



CIGNA HEALTHCARE COVERAGE POSITION

Subject **Botulinum Toxin Type B (Myobloc®)**

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Botox® A

INSTRUCTIONS FOR USE

Coverage Positions are intended to supplement certain **standard** CIGNA HealthCare benefit plans. 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 Positions are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Position. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Positions. 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 Positions and; 4) the specific facts of the particular situation. Coverage Positions relate exclusively to the administration of health benefit plans. Coverage Positions are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2008 CIGNA

Coverage Position

CIGNA HealthCare covers botulinum toxin type B (Myobloc®) as medically necessary when the following indication is met:

- treatment of patients with cervical dystonia
- ptyalism/sialorrhea (excessive salivation) associated with parkinsonism and cerebral palsy, refractory to pharmacotherapy (including anticholinergics)

CIGNA HealthCare does not cover botulinum toxin type B (Myobloc®) because it is considered experimental, investigational or unproven (this list may not be all-inclusive).

- chronic pain including: 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
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General Background

FDA Approved Indications

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

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 botulinum toxin type B 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 presynaptic 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 botulinum toxin type B. Systemic concentrations of botulinum toxin following intradermal or intramuscular injection are not expected.

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 botulinum toxin type B; in another study, patients were randomized to receive placebo or 10,000 U of botulinum toxin type B. 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 botulinum toxin type B 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 botulinum toxin type B 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 botulinum toxin type B, 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.

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.

Co-administration of botulinum toxin type B and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like compounds) should only be performed with caution, as the effect of the toxin may be potentiated.

The most commonly reported adverse events associated with botulinum toxin type B 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.

The recommended initial dose of botulinum toxin type B for patients with a prior history of tolerating botulinum toxin injections is 2500–5000 U, administered by intramuscular (IM) injection, 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.

Coding/Billing Information

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

Covered when medically necessary:

CPT ^{®*} Codes	Description

HCPCS Codes	Description

ICD-9-CM Diagnosis Codes	Description

Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description

HCPCS Codes	Description

ICD-9-CM Diagnosis Codes	Description

***Current Procedural Terminology (CPT[®]) © 2007 American Medical Association: Chicago, IL.**

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