



CIGNA MEDICAL 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 RimabotulinumtoxinB (Myobloc®)

Effective Date..... 9/15/2009
Next Review Date.....9/15/2010
Coverage Policy Number 5107

Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	4
References.....	5
Policy History	9

Hyperlink to Related Coverage Policies

[OnabotulinumtoxinA \(Botox®\)](#)

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 ©2009 CIGNA

Coverage Policy

CIGNA covers rimabotulinumtoxinB (Myobloc®) as medically necessary for treatment of EITHER of the following indications:

- cervical dystonia
- ptyalism/sialorrhea (excessive salivation) associated with parkinsonism and cerebral palsy that is refractory to pharmacotherapy (including anticholinergics)

CIGNA does not cover rimabotulinumtoxinB (Myobloc®) for the following because it is considered experimental, investigational, or unproven (this list may not be all-inclusive):

- chronic pain including **ANY** of the following:
 - low back pain
 - mastectomy reconstruction pain
 - hemorrhoid pain
 - myofascial pain
 - chronic prostate pain
 - tennis elbow
 - chronic neck pain

- temporo-mandibular dysfunction or chronic orofacial pain
 - headache (tension-type headache, chronic daily headache)
 - migraine
 - rhinitis
 - tics
 - paralytic scoliosis
 - diabetic gastroparesis
 - sphincter of Oddi dysfunction
 - voiding dysfunction associated with **ANY** of the following:
 - benign prostatic hyperplasia
 - detrusor hyperreflexia due to myelomeningocele
 - urge incontinence refractory to anticholinergic therapy
 - intracranial lesions or cerebrovascular accident-induced voiding difficulty
 - detrusor sphincter dyssynergia due to spinal cord injury
-

General Background

FDA Approved Indications

Myobloc is indicated for the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.

FDA Recommended Dosing

The recommended initial dose of Myobloc for patients with a prior history of tolerating botulinum toxin injections is 2,500 to 5,000 Units divided among affected muscles. Patients without a prior history of tolerating botulinum toxin injections should receive a lower initial dose. Subsequent dosing should be optimized according to the patient's individual response.

Pharmacology

Botulinum toxins work in the peripheral and autonomic nervous systems by preventing the release of acetylcholine. This effect results in disrupted neurotransmission and muscle paralysis. Clostridium botulinum (*C. botulinum*), *C. baratii*, and *C. butyricum* all produce the neurotoxin, botulinum. The available formulation of rimabotulinumtoxinB is derived from Clostridium botulinum. It specifically has been demonstrated to cleave synaptic vesicle associated membrane protein (VAMP, i.e. synaptobrevin), which is a component of the protein complex responsible for docking and fusion of the synaptic vesicle to the pre-synaptic membrane, a necessary step to neurotransmitter release.

There are seven antigenically different types of botulinum toxin: A, B, C, D, E, F, and G. Antitoxin to a specific botulinum toxin such as anti-A botulinum does not neutralize the effects of other types of toxins such as types B through G. Botulinum toxin doses are expressed in units of biologic activity, with one unit corresponding to the lethal dose for female Swiss-Webster mice. However, the different botulinum formulations are not interchangeable because assays measuring the lethal dose differ. Pharmacokinetic data such as absorption, distribution, metabolism, and elimination are not available for rimabotulinumtoxinB. Systemic concentrations of botulinum toxin following intradermal or intramuscular injection are not expected.

Clinical Efficacy

Two phase III, randomized, multi-center, double-blind, placebo-controlled studies were conducted in adults with cervical dystonia who had a history of receiving botulinum toxin type A in an open-label manner, with a perceived good response and tolerable adverse effects. Patients in one study were randomized to receive placebo, 5000 units (U) or 10,000 U of rimabotulinumtoxinB; in another study, patients were randomized to receive placebo or 10,000 U of rimabotulinumtoxinB. Patients selected for the phase III studies had cervical dystonia of at least moderate severity for at least one year. The primary efficacy measure in these studies was combined improvement in the severity, pain, and disability subscales of the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) Total Score (scale

range of possible scores is 0–87) at four weeks after a single treatment session consisting of 1–5 injections divided among 2–4 muscles in each patient. The secondary endpoints were the Patient Global and Physician Global Assessments of change at week four. Both Global Assessments used a 100 point visual-analog scale (VAS). The Patient Global Assessment allows a patient to indicate how they feel at the time of the evaluation compared to the pre-injection baseline. Patients receiving rimabotulinumtoxinB doses of 5000 or 10,000 units had greater improvement in dystonic manifestations and associated pain and disability than those receiving placebo. In one of the studies in which both doses of rimabotulinumtoxinB were evaluated, there were no statistically significant differences in results between the 5000 U and 10,000 U doses. Exploratory analyses of these two studies suggested that the majority of patients who showed a beneficial response by week four had returned to their baseline status between weeks 12–16 post-injection. Although there was a decrease in pain with the use of rimabotulinumtoxinB, there remained many patients who experienced an increase in dystonia-related neck pain irrespective of treatment group. TWSTRS Total Score at week four and Patient Global Assessment among subgroups by gender or age showed consistent treatment-associated effects across these subgroups.

Clinical Efficacy for Off-Label Uses

In a double-blind, placebo-controlled study, the safety and efficacy of botulinum toxin B was evaluated for the treatment of sialorrhea in patients with Parkinson's disease (PD). Patients were randomized to receive either 1000 units of botulinum toxin B into each parotid gland and 250 units into each submandibular gland or a pH-matched placebo, using only anatomic landmarks. Patients returned after one month to undergo an identical assessment. Compared with placebo, those randomized to drug reported improvement on the Visual Analogue Scale ($p < 0.001$), global impressions of change ($p < 0.005$), Drooling Rating Scale ($p < 0.05$), and Drooling Severity and Frequency Scale ($p < 0.001$). Adverse events were mild and included dry mouth, worsened gait, diarrhea, and neck pain in the botulinum toxin B group. Anatomically guided injections of botulinum toxin B into the parotid and submandibular glands appear to effectively improve sialorrhea without compromising dysphagia in patients with PD.

Ongoing Studies for Investigational Uses

Chronic Pain

Preliminary data suggest that rimabotulinumtoxinB may be useful in the treatment of myofascial pain syndrome. RimabotulinumtoxinB also reportedly has been used in patients with chronic low back pain and in patients with pain associated with brachial plexopathy. However, additional study is needed to determine optimal injection technique and dosing as well as the relative safety and efficacy of rimabotulinumtoxinB in these disorders.

Temporomandibular Dysfunction or Chronic Orofacial Pain

Efficacy evidence and experience with rimabotulinumtoxinB in the management of temporomandibular dysfunction or chronic orofacial pain are limited. Additional research is needed and reportedly is under way to confirm the safety and efficacy and determine optimal doses of rimabotulinumtoxinB for these disorders.

Headache (tension-type headache, chronic daily headache) / Migraine

Efficacy evidence and experience with botulinum toxin type B in the management of disabling headaches (e.g., migraine, cluster headache) are limited. As with botulinum toxin type A, some clinicians consider treatment with botulinum toxin type B appropriate in patients who have disabling headaches that are refractory to other therapies or in patients who cannot tolerate such therapies. Additional research is needed and reportedly is under way to confirm the safety and efficacy and determine optimal doses of botulinum toxin type B in patients with various types of headache.

Voiding Dysfunction

Efficacy evidence for botulinum toxin type B in neurogenic voiding dysfunction (e.g., detrusor hyperreflexia secondary to multiple sclerosis) is limited.

Adverse Reactions

Postmarketing reports indicate that the effects of Myobloc and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects.

These may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have underlying conditions that would predispose them to these symptoms. In unapproved uses, including spasticity in children and adults, and in approved indications, cases of spread of effect have occurred at doses comparable to those used to treat cervical dystonia and at lower doses.

The most commonly reported adverse events associated with Myobloc treatment in all studies were dry mouth, dysphagia, dyspepsia, and injection site pain. Dry mouth and dysphagia were the adverse reactions most frequently resulting in discontinuation of treatment. There was an increased incidence of dysphagia with increased dose in the sternocleidomastoid muscle. The incidence of dry mouth showed some dose-related increase with doses injected into the splenius capitis, trapezius and sternocleidomastoid muscles.

The potency units of Myobloc are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of Myobloc cannot be compared to or converted into units of any other botulinum toxin products assessed with any other specific assay method.

Coding/Billing Information

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

Covered when medically necessary:

CPT®* Codes	Description
64613	Chemodenervation of muscle(s); neck muscle(s) (eg, for spasmodic torticollis, spasmodic dysphonia)

HCPCS Codes	Description
J0587	Botulinum toxin type B, per 100 units

ICD-9-CM Diagnosis Codes	Description
333.83	Spasmodic torticollis
527.7†	Disturbance of salivary gland

†**Note:** Covered when medically necessary and when used to treat ptialism/sialorrhea associated with parkinsonism and cerebral palsy that is refractory to pharmacotherapy (including anticholinergics).

Experimental/Investigational/Unproven/Not Covered:

ICD-9-CM Diagnosis Codes	Description
307.20	Tic disorder, unspecified
307.21	Transient tic disorder

307.22	Chronic motor or vocal tic disorder
307.23	Tourette's disorder
307.81	Tension headache
333.3	Tics of organic origin
339.10- 339.12	Tension type headache
344.61	Cauda equine syndrome with neurogenic bladder
346.00 - 346.93	Migraine
350.1	Trigeminal neuralgia
455.0 – 455.8	Hemorrhoids
472.0	Chronic rhinitis
477.0 – 477.9	Allergic rhinitis
524.60	Unspecified temporomandibular joint disorders
524.62	Arthralgia of temporomandibular joint
536.3	Gastroparesis
564.00- 564.09	Constipation
723.1	Cervicalgia
724.2	Lumbago
726.32	Lateral epicondylitis of elbow
729.1	Myalgia and myositis unspecified
737.9	Unspecified curvature of spine
784.0	Headache
788.31	Urge incontinence

Current Procedural Terminology (CPT®) © 2008 American Medical Association: Chicago, IL.

References

1. Adler CH, Bansberg SF, Krein-Jones K, Hentz JG. Safety and efficacy of rimabotulinumtoxinB (Myobloc) in adductor spasmodic dysphonia. *Mov Disord.* Sep 2004;19(9):1075-1079.
2. Birklein F, Eisenbarth G, Erbguth F, Winterholler M. RimabotulinumtoxinB blocks sudomotor function effectively: a 6 month follow up. *J Invest Dermatol.* Dec 2003;121(6):1312-1316.
3. Brashear A, McAfee AL, Kuhn ER, Fyffe J. RimabotulinumtoxinB in upper-limb poststroke spasticity: a double-blind, placebo-controlled trial. *Arch Phys Med Rehabil.* May 2004;85(5):705-709.
4. Callaway JE, Arezzo JC, Grethlein AJ. RimabotulinumtoxinB: an overview of its biochemistry and preclinical pharmacology. *Semin Cutan Med Surg.* Jun 2001;20(2):127-136.
5. Callaway JE, Arezzo JC, Grethlein AJ. RimabotulinumtoxinB: an overview of its biochemistry and preclinical pharmacology. *Dis Mon.* May 2002;48(5):367-383.
6. Callaway JE. RimabotulinumtoxinB (Myobloc): pharmacology and biochemistry. *Clin Dermatol.* Jan-Feb 2004;22(1):23-28.
7. Chen YH, Kuo HC. Botulinum A toxin treatment of urethral sphincter pseudodyssynergia in patients with cerebrovascular accidents or intracranial lesions. *Urol Int.* 2004;73(2):156-161; discussion 161-152.

8. Conway S, Delplanche C, Crowder J, Rothrock J. Botox Therapy for Refractory Migraine. Headache. 2005;45:355-357.
9. Davies J, Duffy D, Boyt N, Aghahoseini A, Alexander D, Leveson S. Botulinum toxin (botox) reduces pain after hemorrhoidectomy: results of a double-blind, randomized study. Dis Colon Rectum. Aug 2003;46(8):1097-1102.
10. De Andres J, Cerda-Olmedo G, Valia JC, Monsalve V, Lopez A, Minguez A. Use of botulinum toxin in the treatment of chronic myofascial pain. Clin J Pain. Jul-Aug 2003;19(4):269-275.
11. de Seze M, Petit H, Gallien P, et al. Botulinum a toxin and detrusor sphincter dyssynergia: a double-blind lidocaine-controlled study in 13 patients with spinal cord disease. Eur Urol. Jul 2002;42(1):56-62.
12. Dodick DW, Mauskop A, Elkind AH, et al. Botulinum Toxin Type A for the Prophylaxis of Chronic Daily Headache: Subgroup Analysis of Patients Not Receiving Other Prophylactic Medications: A Randomized Double-Blind, Placebo-Controlled Study. Headache. 2005;45:315-324.
13. Evers S, Vollmer-Haase J, Schwaag S, Rahmann A, Husstedt IW, Frese A. Botulinum toxin A in the prophylactic treatment of migraine--a randomized, double-blind, placebo-controlled study. Cephalalgia. Oct 2004;24(10):838-843.
14. Ezzeddine D, Jit R, Katz N, Gopalswamy N, Bhutani MS. Pyloric injection of botulinum toxin for treatment of diabetic gastroparesis. Gastrointest Endosc. Jun 2002;55(7):920-923.
15. Foster L, Clapp L, Erickson M, Jabbari B. Botulinum toxin A and chronic low back pain: a randomized, double-blind study. Neurology. May 22 2001;56(10):1290-1293.
16. Freund B, Schwartz M, Symington JM. Botulinum toxin: new treatment for temporomandibular disorders. Br J Oral Maxillofac Surg. Oct 2000;38(5):466-471.
17. Freund BJ, Schwartz M. Treatment of chronic cervical-associated headache with botulinum toxin A: a pilot study. Headache. Mar 2000;40(3):231-236.
18. Freund BJ, Schwartz M. Treatment of whiplash associated neck pain [corrected] with botulinum toxin-A: a pilot study. J Rheumatol. Feb 2000;27(2):481-484.
19. Gassner HG, Sherris DA. Addition of an anesthetic agent to enhance the predictability of the effects of botulinum toxin type A injections: a randomized controlled study. Mayo Clin Proc. Jul 2000;75(7):701-704.
20. Hecht MJ, Birklein F, Winterholler M. Successful treatment of axillary hyperhidrosis with very low doses of botulinum toxin B: a pilot study. Arch Dermatol Res. Feb 2004;295(8-9):318-319.
21. Jankovic J, Vuong KD, Ahsan J. Comparison of efficacy and immunogenicity of original versus current botulinum toxin in cervical dystonia. Neurology. Apr 8 2003;60(7):1186-1188.
22. Jongerius PH, van den Hoogen FJ, van Limbeek J, Gabreels FJ, van Hulst K, Rotteveel JJ. Effect of botulinum toxin in the treatment of drooling: a controlled clinical trial. Pediatrics. Sep 2004;114(3):620-627.
23. Keizer SB, Rutten HP, Pilot P, Morre HH, v Os JJ, Verburg AD. Botulinum toxin injection versus surgical treatment for tennis elbow: a randomized pilot study. Clin Orthop. Aug 2002(401):125-131.
24. Kwiat DM, Bersani TA, Bersani A. Increased patient comfort utilizing botulinum toxin type a reconstituted with preserved versus nonpreserved saline. Ophthal Plast Reconstr Surg. May 2004;20(3):186-189.

25. Lacy BE, Crowell MD, Schettler-Duncan A, Mathis C, Pasricha PJ. The treatment of diabetic gastroparesis with botulinum toxin injection of the pylorus. *Diabetes Care*. Oct 2004;27(10):2341-2347.
26. Layeeque R, Hochberg J, Siegel E, et al. Botulinum toxin infiltration for pain control after mastectomy and expander reconstruction. *Ann Surg*. Oct 2004;240(4):608-613; discussion 613-604.
27. Lipp A, Trottenberg T, Schink T, Kupsch A, Arnold G. A randomized trial of botulinum toxin A for treatment of drooling. *Neurology*. Nov 11 2003;61(9):1279-1281.
28. Mancini F, Zangaglia R, Cristina S, et al. Double-blind, placebo-controlled study to evaluate the efficacy and safety of botulinum toxin type A in the treatment of drooling in parkinsonism. *Mov Disord*. Jun 2003;18(6):685-688.
29. Maria G, Brisinda G, Civello IM, Bentivoglio AR, Sganga G, Albanese A. Relief by botulinum toxin of voiding dysfunction due to benign prostatic hyperplasia: results of a randomized, placebo-controlled study. *Urology*. Aug 2003;62(2):259-264; discussion 264-255.
30. Marras C, Andrews D, Sime E, Lang AE. Botulinum toxin for simple motor tics: a randomized, double-blind, controlled clinical trial. *Neurology*. Mar 13 2001;56(5):605-610.
31. Mathew NT, Frishberg BM, Gawel M, et al. Botulinum Toxin Type A (BOTOX) for the Prophylactic Treatment of Chronic Daily Headache: A Randomized, Double-Blind, Placebo-Controlled Trial. *Headache*. 2005;45:293-307.
32. McEvoy GK, ed. *AHFS 2009 Drug Information*. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2009.
33. Naumann M, Jankovic J. Safety of botulinum toxin type A: a systematic review and meta-analysis. *Curr Med Res Opin*. Jul 2004;20(7):981-990.
34. Nixdorf DR, Heo G, Major PW. Randomized controlled trial of botulinum toxin A for chronic myogenous orofacial pain. *Pain*. Oct 2002;99(3):465-473.
35. Ondo WG, Hunter C, Moore W. A double-blind placebo-controlled trial of botulinum toxin B for sialorrhea in Parkinson's disease. *Neurology*. Jan 13 2004;62(1):37-40.
36. Ondo WG, Vuong KD, Derman HS. Botulinum toxin A for chronic daily headache: a randomized, placebo-controlled, parallel design study. *Cephalalgia*. Jan 2004;24(1):60-65.
37. Padberg M, de Bruijn SF, de Haan RJ, Tavy DL. Treatment of chronic tension-type headache with botulinum toxin: a double-blind, placebo-controlled clinical trial. *Cephalalgia*. Aug 2004;24(8):675-680.
38. Pal PK, Calne DB, Calne S, Tsui JK. Botulinum toxin A as treatment for drooling saliva in PD. *Neurology*. Jan 11 2000;54(1):244-247.
39. Porta M. A comparative trial of botulinum toxin type A and methylprednisolone for the treatment of myofascial pain syndrome and pain from chronic muscle spasm. *Pain*. Mar 2000;85(1-2):101-105.
40. Rapp DE, Lucioni A, Katz EE, O'Connor RC, Gerber GS, Bales GT. Use of botulinum-A toxin for the treatment of refractory overactive bladder symptoms: an initial experience. *Urology*. Jun 2004;63(6):1071-1075.
41. Relja M, Telarovic S. Botulinum toxin in tension-type headache. *J Neurol*. Feb 2004;251 Suppl 1:112-14.

42. Rundle RL. Allergan's Botox May Offer Relief From Migraines. *The Wall Street Journal*. April 8, 2005: B.3.
43. Schmitt WJ, Slowey E, Fravi N, Weber S, Burgunder JM. Effect of botulinum toxin A injections in the treatment of chronic tension-type headache: a double-blind, placebo-controlled trial. *Headache*. Jul-Aug 2001;41(7):658-664.
44. Schulte-Baukloh H, Michael T, Schobert J, Stolze T, Knispel HH. Efficacy of botulinum-a toxin in children with detrusor hyperreflexia due to myelomeningocele: preliminary results. *Urology*. Mar 2002;59(3):325-327; discussion 327-328.
45. Silberstein S, Mathew N, Saper J, Jenkins S. Botulinum toxin type A as a migraine preventive treatment. For the BOTOX Migraine Clinical Research Group. *Headache*. Jun 2000;40(6):445-450.
46. Solstice Neurosciences, Inc. Myobloc® (rimabotulinumtoxinB) Injectable Solution package insert. South San Francisco, CA: Solstice Neurosciences, Inc. July 2009.
47. Thakker MM, Rubin PA. Pharmacology and clinical applications of botulinum toxins A and B. *Int Ophthalmol Clin*. Summer 2004;44(3):147-163.
48. Tyler LS, Le Ber J. Evaluating Clinical Studies in Pain Management: Pearls and Pitfalls. In: Lipman AG, ed. *Pain Management for Primary Care Clinicians*. Bethesda, MD: American Society of Health-System Pharmacists; 2004:346 - 366.
49. Unal M, Sevim S, Dogu O, Vayisoglu Y, Kanik A. Effect of botulinum toxin type A on nasal symptoms in patients with allergic rhinitis: a double-blind, placebo-controlled clinical trial. *Acta Otolaryngol*. Dec 2003;123(9):1060-1063.
50. van Laborde S, Dover JS, Moore M, Stewart B, Arndt KA, Alam M. Reduction in injection pain with RimabotulinumtoxinB further diluted using saline with preservative: a double-blind, randomized controlled trial. *J Am Acad Dermatol*. Jun 2003;48(6):875-877.
51. von Lindern JJ, Niederhagen B, Berge S, Appel T. Type A botulinum toxin in the treatment of chronic facial pain associated with masticatory hyperactivity. *J Oral Maxillofac Surg*. Jul 2003;61(7):774-778.
52. Wehrmann T, Schmitt TH, Arndt A, Lembcke B, Caspary WF, Seifert H. Endoscopic injection of botulinum toxin in patients with recurrent acute pancreatitis due to pancreatic sphincter of Oddi dysfunction. *Aliment Pharmacol Ther*. Nov 2000;14(11):1469-1477.
53. Wheeler AH, Goolkasian P, Gretz SS. Botulinum toxin A for the treatment of chronic neck pain. *Pain*. Dec 2001;94(3):255-260.
54. Zermann D, Ishigooka M, Schubert J, Schmidt RA. Perisphincteric injection of botulinum toxin type A. A treatment option for patients with chronic prostatic pain? *Eur Urol*. Oct 2000;38(4):393-399.

Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare (Myobloc®)	9/15/2008	5107	RimabotulinumtoxinB
Great-West Healthcare	12/2006	P04.104.2	Botox, Myobloc

"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.