BJ, McGowan EM, Feeney WP, Chu SH, et al. Substance P receptor antagonist 1: Conversion of phosphoramidate prodrug after I.V. administration to rats and dogs. *Drug Metab Dispos*. 1999;27:1367-73.
12. Kramer MS, Cutler N, Feighner J, et al. Distinct mechanism for antidepressant activity by blockade of central substance P receptors. *Science*. 1998;281:1640-5.
13. Kris, MG, Hesketh, PJ, Somerfield, MR American Society of Clinical Oncology Guideline for Antiemetics in Oncology. *J Clin Oncol* 2006; 24(18). Published Ahead of Print on May 22, 2006 as 10.1200/JCO.2006.06.9591
14. Merck and Co., Inc. EMEND (fosaprepitant dimeglumine) for injection package insert. Whitehouse Station, NJ: Merck and Co., Inc. October 2009.
15. Merck and Co., Inc. Emend (aprepitant capsules) package insert. Whitehouse Station, NJ: Merck and Co., Inc. July 2009.
16. McEvoy GK, ed. AHFS 2008 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2008.
17. Navari RM, Reinhardt RR, Gralla R, et al. Reduction of cisplatin-induced emesis by a selective neurokinin-1-receptor antagonist. *N Engl J Med*. 1999;340:190-5.
18. Nutt D. Substance-P antagonists: a new treatment for depression? *Lancet*. 1998;352:1644-6.
19. Poli-Bigelli S, Rodrigues-Pereira, Carides AD, et al. Addition of the neurokinin 1 receptor antagonist aprepitant to standard antiemetic therapy improves control of chemotherapy-induced nausea and vomiting. Results from a randomized, doubleblind, placebo-controlled trial in Latin America. *Cancer* 2003;97:3090-3098.
20. Tattersall FD, Rycroft W, Cumberbatch M, et al. The novel NK₁ receptor antagonist MK-0869 (L-754,030) and its water soluble phosphoryl prodrug, L-758,298, inhibit acute and delayed cisplatin-induced emesis in ferrets. *Neuropharmacology*. 2000;39:652-63.

21. Urban LA, Fox AJ. NK1 receptor antagonists – are they really without effect in the pain clinic? Trends Pharmacol Sci. 2000;21:462-4.
22. Van Belle S, Lichinitser MR, Navari RM, et al. Prevention of cisplatin-induced acute and delayed emesis by the selective neurokinin-1 antagonists, L-758,298 and MK-869. Cancer. 2002;94:3032-41.

Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	12/15/2007	4018	Aprepitant (Emend®)
Great-West Healthcare	6/2007	MDL04.100.2	Emend

“CIGNA” and the “Tree of Life” logo are registered service marks of CIGNA Intellectual Property, Inc., licensed for use by CIGNA Corporation and its operating subsidiaries. All products and services are provided exclusively by such operating subsidiaries and not by CIGNA Corporation. Such operating subsidiaries include Connecticut General Life Insurance Company, CIGNA Behavioral Health, Inc., Intracorp, and HMO or service company subsidiaries of CIGNA Health Corporation and CIGNA Dental Health, Inc. In Arizona, HMO plans are offered by CIGNA HealthCare of Arizona, Inc. In California, HMO plans are offered by CIGNA HealthCare of California, Inc. and Great-West Healthcare of California, Inc. In Connecticut, HMO plans are offered by CIGNA HealthCare of Connecticut, Inc. In North Carolina, HMO plans are offered by CIGNA HealthCare of North Carolina, Inc. In Virginia, HMO plans are offered by CIGNA HealthCare Mid-Atlantic, Inc. All other medical plans in these states are insured or administered by Connecticut General Life Insurance Company.

Connecticut General Life Insurance Company has acquired the business of Great-West Healthcare from Great-West Life & Annuity Insurance Company (GWLA). Certain products continue to be provided by GWLA (Life, Accident and Disability, and Excess Loss). GWLA is not licensed to do business in New York. In New York, these products are sold by GWLA’s subsidiary, First Great-West Life & Annuity Insurance Company, White Plains, N.Y.