Clinical Policy: OnabotulinumtoxinA (Botox)

Reference Number: CP.PHAR.232
Effective Date: 07.01.16
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Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

OnabotulinumtoxinA (Botox®) is an acetylcholine release inhibitor and a neuromuscular blocking agent.

FDA Approved Indication(s)

Botox is indicated for:

- Treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication
- Treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition [e.g., spinal cord injury (SCI), multiple sclerosis (MS)] in adults who have an inadequate response to or are intolerant of an anticholinergic medication
- Prophylaxis of headaches in adult patients with chronic migraine (≥ 15 days per month with headache lasting 4 hours a day or longer)
- Treatment of spasticity in adult patients
- Treatment of cervical dystonia (CD) in adult patients, to reduce the severity of abnormal head position and neck pain
- Treatment of severe axillary hyperhidrosis that is inadequately managed by topical agents in adult patients
- Treatment of blepharospasm associated with dystonia in patients ≥ 12 years of age
- Treatment of strabismus in patients ≥ 12 years of age

Limitation(s) of use:

- Safety and effectiveness of Botox have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) in seven placebo-controlled studies.
- Safety and effectiveness of Botox have not been established for the treatment of other upper or lower limb muscle groups. Safety and effectiveness of Botox have not been established for the treatment of spasticity in pediatric patients under age 18 years. Botox has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture. Treatment with Botox is not intended to substitute for usual standard of care rehabilitation regimens.
- The safety and effectiveness of Botox for hyperhidrosis in other body areas have not been established. Weakness of hand muscles and blepharoptosis may occur in patients who receive Botox for palmar hyperhidrosis and facial hyperhidrosis, respectively. Patients should be evaluated for potential causes of secondary hyperhidrosis (e.g., hyperthyroidism) to avoid symptomatic treatment of hyperhidrosis without the diagnosis and/or treatment of the underlying disease. Safety and effectiveness of Botox have not been established for the treatment of axillary hyperhidrosis in pediatric patients under age 18.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Botox is **medically necessary** when one of the following criteria is met:

I. Initial Approval Criteria

A. Cervical Dystonia (must meet all):

1. Diagnosis of CD (*see Appendix C*):
2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;

3. Age ≥ 16 years;
4. Experiencing involuntary contractions of the neck and shoulder muscles (e.g., splenius, sternocleidomastoid, levator scapulae, scalene, trapezius, semispinalis capitis) resulting in abnormal postures or movements of the neck, shoulder or head;
5. Contractions are causing pain and functional impairment;
6. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
7. Dose does not exceed 400 units per treatment session.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

B. Blepharospasm *(a focal dystonia)* or Strabismus (must meet all)**:**

1. Diagnosis (a or b):
   a. Blepharospasm (i.e., abnormal contraction of eyelid muscles);
   b. Strabismus (i.e., misalignment of the eyes);
2. Prescribed by or in consultation with a neurologist or ophthalmologist;
3. Age ≥ 12 years;
4. Member has significant disability in daily functional activities due to interference with vision;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed (a or b):
   a. Blepharospasm: 5 units per site per treatment session (maximum of 200 units total in a 30-day period);
   b. Strabismus: 25 units per muscle per treatment session.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

C. Other Dystonias (off-label) (must meet all)**:**

1. Diagnosis of dystonia (*see definitions and types in Appendices C and D*);
2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;
3. Failure of a trial of carbidopa/levodopa or trihexyphenidyl unless contraindicated or clinically significant adverse effects are experienced;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
5. Dose does not exceed 400 units per single treatment with the following exceptions:
   a. Oromandibular dystonia: 25 units per muscle per treatment session;
   b. Laryngeal dystonia (spasmodic dysphonia): 3 units per treatment session.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)

Commercial – 6 months or to member's renewal date, whichever is longer

D. Upper and Lower Limb Spasticity (must meet all)**:**
1. Diagnosis of upper or lower limb spasticity;
2. Prescribed by or in consultation with a neurologist, orthopedist , physiatrist, or physical medicine and rehabilitation specialist ;
3. Age ≥ 18 years;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
5. Dose does not exceed 400 units per treatment session.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

E. Spasticity Associated with Cerebral Palsy (off-label) (must meet all)**:**
1. Diagnosis of spasticity associated with cerebral palsy (CP);
2. Prescribed by or in consultation with a neurologist , physiatrist, or physical medicine and rehabilitation specialist;
3. Age ≥ 2 years;
4. Focal increased muscle tone interferes with function or is likely to lead to joint contracture with growth;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed 400 units per treatment session.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

F. Chronic Migraine (must meet all)**:**
1. Diagnosis of chronic migraine (≥ 15 days per month for at least 3 months with headache lasting 4 hours a day or longer);
2. Prescribed by or in consultation with a neurologist or pain specialist;
3. Age ≥ 18 years;
4. Failure of an 8-week trial of at least 2 oral migraine preventative therapies (e.g., antiepileptic drugs: divalproex sodium, sodium valproate, topiramate; beta-blockers: metoprolol, propranolol, timolol; antidepressants: amitriptyline, venlafaxine), unless contraindicated or clinically significant adverse effects are experienced;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed 200 units per treatment session.

Approval duration:
Medicaid/HIM - 24 weeks (two 12-week treatment sessions)
Commercial – 6 months or to member's renewal date, whichever is longer

G. Primary Axillary Hyperhidrosis (must meet all)**:**
1. Diagnosis of severe primary axillary hyperhidrosis (e.g., resulting in medical complications such as skin maceration and infection or significant disruption of professional/social life);
2. Prescribed by or in consultation with a neurologist or dermatologist;
3. Age ≥ 18 years;
4. Failure of a 6-month trial of topical aluminum chloride, unless contraindicated or clinically significant adverse effects are experienced;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed 50 units per axilla per treatment session.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

H. Overactive Bladder and Urinary Incontinence (must meet all)**:**
1. Diagnosis (a or b):
   a. Overactive bladder
   b. Urinary incontinence associated with a neurologic condition (e.g., spinal cord injury, MS);
2. Prescribed by or in consultation with a neurologist or urologist;
3. Age ≥ 18 years;
4. Failure of a trial of at least two anticholinergic agents and one oral beta-3 agonist medication (e.g., oxybutynin chloride, tolterodine tartrate, mirabegron), each used for at least 30 days, unless contraindicated or clinically significant adverse effects are experienced;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed (a or b):
   a. Overactive bladder: 100 units per treatment session;
   b. Urinary incontinence: 200 units per treatment session.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

I. Esophageal Achalasia (off-label) (must meet all)**:**
1. Diagnosis of esophageal achalasia (i.e., failure of relaxation of the lower esophageal sphincter accompanied by loss of peristalsis in the distal esophagus);
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Member is not a good candidate for pneumatic dilation or myotomy (e.g., high surgical risk due to age, comorbidities);

5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed 100 units.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

J. Hirschsprung's Disease and Internal Anal Sphincter Achalasia (off-label) (must meet all):

1. Diagnosis (a or b):
   a. Hirschsprung's disease (HD) (i.e., heritable motor disorder of the gut with failure of the colon to relax causing functional obstruction; usually diagnosed infancy or childhood) (i or ii):
      i. Botox will be used for constipation due to increased internal anal sphincter tone after surgery;
      ii. Member is diagnosed with ultra-short segment HD;
   b. Internal anal sphincter (IAS) achalasia (i.e., lack of rectoanal inhibitory reflex on anal manometry; presents in infancy – may mimic HD);
2. Prescribed by or in consultation with a gastroenterologist;
3. Failure of a trial of stool softeners and laxatives;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
5. Dose does not exceed 100 units.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

K. Chronic Anal Fissure (off-label) (must meet all)**:**

1. Diagnosis of chronic anal fissures;
2. Prescribed by or in consultation with a gastroenterologist or colorectal surgeon;
3. Age ≥ 18 years;
4. Failure of a trial of nitroglycerin 0.2% ointment, unless contraindicated or clinically significant side effects are experienced;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed 100 units.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

L. Other diagnoses/indications:

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Approval

A. Chronic Migraine (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. If member has received 2 or more Botox treatment sessions, has experienced and maintained a 30% reduction in monthly migraine headache frequency from baseline;
4. It has been at least 12 weeks since the last injection of Botox;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. If request is for a dose increase, new dose does not exceed 200 units per treatment session.

Approval duration:
Medicaid/HIM – 24 weeks (two 12-week treatment sessions)
Commercial – 6 months or to member's renewal date, whichever is longer

B. Esophageal Achalasia (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. It has been at least 24 weeks since the last injection of Botox;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
5. If request is for a dose increase, new dose does not exceed 100 units per treatment session.

Approval duration:
Medicaid/HIM - 24 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

C. All Other Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. It has been at least 12 weeks since the last injection of Botox;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
5. Botox administration has not exceeded 400 units over the last 3 months;
6. If request is for a dose increase, new dose does not exceed the following indication-specific maximums if applicable:
   a. Dystonias:

i. CD, upper/lower limb spasticity, CP: 400 units per treatment session;
ii. Blepharospasm: 5 units per site per treatment session (maximum of 200 units total in a 30-day period);
iii. Strabismus: 25 units per muscle per treatment session;
iv. Oromandibular dystonia: 25 units per muscle per treatment session;
v. Laryngeal dystonia (spasmodic dysphonia): 3 units per treatment session;

b. Primary axillary hyperhidrosis: 50 units per axilla per treatment session;
c. Overactive bladder, HD, IAS achalasia, chronic anal fissures: 100 units per treatment session;
d. Urinary incontinence: 200 units per treatment session.

Approval duration:
Medicaid/HIM - 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

D. Other diagnoses/indications (1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: 12 weeks (single treatment session); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
B. Cosmetic treatment of hyperfunctional wrinkles of the upper face including glabellar frown lines, deep forehead wrinkles and periorbital wrinkles (crow's feet).

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CD: cervical dystonia
CP: cerebral palsy
HD: Hirschsprung's disease
IAS: internal anal sphincter
MS: multiple sclerosis
SCI: spinal cord injury
TMD: temporomandibular disorders
TMJ: temporomandibular joint

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
carbidopa/levodopa (Sinemet®, Duopa®, Rytary®)	**Other Dystonias** (*see appendices C and D*) 25 mg/100 mg PO QD, and increase by 1 tablet every 3 to 5 days.	1,200 mg/day of levodopa
trihexyphenidyl	**Other Dystonias** (*see appendices C and D*) 30 mg PO QD	30 mg/day
lactulose	**Hirschsprung's Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure** 15-30 ml PO QD	60 mL/day
Senokot® (sennosides)	**Hirschsprung's Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure** Two 8.6 mg tabs PO QD-BID	34.4 mg/day
Metamucil® (psyllium)	**Chronic anal fissure** One rounded tsp in 8 oz liquid PO up to TID	3 doses/day
Dulcolax® (bisacodyl)	**Hirschsprung's Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure** 5 to 15 mg PO or 10 mg PR QD	30 mg/day
FiberCon® (Calcium polycarbophil)	**Chronic anal fissure** Two 625 mg tabs PO QD-QID	5000 mg/day
Citrucel® (Methylcellulose)	**Chronic anal fissure** Caplet: 2 caplets up to 6 times daily Powder: 2 grams in 8 oz of cold water by mouth up to 3 times daily	12 caplets/day or 6 grams/day
MiraLax® (Polyethylene glycol 3350)	**Hirschsprung's Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure** 17 grams of polyethylene glycol 3350 in 4-8 oz water by mouth once daily	17 grams/day
Colace® (Docusate sodium)	**Hirschsprung's Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure** 50-200 mg PO QD-QID	200 mg/day
nitroglycerin 0.2% ointment (Rectiv®)	**Chronic anal fissure** 15 to 30 mg (2.5 to 5 cm as squeezed from the tube, about 1 to 2 inches), applied topically to the skin every 8 hours while awake and at bedtime;	75 mg (12.5 cm as squeezed from the tube)/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	frequency of application may be increased to every 6 hours if needed. Alternatively, a regimen providing a 12-hour nitrate-free interval may be used; apply dosage once each morning, then reapply 6 hours later	
oxybutynin (Ditropan®/XL, Gelnique®)	**Overactive Bladder** Immediate-release tablets: 5 mg orally two to three times daily Extended-release tablets: 5-10 mg orally once daily Topical gel: Apply contents of one sachet topically once daily	Immediate-release: 20 mg/day Extended-release: 30 mg/day Gel: one sachet/day
tolterodine tartrate (Detrol®/LA)	**Overactive Bladder** Immediate-release tablets: 2 mg orally twice daily Extended-release tablets: 4 mg orally once daily	4 mg/day
Myrbetriq® (mirabegron)	**Overactive Bladder** 25 mg orally once daily	50 mg/day
Anticonvulsants such as: divalproex (Depakote®), topiramate (Topamax®)	**Chronic Migraines** *Refer to prescribing information*	*Refer to prescribing information*
Beta blockers such as: propranolol (Inderal®), metoprolol (Lopressor®), timolol	**Chronic Migraines** *Refer to prescribing information*	*Refer to prescribing information*
Antidepressants/tricyclic antidepressants such as: amitriptyline (Elavil®), venlafaxine (Effexor®)	**Chronic Migraines** *Refer to prescribing information*	*Refer to prescribing information*
Non-steroidal anti-inflammatory drugs (NSAIDs) such as: fenoprofen (Nalfon®), ibuprofen (Motrin®), ketoprofen (Orudis®), naproxen (Naprosyn®)	**Chronic Migraines** *Refer to prescribing information*	*Refer to prescribing information*
Drysol ® (aluminum chloride)	**Primary Axillary Hyperhidrosis** Apply topically once daily	One application/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Definition and Classification of Dystonia[11]

Dystonia is defined as a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both.

- Dystonic movements are typically patterned and twisting, and may be tremulous.
- Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation.

Dystonia is classified along two axes:

- Clinical characteristics: Age at onset, body distribution, temporal pattern, associated features (additional movement disorders or neurological features) - *the clinical characteristics fall into several specific dystonia syndromes that help to guide diagnosis and treatment*;
- Etiology: Nervous system pathology, inheritance.

*Appendix D: Descriptions and Examples of Dystonia Syndromes**

Category	Subcategory	Description and Examples
Isolated dystonias	Early-onset generalized isolated dystonia	Dystonia with focal-onset in childhood often progresses to generalized involvement. Cases may be sporadic, familial, genetically defined or without known cause. • Early-onset generalized dystonia (DYT-TOR1A) • Adolescent-onset dystonia of mixed type (DYT-THAP1)
	Adult-onset focal or segmental isolated dystonia	Usually begins after age 30 years. Most are sporadic without identifiable cause. Rarely progress to generalized dystonia but can extend to contiguous body regions. • Adult-onset segmental dystonia (DYT-GNAL) • Cervical dystonia • Blepharospasm • Writer's cramp • Oromandibular dystonia • Laryngeal dystonia (spasmodic dysphonia) • Limb dystonia
Combined dystonias	Dystonia-parkinsonism	Disorders that combine dystonia and parkinsonian features. May be accompanied by pyramidal tract involvement or nonmotor features including cognitive decline. Many are inherited. • Dopa-responsive dystonia (DYT-GCH1, DYT-TH, and DYT-SPR) • Wilson disease • Early-onset parkinsonism (PARK-PARKIN) • Conditions associated with neurodegeneration with brain iron accumulation
	Myclonus-dystonia	Disorders in which there is a combination of dystonia and myoclonus. Dystonia may be mild and myoclonus generally predominates.

Category	Subcategory	Description and Examples
		• Myoclonus-dystonia (DYT-SGCE)
	Paroxysmal dyskinesia with dystonia	Disorders characterized by episodes of spontaneous or induced dyskinesia with dystonia. • Paroxysmal nonkinesigenic dyskinesia (DYT-MR1)

**Table adapted with permission from: Comella C. Classification and evaluation of dystonia. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available at www.uptodate.com. Accessed on June 22, 2017.*

Appendix E: General Information

- All botulinum toxin products have a black box warning which cautions patients that the effects of the drug may spread from the area of injection and cause symptoms similar to botulism, including potentially life-threatening swallowing and breathing difficulty.
- The potency units of botulinum toxin products 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 one product cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method.
- Safety and effectiveness have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) and is a Class III recommendation in Micromedex.
- Indication specific dosage and administration recommendations should be followed for Botox. When initiating treatment, the lowest recommended dose should be used. In treating adult patients for one or more indications, the maximum cumulative dose should not exceed 400 Units, in a 3 month interval.
- For detrusor overactivity associated with a neurologic condition there was no additional benefit of Botox 300 Units over 200 Units.
- Safety and effectiveness have not been uniformly established for the treatment of temporomandibular disorders (TMD). Use of botulinumtoxin for this indication is a Class IIb recommendation in Micromedex based on a single study from 1999. A review of two clinical studies (from 2002 and 2011) (15 and 21 patients) found no significant differences in pain reduction between botulinumtoxin and placebo. Other small studies (from 2005 - Italy and 2008 - Turkey) have been performed and showed improvement in objective measures of pain (20 patients and 26 patients). The most common total dose of BTX-A used in the studies was 25u for each temporalis muscle and 50u for each masseter muscle. The studies did not repeat the dosing, but measured efficacy at 16 weeks post dose. The 2003 Guidelines for diagnosis and management of disorders involving the temporomandibular joint and related musculoskeletal structures mention Botox as a possible treatment option for temporomandibular joint (TMJ) based on its mechanism of action and the pathophysiology of TMD.
  - TMD "gold standard" treatment continues to be: 1) TMJ intraoral orthotic; 2) Muscle relaxants by mouth; and 3) Home muscle relaxation exercises/techniques.
- Limb spasticity may be caused by Heredity spastic paraplegia; multiple sclerosis or other demyelinating diseases of the central nervous system; Spastic hemiplegia; infantile cerebral palsy; Stroke.

V. Dosage and Administration

Botox (onabotulinumtoxin A) Dose Chart			
Condition	**Average Duration of Effect**	**Average Dose**	**Maximum dose per treatment session**
Blepharospasm	12.5 weeks	5 units per site	200 units total in a 30-day period
Strabismus	6-8 weeks to 6-12 months	2.5 to 5 units per muscle (max 25 units)	25 units
Cervical dystonia	4 weeks to 3 months	200 to 300 units divided among affected muscles	400 units
Oromandibular dystonia*	10 to 14 weeks	25 units per muscle per treatment	100 units
Spasmodic dysphonia*	3-6 months	0.031 to 10 units per vocal cord. 5 to 30 units in abductor muscle	400 units
Overactive bladder	12 weeks	Total dose 100 Units, as 0.5 mL (5 Units) injections across 20 sites into the detrusor. Repeat doses should be 12 weeks apart	400 units
Spastic muscle contracture of pediatric cerebral palsy*	1-6 months	3 to 6 units/kg (maximum 12 units/kg). total dose 82 to 220 units divided among affected muscles	100 units
Childhood myoclonus following failure of Baclofen, benzodiazepines, and antiseizure medications*	4-8 months	8 to 80 units/kg	400 units
Chronic anal fissure*	Single Injection	20 units both sides	80 units/kg
Internal anal sphincter achalasia*	Single treatment. Patient may require repeat treatment. Adults or children	15 units to 25 units in each quadrant or up to 50 units on either side of IAS	100 units
Axillary Hyperhidrosis	4-12 months	50 units per axilla	100 units
Migraines	3-4 months	155 to 195 total units given in 5 to 40 units/site	200 units
Neurogenic bladder	8-12 months	200 units given in multiple sites	200 units

Botox (onabotulinumtoxin A) Dose Chart			
Condition	**Average Duration of Effect**	**Average Dose**	**Maximum dose per treatment session**
Upper Limb Spasticity	12 weeks	12.5 Units-50 Units in one site	400 units

**off-label uses*

VI. Product Availability

Vial of powder for solution for injection: 100 units, 200 units

VII. References

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Dystonias, Spasticity, Chronic Migraine

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Primary Axillary Hyperhidrosis, Overactive Bladder, Urinary Incontinence

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Esophageal Achalasia

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Hirschsprung's Disease, Internal Anal Sphincter Achalasia

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Chronic Anal Fissures

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Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0585	Injection, onabotulinumtoxinA, 1 unit

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.09. Added new FDA indication of lower limb spasticity per FDA labeling. Added compendial indication of laryngeal spasm/spasmodic dysphonia. -Overactive bladder: modified requirement for trial/failure of previous therapy to include oral beta-3 agonist medications per AUA guidelines. -Migraine: modified continuation criteria to require 30% reduction in headache frequency after 2 injections rather than just 1 per literature review and NICE guidelines. -Added general max dosing limit for cerebral palsy and spastic conditions and indication-specific max dosing limit for cervical dystonia, strabismus, primary axillary hyperhidrosis, upper limb spasticity, overactive bladder, urinary incontinence, and chronic migraine per PI. -Added indication-specific max dosing limit for chronic anal fissures, esophageal achalasia, laryngeal spasm/spasmodic dysphonia, Hirschsprung's disease, and dystonias per literature review. -Added prescriber requirement for overactive bladder, urinary incontinence, chronic migraines, upper limb spasticity, primary axillary hyperhidrosis, chronic anal fissures, cerebral palsy, esophageal achalasia, dystonias, Hirschsprung's disease, and spastic conditions. -Added age restriction for upper limb spasticity and primary axillary hyperhidrosis per PI, and for chronic anal fissures, esophageal achalasia, and Hirschsprung's disease per literature review. -Added route of administration for each labeled indication per PI. -Removed reauthorization criteria requiring attestation of significant improvement in symptoms and/or health-related quality of life. Added positive response to therapy to continuation criteria.	05.16	07.16
-Chronic migraine initial approval duration lengthened from 12 to 24 weeks (from one to two treatment sessions) to allow assessment of response as outlined in continuation criteria.	11.16	
The off-label criteria set entitled "Spastic Conditions" is deleted due to its broad scope; off-label requests not covered elsewhere in the policy are referred to the CP.PHAR.57.Global Biopharm policy so that they may be reviewed individually. Requirement that provider submits detailed treatment plan added to curtail abuse	02.17	
Indications reorganized. Definition of CD is edited per AAN guidelines. Laryngeal dystonia is merged with off-label dystonias which in turn are entitled "Other Dystonias". Clarified "blepharospasm" as a focal dystonia. Deleted causes and classifications of blepharospasm; blepharospasm and strabismus definitions are added. Dystonia information is added at Appendices B and C. Added	06.17	07.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
esophageal achalasia definition. IAS achalasia is given its own line item. HD and IAS achalasia definitions added. Background FDA indication section and references categorized. "Non-cosmetic" parenthetical added to the background FDA indication section; cosmetic coverage restriction reworded under the "Other Diagnoses/Indications" section to include notation of glabellar lines.		
2Q 2018 annual review: combined Medicaid and Commercial lines of business; added HIM line of business; expanded maximum dose for chronic migraine treatment to 200 units per treatment per 2012 NICE guidelines; Hirschsprung's Disease and Internal Anal Sphincter Achalasia: removed requirement for dietary and fluid control; added physical medicine and rehabilitation specialist for cervical dystonia, other dystonia, upper and lower limb spasticity, and spasticity associated with CP; added pain specialist for migraine; Medicaid: lowered age limit for CD to 16 from 18 years; added physiatrist to accepted specialist for spasticity associated with CP; Commercial: approval durations changed from length of benefit to 6 months or to member's renewal date, whichever is longer for initial and continued approval; references reviewed and updated.	04.24.18	05.18

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to

applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.