



CIGNA MEDICAL COVERAGE POLICY

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

Subject **IncobotulinumtoxinA (Xeomin®)**

Effective Date 4/15/2011
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Hyperlink to Related Coverage Positions

- AbobotulinumtoxinA (Dysport®)
- OnabotulinumtoxinA (Botox® A)
- RimabotulinumtoxinB (Myobloc®)

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer'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 customer'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 customer'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 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 ©2011 CIGNA

Coverage Policy

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

- blepharospasm in adults previously treated with onabotulinumtoxinA (Botox)
- cervical dystonia (including spasmodic torticollis) causing persistent pain or interfering with the ability to perform age-related activities of daily living

When criteria are met for coverage, approval consists of a quantity of four (4) treatments in a 12 month period (one (1) treatment every 90 days).

If the initial approval criteria (listed above) are met AND clinical improvement with previous botulinum toxin treatment is documented but duration of benefit is < 90 days/treatment, then up to six treatments in a 12 month period (one treatment per 60 days) may be considered on a case-by-case basis.

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to incobotulinumtoxinA (Xeomin®).

FDA Approved Indications

Blepharospasm

Xeomin (incobotulinumtoxinA) is indicated for the treatment of adults with blepharospasm who were previously treated with onabotulinumtoxinA (Botox).

Cervical Dystonia

Xeomin (incobotulinumtoxinA) is indicated for the treatment of adults with cervical dystonia to decrease the severity of abnormal head position and neck pain in both botulinum toxin-naïve and previously treated patients.

FDA Recommended Dosing

The potency Units of Xeomin (incobotulinumtoxinA) for injection 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 Xeomin cannot be compared to or converted into units of any other botulinum toxin products assessed with any other specific assay method.

Blepharospasm

The recommended initial total dose of Xeomin should be the same dose as the patient's previous treatment of onabotulinumtoxinA (Botox), although responses to Xeomin and onabotulinumtoxinA (Botox) may differ in individual patients. In a placebo-controlled trial in which patients were dosed with the same number of Units as they had received previously with onabotulinumtoxinA (Botox), the mean dose per eye was about 33 Units (range 10-50 Units), and the mean number of injections per eye was 6. The maximum dose per eye in the controlled trials was 50 Units, with a range of 10-50 Units. In the controlled trial, few patients received a total dose of greater than 75 Units. The total initial dose of Xeomin in both eyes should not exceed 70 Units (35 Units/eye). Subsequent dosing should be tailored to the individual patient, based on response, up to a maximum dose of 35 Units per eye. Xeomin dosing has not been established in patients with blepharospasm who have not been previously treated with onabotulinumtoxinA (Botox).

Cervical Dystonia

The recommended initial total dose of Xeomin for cervical dystonia is 120 Units. In a placebo-controlled trial utilizing initial Xeomin doses of 120 Units and 240 Units, no meaningful difference in effectiveness was demonstrated between the doses. In the treatment of cervical dystonia, Xeomin is usually injected into the sternocleidomastoid, levator scapulae, splenius capitis, scalenus, and/or the trapezius muscle(s). The dose and number of injection sites in each treated muscle should be individualized based on the number and location of the muscle(s) to be treated, the degree of spasticity/dystonia, muscle mass, body weight, and response to any previous botulinum toxin injections.

Black Box Warning

Postmarketing reports indicate that the effects of Xeomin 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 been reported at doses comparable to those used to treat cervical dystonia and at lower doses.

Drug Availability

Type 1 borosilicate glass single-use vials with latex-free bromobutyl rubber closures and tamper-proof aluminum seals come in single vial pack sizes of 50 units and 100 units.

General Background

Pharmacology

IncobotulinumtoxinA (Xeomin) is a botulinum toxin type A product labeled for the treatment of cervical dystonia and for the treatment of blepharospasm in patients who have previously received onabotulinumtoxinA. Botulinum toxins work by preventing the release of acetylcholine. This effect results in disrupted neurotransmission and muscle paralysis. IncobotulinumtoxinA differs from the other botulinum products, in that it contains only the active neurotoxin without accessory proteins (hemagglutinin and non-hemagglutinin complexing proteins). IncobotulinumtoxinA is not detectable in the blood stream after intramuscular injection at normal doses. The median onset of action is ≤ 7 days, with effects typically up to 3 months.

Clinical Efficacy

IncobotulinumtoxinA has been directly compared to onabotulinumtoxinA for cervical dystonia (1 trial) and blepharospasm (2 trials). In cervical dystonia for the primary end point (change from baseline in TWSTRS severity score at 4 weeks post-injection), incobotulinumtoxinA (-6.6 points) was non-inferior to onabotulinumtoxinA (-6.4 points). In blepharospasm, one trial found no significant difference for the primary endpoint (mean change from baseline in BSDI at 4 weeks) between incobotulinumtoxinA (-1.3 points) and onabotulinumtoxinA (-2.8 points). In a second blepharospasm trial, for the primary endpoint (mean change from baseline in JRS sum score at 3 weeks) incobotulinumtoxinA (-2.83 points) was non-inferior to onabotulinumtoxinA (-2.65 points). The basis used to determine the non-inferiority margin was not specified in either non-inferiority study. The three trials all used a dosing ratio of 1:1 for incobotulinumtoxinA and onabotulinumtoxinA and reported similar duration of effect and adverse event profiles when comparing the two agents.

Ongoing Studies

Post-Stroke Upper Limb Spasticity

One hundred forty-eight patients with an Ashworth Scale score of 2 or higher for wrist and finger flexors and at least moderate disability in their principal therapeutic target of the Disability Assessment Scale were treated either with Xeomin or placebo and followed up for up to 20 weeks Kanovsky, et al. (2009). Treatment of the wrist and finger muscles was mandatory. A significantly higher proportion of patients treated with Xeomin were responders (improvement of $>$ or $= 1$ point in the Ashworth Scale score), as observed in comparison to placebo 4 weeks after treatment in wrist flexors (odds ratio, 3.97; 95% confidence interval, 1.9-8.3; $P < 0.001$, intent to treat). For all treated flexor muscle groups, statistically significant odds ratios in favor of Xeomin were observed at week 4 ($P < 0.009$). Statistically significant results in favor of Xeomin were observed at all postinjection visits until week 12 in the principal therapeutic target ($P < 0.005$), in the global assessment of efficacy ($P < 0.001$), and in some tasks of the Carer Burden Scale ($P < 0.05$). Similar numbers of patients in each group experienced at least 1 adverse event (NT 201, $n = 21$; placebo, $n = 20$). Importantly, none of the patients developed neutralizing antibodies. Xeomin led to statistically significant improvements in muscle tone and disability and was well tolerated in patients with post-stroke upper limb spasticity.

Adverse Drug Reactions / Drug Interactions

All botulinum toxin products carry a black box warning regarding the distant spread of the medication resulting in swallowing and breathing difficulties; respiratory failure and death have occurred. Adverse effects on the cornea (exposure and ulceration) due to reduced blinking may occur in patients treated for blepharospasm. The most common adverse events reported with incobotulinumtoxinA in placebo-controlled trials in cervical dystonia include dysphagia, injection site pain, neck pain, muscle weakness, and musculoskeletal pain. In blepharospasm, the most common adverse events were eyelid ptosis, dry eye, dry mouth, visual impairment. IncobotulinumtoxinA is contraindicated in the setting of infection and in patients with a history of hypersensitivity to any botulinum toxin product. Neutralizing antibodies to botulinum toxin developed in 1.1% of incobotulinumtoxinA-treated patients. The neuromuscular effects of incobotulinumtoxinA may be increased by aminoglycosides or neuromuscular blocking agents. Anticholinergic effects may be increased with anticholinergic medications. The use of two botulinum neurotoxin products concomitantly or within several months of each other has not been studied and may lead to excessive weakness.

Coding/Billing Information

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

Covered when medically necessary:

CPT [®] * Codes	Description
64612	Chemodenervation of muscle(s); muscle(s) innervated by facial nerve (eg, for blepharospasm, hemifacial spasm)
64613	Chemodenervation of muscle(s); neck muscle(s) (eg, for spasmodic torticollis, spasmodic dysphonia)

HCPCS Codes	Description
C9278	Injection, incobotulinumtoxin A, 1 mg (Code deleted 03/31/2011)
Q2040	Injection, incobotulinumtoxin A, 1 mg (Code effective 04/01/2011)

ICD-9-CM Diagnosis Codes	Description
333.81	Blepharospasm
333.83	Spasmodic torticollis

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