Clinical Policy: OnabotulinumtoxinA (Botox)

Reference Number: PA.CP.PHAR.232
Effective Date: 01/18
Last Review Date: 04/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for onabotulinumtoxinA (Botox®).

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
It is the policy of Pennsylvania Health and Wellness® that Botox is **medically necessary** when one of the following criteria is met:

ContentsDescription

I. Initial Approval Criteria

A. Cervical Dystonia (must meet all):

1. Prescribed by or in consultation with a neurologist, orthopedist or physiatrist;
2. Age ≥ 16years;
3. Diagnosis of cervical dystonia (CD) (see definition in Appendix B):
4. Experiencing involuntary contractions of the neck and shoulder muscles (e.g., splenius, sternocleidomastoid, levator scapulae, scalene, trapezius, posterior cervical) resulting in abnormal postures or movements of the neck, shoulder or head;
5. Contractions are causing pain or functional impairment;

1. 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. Prescribed dose of Botox does not exceed 400 units per treatment session.

Approval duration: 12 weeks (single treatment session)

B. Blepharospasm *(a focal dystonia)* or Strabismus (must meet all)**:**
1. Prescribed by or in consultation with a neurologist or ophthalmologist;
2. Age ≥ 12 years;
3. Diagnosis (a or b):
   a. Blepharospasm (i.e., abnormal contraction of eyelid muscles);
   b. Strabismus (i.e., misalignment of the eyes);
4. Member hasdisability in daily functional activities due to interference with vision;
2. 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. Prescribed dose of Botox 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: 12 weeks (single treatment session)

C. Other Dystonias – Off Label Use (must meet all)**:**
1. Prescribed by or in consultation with a neurologist, orthopedist or physiatrist;
2. Diagnosis of dystonia (see definitions and types in Appendices B and C);
3. If not contraindicated, member has tried and failed or is intolerant to carbidopa/levodopa and trihexyphenidyl;
3. 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;
4. Prescribed dose of Botox 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: 12 weeks (single treatment session)

D. Upper and Lower Limb Spasticity (must meet all)**:**
1. Prescribed by or in consultation with a neurologist, orthopedist or physiatrist;
2. Age ≥ 18 years;
3. Diagnosis of upper or lower limb spasticity (a or b):
   a. Upper limb: intent of treatment is to decrease severity of increased muscle tone in elbow flexors (i.e., biceps brachii, brachialis, pronator teres, brachioradialis), wrist flexors (i.e., flexor carpi radialis, flexor carpi ulnaris), finger flexors (i.e.,

flexor digitorum profundus, flexor digitorum sublimis [superficialis]), or thumb flexors (i.e., adductor pollicis, flexor pollicis longus);
   b. Lower limb: intent of treatment is to decrease severity of increased muscle tone in ankle or toe flexors (i.e., gastrocnemius, soleus, tibialis posterior, flexor hallucis longus, flexor digitorum longus);
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;
4. Prescribed dose of Botox does not exceed 400 units per treatment session.

Approval duration: 12 weeks (single treatment session)

E. Spasticity Associated with Cerebral Palsy – Off Label Use (must meet all)**:**
1. Prescribed by or in consultation with a neurologist;
2. Age ≥ 2 years;
3. Diagnosis of spasticity associated with cerebral palsy (CP);
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;
5. Prescribed dose of Botox does not exceed 400 units per treatment session.
6. Pediatric approved dosing:
   a. 2-16 years old: 4units/kg administered IM into the gastrocnemius muscle of the affected leg(s)
   b. 3-9 years old: 2-6 units/kg into at least 1 of 3 muscle groups (biceps, volar forearm muscles, or adductor pollicis muscle)

Approval duration: 12 weeks (single treatment session)

F. Chronic Migraine (must meet all)**:**
1. Prescribed by or in consultation with a neurologist;
2. Age ≥ 18 years;
3. Diagnosis of chronic migraine (≥ 15 days per month with headache lasting 4 hours a day or longer);
4. Member has tried and failed, or is intolerant or contraindicated to, at least 2 oral migraine preventative therapies, each for at least 8 weeks (e.g., antiepileptic drugs: divalproex sodium, sodium valproate, topiramate; beta-blockers: metoprolol, propranolol, timolol; antidepressants: amitriptyline, venlafaxine);
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;
5. Prescribed dose of Botox does not exceed 200 units per treatment session.

Approval duration: 24 weeks (two 12-week treatment sessions)

G. Primary Axillary Hyperhidrosis (must meet all)**:**

1. Prescribed by or in consultation with a neurologist or dermatologist;
2. Age ≥ 18 years;
3. Diagnosis of severe primary axillary hyperhidrosis (e.g., resulting in medical complications such as skin maceration and infection or disruption of professional/social life);
4. Member has tried and failed 6 months of topical aluminum chloride;
7. 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. Prescribed dose of Botox does not exceed 50 units per axilla per treatment session.

Approval duration: 12 weeks (single treatment session)

H. Overactive Bladder and Urinary Incontinence (must meet all)**:**

1. Prescribed by or in consultation with a neurologist or urologist;
2. Age ≥ 18 years;
3. Diagnosis (a or b):
   a. Overactive bladder with symptoms of urge urinary incontinence, urgency and frequency;
   b. Urinary incontinence due to detrusor over activity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis);
4. Member has tried and failed behavioral therapy (e.g., bladder training, pelvic floor muscle training, fluid management) for at least 8 weeks;
5. Member has tried and failed, or is intolerant or contraindicated to, at least 2 anticholinergic or oral beta-3 agonist medications (e.g., oxybutynin chloride, tolterodine tartrate; mirabegron) at the maximum tolerated dose for at least 30 days;
8. 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. Prescribed dose of Botox does not exceed (a or b):
   a. Overactive bladder: 100 units per treatment session;
   b. Urinary incontinence: 200 units per treatment session.

Approval duration: 12 weeks (single treatment session)

I. Esophageal Achalasia – Off Label Use (must meet all)**:**

1. Prescribed by or in consultation with a gastroenterologist;
2. Age ≥ 18 years;
3. Diagnosis of esophageal achalasia (i.e., failure of relaxation of the lower esophageal sphincter accompanied by loss of peristalsis in the distal esophagus);
4. Member is not a good candidate for pneumatic dilation or myotomy;
9. 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. Prescribed dose of Botox does not exceed 100 units.

Approval duration: 24 weeks (single treatment session)

J. Hirschsprung's Disease and Internal Anal Sphincter Achalasia – Off Label Use (must meet all):

10. Prescribed by or in consultation with a gastroenterologist;
11. 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);
12. 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;
13. Prescribed dose of Botox does not exceed 100 units.

Approval duration: 12 weeks (single treatment session)

K. Chronic Anal Fissure – Off Label Use (must meet all)**:**

1. Prescribed by or in consultation with a gastroenterologist or colorectal surgeon;
2. Age ≥ 18 years;
3. Diagnosis of chronic anal fissures;
4. Member has tried and failed, or is intolerant or contraindicated to, at least 2 months of conventional therapy (e.g., high fiber diet and adequate fluids, bulk fiber supplements, stool softeners, warm sitz baths, nitroglycerin 0.2% ointment);
14. 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. Prescribed dose of Botox does not exceed 100 units.

Approval duration: 12 weeks (single treatment session)

L. Other diagnoses/indications:

1. Refer to PA.CP.PHAR.57 - Global Biopharm Policy if requested indication is non-cosmetic.

II. Continued Approval

A. Chronic Migraine (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;

2. Member is responding positively to therapy;
3. If member has received 2 or more Botox treatment sessions, has experienced and maintained a reduction in monthly migraine headache frequency from baseline;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
5. Prescribed dose of Botox does not exceed 155 units per treatment session.

Approval duration: 12 weeks (single treatment session)

B. Esophageal Achalasia (must meet all):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
15. 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;
3. Prescribed dose of Botox does not exceed 100 units per treatment session.

Approval duration: 24 weeks (single treatment session)

C. All Other Indications in Section I (must meet all):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
16. 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;
3. Botox administration has not exceeded 400 units over the last 3 months;
4. Prescribed dose of Botox does not exceed the following indication-specific maximums:
    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: 12 weeks (single treatment session)

D. Other diagnoses/indications (1 or 2):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy; coverage is not approved for cosmetic use, including for treatment of glabellar lines.

Background

Description/Mechanism of Action:
OnabotulinumtoxinA is a purified botulinum toxin type A produced from fermentation of Clostridium botulinum. It blocks neuromuscular transmission by binding to acceptor sites on motor or sympathetic nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. This inhibition occurs as the neurotoxin cleaves SNAP-25, a protein integral to the successful docking and release of acetylcholine from vesicles situated within nerve endings.

Formulations:
Botox: Vacuum-dried powder for reconstitution in single-use vials containing 100 units or 200 units of onabotulinumtoxinA.

Appendices

Appendix A: Abbreivation Key
CD: cervical dystonia
CNS: central nervous system
CP: cerebral palsy
HD: Hirschsprung's disease
IAS: internal anal sphincter
MS: multiple sclerosis
SCI: spinal cord injury

Appendix B: 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 C: Descriptions and Examples of Dystonia Syndromes**

Category	Subcategory	Description and Examples
Isolated dystonias	Early-onset generalized	Dystonia with focal-onset in childhood often progresses to generalized involvement. Cases may be sporadic, familial, genetically defined or without known cause.

Category	Subcategory	Description and Examples
	isolated dystonia	• 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. • 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.*

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	Approval Date
2Q 2018 annual review: 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; removed requirement of at least 12 weeks have passed since last treatment; references reviewed and updated.	2.20.18	

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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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