



CIGNA HEALTHCARE COVERAGE POSITION

**Subject Botulinum Toxin Type A
 (Botox® A)**

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Coverage Position Number 5018**

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Myobloc® (botulinum toxin type B)

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 A (Botox® A) as medically necessary when ANY of the following indications are met:

- **dystonias, spasticities, and neuro-ophthalmological conditions, including:**
 - **cervical dystonia**, including spasmodic torticollis, causing persistent pain or interfering with the patient's ability to perform age-related activities of daily living
 - **focal dystonias**
 - treatment of blepharospasm
 - focal hand dystonia (e.g., writer's cramp) causing persistent pain or interfering with the patient's ability to perform age-related activities of daily living
 - adductor spasmodic dysphonia/laryngeal dystonia
 - jaw-closing oromandibular dystonia causing any one of the following: persistent pain, interference with nutritional intake (e.g., masticatory dysfunction that results in weight loss or malnutrition), or significant speech impairment/interference with the ability to communicate effectively
 - Meige's syndrome/cranial dystonia (i.e., blepharospasm with jaw-closing oromandibular cervical dystonia), when jaw-closing oromandibular dystonia is causing any one of the following: persistent pain, interference with nutritional or significant speech impairment/interference with the ability to communicate effectively

- **spastic conditions**
 - cerebral palsy (including spastic equinus foot deformities)
 - cerebrovascular accident
 - localized adductor muscle spasticity in multiple sclerosis
 - spinal cord injury
 - traumatic brain injury
 - hereditary spastic paraplegia
- **hemifacial spasms/seventh cranial nerve palsy/gaze palsies,,** causing persistent pain or vision impairment
- **strabismus disorders in adults, in situations when:**
 - (a) One of the following is present:
 - horizontal strabismus up to 50 prism diopters
 - vertical strabismus
 - persistent sixth nerve palsy of one month or longer duration

AND

- (b) One the following is present:
 - diplopia
 - impaired depth perception
 - impaired peripheral vision
 - impaired ability to maintain fusion
- **strabismus disorders in children,** to achieve normal binocular motor alignment
- **gastrointestinal conditions, including:**
 - **primary esophageal achalasia in patients who have ANY of the following:**
 - concomitant illness and/or who are at high risk for complications such as esophageal reflux or perforation
 - have not responded to prior myotomy or dilation
 - have a history of perforation caused by previous pneumatic dilatation
 - have an epiphrenic diverticulum
 - **chronic anal fissure,** in patients who have failed conventional nonsurgical treatment (e.g., nitrate preparations, sitz baths, stool softeners, bulk agents, diet modifications)
- **hyperhidrosis,** when **ANY** of the following indications are met:
 - primary axillary hyperhidrosis that is inadequately managed with a prescription topical agent
 - palmar hyperhidrosis **OR** gustatory sweating (Frey's syndrome, diabetic gustatory sweating) when the condition is refractory to conventional medical treatment, including an attempt at both topical and pharmacotherapy (unless clinically contraindicated)

AND when **ONE** of the following criteria is met:

 - The condition is significantly interfering with the patient's ability to perform age-appropriate activities of daily living.
 - The condition is causing persistent or chronic cutaneous conditions such as skin maceration, dermatitis, fungal infections and secondary microbial conditions.
- **disabling essential tremor, including head and neck, hand, and voice tremor**

- **excessive glandular secretion**
 - cholinergic-mediated secretions associated with various types of fistulas (e.g., parotid gland, pharyngocutaneous) **OR** ptyalism/sialorrhea (excessive salivation) associated with parkinsonism and cerebral palsy, refractory to pharmacotherapy (including anticholinergics)
- **voiding dysfunction associated with any of the following:**
 - intracranial lesions or cerebrovascular accident-induced voiding difficulty
 - detrusor sphincter dyssynergia due to spinal cord injury
- **prophylaxis of migraine AND** failure, contraindication, or intolerance to two migraine prophylaxis medications: beta-blockers, calcium channel blockers, tricyclic antidepressants or anticonvulsant medications

Where criteria are met for coverage, approval consists of a quantity of four treatments in a 12 month period (one treatment per 90 days)

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

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

- anismus
- chronic constipation
- chronic pain, including: low back pain, mastectomy reconstruction pain, hemorrhoid pain, myofascial pain, chronic prostate pain, tennis elbow, chronic neck pain
- temporomandibular dysfunction or chronic orofacial pain
- headache (tension-type headache, chronic daily headache)
- treatment of migraine
- rhinitis
- tics
- paralytic scoliosis
- diabetic gastroparesis
- sphincter of Oddi dysfunction
- vaginismus
- Voiding dysfunction associated with **ANY** of the following:
 - benign prostatic hyperplasia
 - detrusor hyperreflexia due to myelomeningocele
 - urge incontinence refractory to anticholinergic therapy

General Background

FDA Approved Indications

Botulinum toxin type A is indicated for the treatment of following:

- **Cervical Dystonia-** in adults to decrease the severity of abnormal head position and neck pain associated with cervical dystonia
- **Severe Primary Axillary Hyperhidrosis** that is inadequately managed with topical agents
- **Strabismus and Blepharospasm-** associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and above

Botulinum toxin type A (Botox A) is available as Botox[®] and Botox Cosmetic[®]. Botulinum toxins work in the peripheral and autonomic nervous systems by preventing the release of acetylcholine. This results in disrupted neurotransmission and muscle paralysis. 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, as assays measuring the lethal dose differ. Pharmacokinetic data such as absorption, distribution, metabolism, and elimination are not available for Botox A. Systemic concentrations of botulinum toxin following intradermal or intramuscular injection are not expected.

Based on peer-reviewed literature and the American Hospital Formulary Service Drug Information (AHFS DI), there is sufficient evidence to support the use of Botulinum Toxin Type A for all of the indications included in the criteria for the coverage policy. Most supporting data for off-label uses are from one or two trials. Few trials had active comparators and most are placebo-controlled or case series data.

Off-label Indications

Voiding Dysfunction

Three trials and two case series are available evaluating Botox A for patients with a variety of problems that can cause voiding dysfunction. All available data demonstrate positive results for Botox A treatment for treatment of voiding dysfunction caused by the following conditions:

- **Benign Prostatic Hyperplasia:** Maria et al. (2003) compared Botox A and placebo in patients with symptomatic benign prostatic hyperplasia. Patients treated with Botox A had decreased American Urological Index scores (65% to 54%) compared to patients treated with placebo who had no changes ($p < 0.05$). Patients treated with Botox A also had decreased post-void residual volumes (83% to 60%) compared to patients treated with placebo who had no changes ($p < 0.05$). No adverse effects or withdrawals were reported.
- **Intracranial Lesions or Cerebrovascular Accident-Induced Voiding Difficulty:** Chen and Kuo (2004) also showed positive results with Botox A when comparing Botox A and no treatment in patients with urinary problems due to intracranial lesions or cerebrovascular accidents. Patients who received a urethral injection of Botox A showed improved voiding pressure and increased maximum urine flow rates (+3.1 mL/sec) compared to baseline ($p < 0.05$). No adverse effects or withdrawals were reported.
- **Detrusor Hyperreflexia Due to Myelomeningocele:** Schulte-Baukloh et al. (2002) administered bladder injections of Botox A to 17 children with detrusor hyperreflexia. These results showed that maximum bladder capacity increased by 56%, maximum detrusor pressure decreased by 32.6%, and detrusor compliance increased by 121% compared to baseline values ($p < 0.05$). No adverse effects or withdrawals were reported.
- **Urge Incontinence Refractory to Anticholinergic Therapy:** Rapp et al. (2000) administered bladder injections of Botox A to a series of patients with urge incontinence and showed that 34% of patients achieved a complete response, 26% had slight improvement, and 40% had no improvement compared to baseline values ($p = \text{not reported}$). Patients showed improvements on the Incontinence Impact Questionnaire and Urogenital Distress Inventory scales compared to baseline ($p < 0.003$). Approximately 20% of patients experienced mild hematuria, pelvic pain, and dysuria; however, no patients withdrew due to these adverse effects.
- **Detrusor Sphincter Dyssynergia Due to Spinal Cord Injury:** de Seze et al. (2002) compared injections of lidocaine 0.5% and Botox A in patients with detrusor sphincter dyssynergia. After 30 days, patients treated with Botox A decreased their post-void residual by 159 mL compared to an increase of 50 mL in patients treated with lidocaine ($p < 0.01$). More patients receiving Botox A improved on Blaivas' classification of detrusor sphincter dyssynergia compared to patients treated with lidocaine ($p < 0.04$). Patients experienced an equal amount of incontinence between groups, and no patients withdrew from the study.

Chronic Pain

Nine trials are available evaluating the effectiveness of Botox A for the treatment of patients with different types of chronic pain. These data show positive results for Botox A in patients with low back pain, mastectomy reconstruction pain, hemorrhoid pain, chronic prostate pain, and myofascial pain syndrome. Botox A therapy is not effective at relieving neck pain and is equivalent to surgery in patients with tennis elbow. All trials reported few or no adverse effects, and no patients withdrew due to side effects.

- **Low Back Pain:** Foster et al. (2001) showed that after three and eight weeks after Botox A injections into the sacral region, low back pain decreases by 50% as measured via visual analog scale (VAS). Patients also showed improvements on the Oswestry Low Back Pain Questionnaire at eight weeks, with 66.7% of patients treated with Botox A showing some improvement from baseline compared to 18.8% of patients treated with placebo ($p=0.011$).
- **Mastectomy Reconstruction Pain:** Layeeque et al. (2004) showed a significant decrease in immediate postoperative pain (mean VAS score 3) in patients who received a Botox A infiltration compared to patients who received standard therapy (mean VAS score 6.8) ($p<0.001$). Patients in the Botox A group also had decreased pain during tissue expansion ($p\leq 0.009$).
- **Hemorrhoid Pain:** Davies et al. (2003) showed that Botox A injections into the internal anal sphincter in patients undergoing Milligan-Morgan hemorrhoidectomy had lower pain scores compared to patients receiving placebo, $p < 0.02$. No differences were noted in the amount of postoperative analgesic required.
- **Myofascial Pain:** Porta (2000) compared trigger point injections of bupivacaine and either Botox A or methylprednisolone in patients with chronic myofascial pain. At baseline, patients in the Botox A group had higher pain scores than the methylprednisolone group, $p = 0.006$. At day 60, there were significant differences in pain scores (Botox A -5.5, methylprednisolone -2.5, $p<0.0001$), but not at day 30.
- **Chronic Prostate Pain:** Zermann et al. (2000) reported case series data that Botox A perisphincteric injection in patients with chronic prostate pain can reduce pain (VAS, 10 cm) by -5.6 compared to baseline (p =not reported). These authors also noted positive improvements compared to baseline in post-void residuals, average urine flow, peak urine flow, urethral sphincter closing pressure, and functional urethral length ($p<0.001$).
- **Tennis Elbow:** Keizer et al. (2002) found no differences in pain, range of motion, or patient satisfaction between patients who received one or two injections of Botox A compared to patients who had surgery (Hohmann modified release). Patients who underwent surgery used less sick leave at three months than patients receiving Botox A injections ($p<0.01$), but there were no differences at six, 12, and 24 months. These authors did not perform a power calculation to determine if their sample size was sufficient to detect a difference.
- **Chronic Neck Pain:** Three trials are available comparing Botox A injections to placebo in patients with chronic neck pain. No trial showed a difference between groups for reduction in neck pain. These trials may have had insufficient sample size to detect a difference. No differences were found between groups using the Vernon-Mior Score, Neck Pain and Disability Scale, Global Assessment Scale, and the SF-36 health survey.

Temporomandibular Dysfunction or Chronic Orofacial Pain

Two trials are available evaluating Botox A in patients with chronic orofacial pain. Nixdorf et al. found no differences between Botox A and placebo for relief of pain. von Lindern et al. (2003) showed a decrease in pain scores of 3.2 on a 10 cm visual analog scale for patients treated with Botox A and a decrease of 0.4 for patients treated with placebo ($p<0.01$). Three case series reports are available evaluating Botox A in patients with temporal mandibular dysfunction. These data show that Botox A treatment can reduce pain scores (VAS, 10 cm) by at least three points compared to baseline ($p<0.05$).

Headache/Migraine

Table 1 summarizes the evidence-based assessment of the efficacy and safety of botulinum neurotoxin (botulinum toxin type A, BoNT-A) in the treatment of head pain reported by the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (AAN) published in Neurology, May 2008.

Table 1

<p>Source: Naumann M, et al. Assessment: Botulinum neurotoxin in the treatment of autonomic disorders and pain: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2008;70;1707-1714</p> <p>Objective: To perform an evidence-based review of the safety and efficacy of botulinum neurotoxin (BoNT) in the treatment of autonomic and urologic disorders and low back and head pain.</p> <p>Method / Study Design: - An evidence-based review: literature search included MEDLINE and Current Contents for therapeutic articles relevant to BoNT. A total of 11 randomized, placebo-controlled studies of BoNT in patients with headache were evaluated. Conclusions and recommendations were developed based on the highest level of evidence and put into current clinical context</p>
Outcome
<p>Episodic migraine</p> <p>Two class I and two Class II studies</p> <ul style="list-style-type: none">- two Class I studies:<ul style="list-style-type: none">- 1st study: There were reductions from baseline in migraine frequency, maximum severity, and duration, but there was no significant difference between BoNT and placebo groups at 1 to 3 months after injection.- 2nd study: BoNT-A and placebo produced a comparable decrease from baseline in migraine frequency and there were no consistent, statistically significant, between-group differences.- two Class II studies:<ul style="list-style-type: none">- 1st study Primary outcome: a change in the frequency of moderate to severe migraines per month. For the primary outcome measures, no significant benefit of BoNT.- 2nd study primary outcome: proportion of patients with 50% or more decrease in the frequency of headaches as compared with baseline. For the primary outcome measures, no significant benefit of BoNT. Rate difference between patients treated with placebo and BoNT experiencing 50% or more reduction in headache frequency was 5%, favoring the BoNT-treated group. However, this difference was not significant. <p>Conclusions. Based on published Class I and Class II studies, BoNT injection is probably ineffective in the treatment of episodic migraine (Level B, labeled as “probably ineffective”).</p>
<p>Chronic tension-type headache:</p> <p>Two Class I studies:</p> <p>1st study primary measure: The area under the headache curve in the subjects’ headache diary.</p> <ul style="list-style-type: none">- There was no significant difference, when compared to a baseline 6-week period, between the BoNT and placebo groups. A post hoc statistical analysis showed that this study was sufficiently powered to detect a difference in reduction of headache frequency of one headache per week. Thus, a clinically meaningful effect of BoNT was excluded. <p>2nd study primary measure: Mean change from baseline in number of headache-free days from day 30 to 60 after injection.</p> <ul style="list-style-type: none">- Both BoNT and placebo groups improved after injection, but BoNT was not more beneficial. A power analysis was not provided. <p>Class II study: used the mean difference in intensity of headache measured by a visual analog scale (VAS) pre- and post-treatment.</p> <ul style="list-style-type: none">- Data showed no significant difference in the severity of pain. <p>Conclusions. Based on the results of two Class I studies, at least one of which was adequately powered, BoNT injection is probably ineffective for patients with chronic tension-type headaches (Level B, labeled as “probably ineffective”).</p>
<p>Chronic daily headache</p> <p>Four Class II studies</p> <ul style="list-style-type: none">- Primary outcome for all 4 studies: the mean change in headache-free days per month.- Two studies demonstrated a significant benefit for the BoNT-treated patients attaining at least a 50% reduction in CDH- The largest study (N=702), showed no significant difference between BoNT-treated patients and placebo. <p>Conclusions. Based on inconsistent results from four Class II studies, there is insufficient evidence to support or refute a benefit of BoNT for the treatment of chronic daily headache (Level U, labeled as “insufficient evidence”).</p>

In addition, table 2 provides the summary of most current published clinical trials evaluating the safety and efficacy of botulinum toxin A for the treatment and prophylactic treatment of various types of headache:

Table2:

Source and Objective	Method / Study Design	Outcome	Grade*
<p>Source: Cady et al. Headache. 48(6):900-913, June 2008.</p> <p>Objective: To examine the efficacy and safety of and satisfaction with botulinum toxin type A for prophylactic treatment of headache in patients previously failing prophylaxis because of issues pertaining to compliance.</p>	<p>- randomized, double-blind, single-center, placebo-controlled study (months 1 to 3) of BoNTA with a cross-over to open-label BoNTA treatment (months 4 to 6). [N=73 subjects screened, 61 (40 BoNTA; 21 placebo)</p> <p>- Pt population: with disabling headache (International Headache Society, International Classification of Headache Disorders [ICHD-I] diagnosis 1.1, 1.2, 1.7, or 2.2, and Headache Impact Test [HIT]-6 scores ≥ 56) previously failing prophylaxis because of compliance, tolerability, or adherence issues</p> <p>-Primary endpoint: reduction of the number of headache episodes or days</p> <p>-Secondary endpoint: headache severity</p>	<p>-No statistical significance at months 1 to 3 for the number of headache episodes or days.</p> <p>- During the open-label study, BoNTA-treated subjects had a decrease in the number of headache episodes at months 5 and 6 ($P < .05$) vs baseline for both) and headache days at months 5 and 6 ($P < .05$ vs baseline).</p> <p>- A decrease in Headache Impact Test (HIT-6) scores was significantly greater for BoNTA-treated subjects than for placebo-treated subjects at month 3 ($P = .0466$).</p> <p>- Within-group decreases in HIT-6 scores were significant in BoNTA-treated subjects during each month of the blinded trial (for months 1 to 3, respectively; $P < .0001$ for all vs baseline) and throughout the open-label portion of the study (months 4 to 6, respectively; $P < .01$ for all vs baseline).</p> <p>- At 3 months, BoNTA was significantly better than placebo ($P = .001$) in the reduction of Migraine Disability Assessment (MIDAS) total score. The change from baseline in the MIDAS total scores was significant in BoNTA-treated subjects ($P < .0001$) but not in placebo recipients.</p> <p>- BoNTA-treated subjects showed improvement in 11 of 13 and 7 of 13 assessments of treatment satisfaction in Migraine Impact Questionnaire (MIQ) at months 3 and 6, respectively, while the placebo group showed no improvement at any measured time interval in the study.</p> <p>- At month 3 (blinded period), there were no treatment-related AEs reported in both groups.</p>	1
<p>Source: Blumenfeld, et al. Headache. 48(2):210-220, February 2008.</p> <p>Objective: To compare the efficacy and safety of botulinum toxin type A and divalproex sodium as prophylaxis in reducing disability and impact associated with migraine</p>	<p>- randomized, double-blind, single-center prospective study.</p> <p>-59 patients received either BoNTA 100 U/placebo-DVPX bid or placebo-BoNTA/DVPX 250 mg bid. BoNTA/placebo injections were given at Day 0 and at Month 3. Patients were evaluated at Months 1, 3, 6, and 9.</p>	<p>- Both treatments showed significant improvements in disability scores and reductions in headache days and headache index.</p> <p>- A trend to decreased headache severity was observed with BoNTA.</p> <p>- A greater percentage of DVPX patients reported adverse events possibly related to treatment (DVPX 75.8% vs BoNTA 50%, $P = .04$) and discontinued because of adverse events (DVPX 27.6% vs BoNTA 3.3%, $P = .012$).</p>	1
<p>Source: Freitag, et al Headache. 48(2):201-209, February 2008.</p> <p>Objective: To examine the effects of botulinum Toxin Type A in the Treatment of Chronic Migraine Without Medication Overuse.</p>	<p>- Double-blind placebo-controlled randomized trial of botulinum Toxin Type A 100 units administered in a fixed dose</p> <p>- Patients: A total of 60 patients were randomized and 41 patients were treated with the study medication or placebo. Five patients failed to complete the study, which lasted 4 months after the study medication was injected.</p>	<p>- Botulinum Toxin Type A was statistically superior to placebo for the primary endpoint of reduction in headache episodes and the secondary endpoints including total headache days, headache index, and quality of life measures</p> <p>- 6 patients on botulinum Toxin Type A compared with 3 patients on Placebo had at least a 50% reduction in their episodes.</p> <p>- It showed numerical superiority to placebo for acute medication use and Disability Assessment Scores.</p> <p>- similar adverse events were report for both treatment groups.</p>	1

*Grade 1.Evidence from randomized, blinded, placebo-controlled, clinical trials in peer reviewed journals

Based on the evidence-based conclusions reported by the AAN, BoNT-A injection is probably ineffective in the treatment of episodic migraine and chronic tension-type headaches and to date there is no consistent evidence to support the use of BoNT-A injection for treatment of chronic daily headache. However, the results from randomized, double-blind, and placebo-controlled published studies show the efficacy of BoNT-A injection for the prophylactic treatment of migraine headache. Future clinical trials appear warranted to evaluate the use of BoNT-A injection for treatment of migraine, chronic tension-type headache, and chronic daily headache.

Rhinitis

Two trials are available comparing Botox A and placebo injections for patients with intrinsic rhinitis and allergic rhinitis. Patients with intrinsic rhinitis treated with Botox A had decreased rhinorrhea during the first four weeks of follow-up compared to patients treated with placebo ($p<0.05$). No differences were noted between groups during the remaining 20 weeks of follow-up. No differences were noted between groups for sneezing and nasal stuffiness symptoms. Patients with allergic rhinitis treated with Botox A had decreased rhinorrhea, nasal obstruction, and sneezing compared to patients treated with placebo. Itching scores did not differ favoring Botox A treatment after two weeks of treatment. No adverse effects or withdrawals were reported in either trial.

Treatment of Tics

One trial is available comparing Botox A and placebo in patients with one or more motor tics due to Tourette Syndrome or idiopathic tic disorder. Botox A treatment decreased the number of tics performed per minute by 39%, while patients treated with placebo experienced an increase in tic performance of 5.8% ($p<0.05$). No differences between groups were noted in the Tourette Syndrome Global Score, Yale Global Tic Severity Scale, or Unified Tic Rating Scale. Approximately 50% of patients experienced muscle weakness, and 10% experienced motor restlessness and the emergence of new tics. One patient withdrew from each group for unspecified reasons.

Paralytic Scoliosis

Nuzzo et al. (1997) administered Botox A to 12 children with paralytic scoliosis requiring surgical intervention. Botox A therapy improved spine curvature from 9–51 degrees and no child worsened.

Diabetic Gastroparesis

Two case series showed positive results with Botox A therapy improving gastric emptying by 112 minutes and subjective symptom scores from baseline ($p<0.05$).

Sphincter of Oddi Dysfunction

Two case series with Dysport[®], a botulinum toxin type A product available in Europe but not the United States, showed some improvement with Botox A therapy decreasing the return of biliary colic or acute pancreatitis.

Sialorrhea

Two trials are available evaluating Dysport[®] (a botulinum toxin type A product not available in the United States), for the treatment of sialorrhea in patients with Parkinson's disease. Observational data are available comparing Botox A and scopolamine for the treatment of sialorrhea in patients with cerebral palsy.

- **Parkinson's Disease Sialorrhea:** Clinical trial data show that injections of the parotid glands with a botulinum toxin type A decrease sialorrhea by 20–50%. Adverse effects include dry mouth, worsened gait, diarrhea, and neck pain. No patients withdrew from these studies due to adverse effects.
- **Cerebral Palsy Sialorrhea:** Jongerius et al. (2004) compared transdermal scopolamine and Botox A in children with cerebral palsy and severe sialorrhea. Both scopolamine and Botox A therapy reduced the drooling quotient by 15–20 points ($p=0.0001$). More patients receiving scopolamine (82%) had anticholinergic adverse effects compared to patients receiving Botox A

(5%). Four patients withdrew due to side effects from scopolamine; no patients withdrew due to adverse effects from Botox A.

Therapy with Botox A is well-tolerated. The most common side effects of Botox A therapy are muscle weakness and injection site pain. Theoretical drug interactions may occur with concomitant use of neuromuscular blockers, but the clinical significance of this interaction is unknown.

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)
64614	Chemodenervation of muscle(s); extremity(s) and/or trunk muscle(s) (eg, for dystonia, cerebral palsy, multiple sclerosis)
67345	Chemodenervation of extraocular muscle

HCPCS Codes	Description
J0585	Botulinum toxin type A, per unit

ICD-9-CM Diagnosis Codes	Description
306.0	Musculoskeletal malfunction arising from mental factors
333.6	Genetic torsion dystonia
333.71	Athetoid cerebral palsy
333.79	Other acquired torsion dystonia
333.81	Blepharospasm
333.82	Orofacial dyskinesia
333.83	Spasmodic torticollis
333.84	Organic writers' cramp
333.89	Other fragments of torsion dystonia
334.1	Hereditary spastic paraplegia
340	Multiple sclerosis
341.0	Neuromyelitis optica
341.1	Schilder's disease
341.8	Other demyelinating diseases of central nervous system
341.9	Unspecified demyelinating disease of central nervous system
342.10	Spastic hemiplegia affecting unspecified side
342.11	Spastic hemiplegia affecting dominant side
342.12	Spastic hemiplegia affecting nondominant side
343.0	Diplegic infantile cerebral palsy
343.1	Hemiplegic infantile cerebral palsy
343.2	Quadriplegic infantile cerebral palsy
343.3	Monoplegic infantile cerebral palsy
343.4	Infantile hemiplegia
343.8	Other specified infantile cerebral palsy

343.9	Unspecified infantile cerebral palsy
351.8	Other facial nerve disorders
368.01	Strabismic amblyopia
368.2	Diplopia
368.32	Simultaneous visual perception without fusion
368.33	Fusion with defective stereopsis
378.00	Unspecified esotropia
378.01	Monocular esotropia
378.02	Monocular esotropia with A pattern
378.03	Monocular esotropia with V pattern
378.04	Monocular esotropia with other noncomitancies
378.05	Alternating esotropia
378.06	Alternating esotropia with A pattern
378.07	Alternating esotropia with V pattern
378.08	Alternating esotropia with other noncomitancies
378.10	Unspecified exotropia
378.11	Monocular exotropia
378.12	Monocular exotropia with A pattern
378.13	Monocular exotropia with V pattern
378.14	Monocular exotropia with other noncomitancies
378.15	Alternating exotropia
378.16	Alternating exotropia with A pattern
378.17	Alternating exotropia with V pattern
378.20	Unspecified intermittent heterotropia
378.21	Intermittent esotropia, monocular
378.22	Intermittent esotropia, alternating
378.23	Intermittent exotropia, monocular
378.24	Intermittent exotropia, alternating
378.50	Unspecified paralytic strabismus
378.51	Paralytic strabismus, third or oculomotor nerve palsy, partial
378.52	Paralytic strabismus, third or oculomotor nerve palsy, total
378.53	Paralytic strabismus, fourth or trochlear nerve palsy
378.54	Paralytic strabismus, sixth or abducens nerve palsy
378.55	Paralytic strabismus, external ophthalmoplegia
378.56	Paralytic strabismus, total ophthalmoplegia
378.60	Unspecified mechanical strabismus
378.61	Mechanical strabismus from Brown's (tendon) sheath syndrome
378.62	Mechanical strabismus from other musculofascial disorders
378.63	Mechanical strabismus from limited duction associated with other conditions
378.71	Duane's syndrome
378.72	Progressive external ophthalmoplegia
378.73	Strabismus in other neuromuscular disorders
378.9	Unspecified disorder of eye movements
478.75	Laryngeal spasm
530.0	Achalasia and cardiospasm
565.0	Anal fissure
596.55	Detrusor sphincter dyssynergia
705.21	Primary focal hyperhidrosis
705.22	Secondary focal hyperhidrosis
723.5	Torticollis, unspecified
736.72	Equinus deformity of foot, acquired
780.8	Generalized hyperhidrosis

Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description

HCPCS Codes	Description

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
346.00	Classical migraine without mention of intractable migraine
346.01	Classical migraine with intractable migraine, so stated
346.10	Common migraine without mention of intractable migraine
346.11	Common migraine with intractable migraine, so stated
346.90	Unspecified migraine without mention of intractable migraine
346.91	Unspecified migraine with intractable migraine, so stated
350.1	Trigeminal neuralgia
455.1	Internal thrombosed hemorrhoids
455.2	Internal hemorrhoids with other complication
455.4	External thrombosed hemorrhoids
455.5	External hemorrhoids with other complication
455.7	Unspecified thrombosed hemorrhoids
455.8	Unspecified hemorrhoids with other complication
472.0	Chronic rhinitis
477.0	Allergic rhinitis due to pollen
477.1	Allergic rhinitis, due to food
477.2	Allergic rhinitis due to animal (cat) (dog) hair and dander
477.8	Allergic rhinitis due to other allergen
477.9	Allergic rhinitis, cause unspecified
524.60	Unspecified temporomandibular joint disorders
524.62	Arthralgia of temporomandibular joint
527.7	Disturbance of salivary secretion
536.3	Gastroparesis
576.5	Spasm of sphincter of Oddi
600.01	Hypertrophy (benign) of prostate with urinary obstruction and other lower urinary tract symptoms [LUTS]
723.1	Cervicalgia
737.30	Scoliosis (and kyphoscoliosis), idiopathic
737.33	Scoliosis due to radiation
724.2	Lumbago
726.32	Lateral epicondylitis of elbow
784.0	Headache
788.20	Unspecified retention of urine
788.21	Incomplete bladder emptying
788.29	Other specified retention of urine

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