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Section:	Prescription Drugs	**Effective Date:**	July 1, 2019
Subsection:	Neuromuscular Drugs	**Original Policy Date:**	October 1, 2001
Subject:	Botox	**Page:**	1 of 11

Last Review Date: June 20, 2019

Botox

Description

Botox (onabotulinum toxin A)

Background
Botulinum toxin (abbreviated either as BTX or BoNT) is a protein neurotoxin produced by the bacterium *Clostridium botulinum.* The botulinum toxins are characterized as 7 separate neurotoxins (labeled as types A, B, C [C1, C2], D, E, F, and G), which are antigenically and serologically distinct but structurally similar. The neuromuscular blockade is achieved through prevention of docking/fusion of neurosecretory with the nerve synapse plasma membrane and release of neurotransmitters (1).

The various botulinum toxins have approved cosmetic and non-aesthetic uses. They possess individual potencies, and care is required to assure proper use and avoid medication errors. Recent changes to the established drug names by the FDA were intended to reinforce these differences and prevent medication errors (1-2).

Regulatory Status
FDA-approved indications: Botox is an acetylcholine release inhibitor and a neuromuscular blocking agent indicated for: (3)

1. 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
2. Treatment of urinary incontinence due to detrusor over-activity 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.

3. Prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer).
4. Treatment of upper or lower limb spasticity in adult patients.
5. Treatment of upper limb spasticity in pediatric patients 2 to 17 years of age.
6. Treatment of cervical dystonia in adult patients, to reduce the severity of abnormal head position and neck pain.
7. Treatment of severe axillary hyperhidrosis that is inadequately managed by topical agents in adult patients.
8. Treatment of blepharospasm associated with dystonia in patients ≥12 years of age.
9. Treatment of strabismus in patients ≥12 years of age.

Limitations of Use:
Safety and effectiveness of Botox have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) (3).

Off-Label Uses: (4-11)
1. Achalasia
2. Chronic anal fissures
3. Essential tremor
4. Excessive salivation secondary to advanced Parkinson's disease
5. Hemifacial spasm
6. Spasmodic dysphonia (laryngeal dystonia)

Safety and effectiveness of Botox have not been established for the treatment of hyperhidrosis in body areas other than axillary (4).

Botulinum toxins are not interchangeable. Total accumulated dose should not exceed 400 IU over a 3 month interval (3).

Some products have cosmetic indications which are excluded from coverage.

Related policies
Dysport, Myobloc, Xeomin

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Botox may be considered **medically necessary** for treatment of the conditions indicated below.

Botox may be considered **investigational** for all other indications.

Prior – Approval Requirements

Age No age restriction

Diagnosis

Patient must have the following:

1. Upper and/or lower limb spasticity
2. Spastic hemiplegia

AND the following:

a. **NO** dual therapy with other botulinum toxins

Age 12 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Blepharospasm associated with dystonia
2. Strabismus

AND the following:

b. **NO** dual therapy with other botulinum toxins

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

A. Spasticity disorders

1. Hereditary spastic paraplegia
2. Hemifacial spasms
3. Spasmodic torticollis (clonic twisting of the head)
4. Facial Nerve (VII) disorders
5. Neuromyelitis optica

B. Movement disorders

1. Dystonia
    a. Cervical
    b. Writer's cramp
    c. Focal task specific
    d. Laryngeal (spasmodic dysphonia)
2. Essential Tremor
3. Orofacial dyskinesia

C. GI/ Sphincter disorders

1. Achalasia
2. Chronic anal fissures
3. Dysphagia
4. Sphincter of Oddi dysfunction
5. Excessive Salivation
    a. Due to Parkinson's disease

D. Bladder

1. Overactive bladder (OAB)
    a. Inadequate response or intolerance to an anticholinergic
2. Incontinence associated with a neurologic condition (spinal cord injury, multiple sclerosis, etc)
    a. Inadequate response or intolerance to an anticholinergic

E. Other Indications

1. Hyperhidrosis
2. Prophylaxis of chronic migraine headaches
    a. Patient is experiencing ≥15 days per month with headache lasting 4 hours a day or longer

b. Patient has completed an adequate trial (≥ 8 weeks) of at least **ONE** of the following
   i. Divalproex Sodium (Depakote, Depakote ER)
   ii. Topiramate (Topamax)
   iii. Gabapentin (Neurontin)
   iv. Amitriptyline (Elavil)
   v. Venlafaxine (Effexor)
   vi. Beta-Blockers: Atenolol/Metoprolol/Propranolol/Timolol/Nadolol
   vii. Nimodipine/Verapamil
   viii. Naproxen/other NSAID
   ix. Other oral migraine prophylactic therapy considered to be appropriate by the requesting physician

c. **NO** dual therapy with a calcitonin gene-related peptide (CGRP) antagonist

AND the following:

1. **NO** dual therapy with other botulinum toxins

Prior – Approval *Renewal* Requirements

Age No age restriction

Diagnosis

Patient must have the following:

1. Upper and/or lower limb spasticity
2. Spastic hemiplegia

AND the following:

c. **NO** dual therapy with other botulinum toxins

Age 12 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Blepharospasm associated with dystonia
2. Strabismus

AND the following:

d. **NO** dual therapy with other botulinum toxins

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

A. Spasticity disorders

1. Hereditary spastic paraplegia
2. Hemifacial spasms
3. Spasmodic torticollis (clonic twisting of the head)
4. Facial Nerve (VII) disorders
5. Neuromyelitis optica

B. Movement disorders

1. Dystonia
   a. Cervical
   b. Writer's cramp
   c. Focal task specific
   d. Laryngeal (spasmodic dysphonia)
2. Essential Tremor
3. Orofacial dyskinesia

C. GI/ Sphincter disorders

1. Achalasia
2. Chronic anal fissures
3. Dysphagia
4. Sphincter of Oddi dysfunction
5. Excessive Salivation
   a. Due to Parkinson's disease

D. Bladder

1. Overactive bladder (OAB)
2. Incontinence associated with a neurologic condition (spinal cord injury, multiple sclerosis, etc)

E. Other Indications

1. Hyperhidrosis
2. Prophylaxis of chronic migraine headaches
    a. Response to therapy has shown a 50% reduction in monthly migraine frequency since starting therapy with Botox
    b. **NO** dual therapy with a calcitonin gene-related peptide (CGRP) antagonist

AND the following:

e. **NO** dual therapy with other botulinum toxins

Policy Guidelines

Pre – PA Allowance

None

Prior – Approval Limits

Quantity	**100 IU vial**	4 vials per 90 days **OR**
	200 IU vial	2 vials per 90 days **OR**
	Any combination that does not exceed 400 IU per 90 days	
Duration	12 months	

Prior – Approval *Renewal* Limits

Quantity	**100 IU vial**	4 vials per 90 days **OR**
	200 IU vial	2 vials per 90 days **OR**
	Any combination that does not exceed 400 IU per 90 days	
Duration	12 months	

Rationale

Summary

Botulinum toxin (abbreviated either as BTX or BoNT) is a protein neurotoxin produced by the bacterium *Clostridium botulinum.* The botulinum toxins are characterized as 7 separate neurotoxins (labeled as types A, B, C [C1, C2], D, E, F, and G), which are antigenically and serologically distinct but structurally similar (3).

The various botulinum toxins have approved cosmetic and non-aesthetic uses. They possess individual potencies, and care is required to assure proper use and avoid medication errors. Recent changes to the established drug names by the FDA were intended to reinforce these differences and prevent medication errors (1-2).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Botox while maintaining optimal therapeutic outcomes.

References

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Policy History

Date	Action
July 2010	Updated ICD-9 codes, addition of ICD-10 codes, separation of criteria for Botox and Myobloc, and addition of the recently FDA approved diagnosis of spasticity in flexor muscles of the elbow, wrist and fingers for Botox. BOTOX (onabotulinumtoxinA) for injection is indicated for the treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris) and finger flexors (flexor digitorum profundus and flexor digitorum sublimis). The efficacy and safety of BOTOX for the treatment of upper limb spasticity were evaluated in three randomized, multi-center, double-blind, placebo-controlled studies. Safety and effectiveness of BOTOX have not been established for the treatment of upper limb spasticity in pediatric patients, and for the treatment of lower limb spasticity in adult and pediatric patients.
October 2010	Updated criteria to mirror newly approved FDA indication for chronic migraine in adults.
September 2011	Updated criteria to mirror newly approved FDA indication for urinary incontinence in people with neurologic conditions such as spinal cord injury and multiple sclerosis who have overactivity of the bladder. Removal of ICD 9 and 10 codes due to lack of specificity. Additional compendial indications for botulinum toxin type A including spasticity (upper and lower limbs) due to multiple causes (i.e. cerebral palsy, stroke, multiple sclerosis and post-traumatic brain and spinal cord injury) in both adults and children, treatment of achalasia in patients who are considered poor candidates for

endoscopic dilation or surgery, chronic anal fissure, sphincter of Oddi dysfunction, dysphagia and hyperhidrosis.

December 2012	Annual Review-no change in policy statement. Reference and editorial updates
April 2013	FDA approval of overactive bladder in adults
September 2014	Annual editorial review and reference update
September 2015	Annual editorial review and reference update
January 2016	Addition of new indication of lower limb spasticity Policy number change from 5.12.01 to 5.75.01
March 2016	Annual review
May 2016	Addition of quantity limits 100 IU vial 4 vials per 90 days or 200 IU vial 2 vials per 90 days or any combination that does not exceed 400 IU per 90 days
June 2016	Annual review
December 2016	Annual editorial review Addition of essential tremor and excessive salivation due to Parkinson's disease to criteria. Additional initiation criteria added to prophylaxis of chronic migraine. Continuation criteria updated for prophylaxis of chronic migraine to quantify reduction of migraine headaches.
September 2017	Annual review and reference update
April 2018	Addition of references for off-label uses and reorganization of the indications
June 2018	Annual review
August 2018	Addition of no dual therapy with a calcitonin gene-related peptide (CGRP) antagonist for migraine prophylaxis
November 2018	Annual review and reference update
May 2019	Removed regulatory status statement regarding upper and lower limb spasticity not being studied in pediatric patients
June 2019	Annual review. Changed spastic hemiplegia indication to have no age limit

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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.