BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
750 9th St NW
Washington, D.C. 20001
202.942.1000
Fax 202.942.1125

5.75.001

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Neuromuscular Drugs	**Original Policy Date:**	October 1, 2001
Subject:	Botox	**Page:**	1 of 11

Last Review Date: March 8, 2024

Botox

Description

Botox (onabotulinumtoxinA)

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. Treatment of neurogenic detrusor overactivity (NDO) in pediatric patients 5 years of age and older who have an inadequate response to or are intolerant of anticholinergic medication.
4. Prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer).
5. Treatment of spasticity in patients 2 years of age and older.
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) or for the treatment of hyperhidrosis in body areas other than axillary (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

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Neuromuscular Drugs	**Original Policy Date:**	October 1, 2001
Subject:	Botox	**Page:**	3 of 11

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** if the conditions indicated below are met.

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

Prior – Approval Requirements

Age No age restriction

Diagnoses

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

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

AND the following:

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

Age 5 – 17 years of age

Diagnosis

Patient must have the following:

1. Neurogenic detrusor overactivity (NDO)
    a. Inadequate response or intolerance to an anticholinergic

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:

a. **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-blocker: atenolol, metoprolol, propranolol, timolol, nadolol
        vii. Nimodipine or verapamil
        viii. Naproxen or other NSAID
        ix. Other oral or injectable migraine prophylactic therapy considered to be appropriate by the requesting physician

AND the following for **ALL** indications:

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

Prior – Approval *Renewal* Requirements

Age No age restriction

Diagnoses

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

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

AND the following:

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

Age 5 – 17 years of age

Diagnosis

Patient must have the following:

1. Neurogenic detrusor overactivity (NDO)

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:

a. **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

AND the following for **ALL** indications:

a. **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

Same as above

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 (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).

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

References

1. Blasi J, Chapman ER, Link E, et al. Botulinum neurotoxin A selectively cleaves the synaptic protein SNAP-25. Nature. Sep 9 1993;365(6442):160-3.
2. Brin MF. Botulinum toxin: chemistry, pharmacology, toxicity, and immunology. Muscle Nerve Suppl. 1997;6:S146-68.
3. Botox [package insert]. Irvine, CA: Allergan Inc.; November 2023.
4. Reisfeld R, Berliner KI. Evidence-based review of the nonsurgical management of hyperhidrosis. *Thorac Surg Clin*. 2008;18: 157-166.
5. Pasricha, P. J., Ravich, W. J., Hendrix, T. R., Sostre, S., Jones, B., & Kalloo, A. N. Intrasphincteric botulinum toxin for the treatment of achalasia. New England Journal of Medicine, 1995. 332(12), 774-778.

6. Menteş, B. B., Irkörücü, O., Akın, M., Leventoğlu, S., & Tatlıcıoğlu, E. Comparison of botulinum toxin injection and lateral internal sphincterotomy for the treatment of chronic anal fissure. *Diseases of the colon & rectum*, 2003. 46(2), 232-237.
7. Ahsan, S. F., Meleca, R. J., & Dworkin James, P. Botulinum toxin injection of the cricopharyngeus muscle for the treatment of dysphagia. *Otolaryngology—Head and Neck Surgery*, 2000. *122*(5), 691-695.
8. Lagalla, G., Millevolte, M., Capecci, M., Provinciali, L., & Ceravolo, M. G. Botulinum toxin type A for drooling in Parkinson's disease: a double-blind, randomized, placebo-controlled study. *Movement Disorders*, 2006.*21*(5), 704-707.
9. Sorgun, M. H., Yilmaz, R., Akin, Y. A., Mercan, F. N., & Akbostanci, M. C. Botulinum toxin injections for the treatment of hemifacial spasm over 16 years. *Journal of Clinical Neuroscience*, 2015. *22*(8), 1319-1325.
10. Slotema, C. W., van Harten, P. N., Bruggeman, R., & Hoek, H. W. Botulinum toxin in the treatment of orofacial tardive dyskinesia: a single blind study. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 2008. *32*(2), 507-509.
11. Wehrmann, T., Seifert, H., Seipp, M., Lembcke, B., & Caspary, W. F. Endoscopic injection of botulinum toxin for biliary sphincter of Oddi dysfunction. *Endoscopy*, 1998. *30*(08), 702-707.

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 recent 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

September 2020	Annual editorial review and reference update
March 2021	Annual review. Addition of indication: neurogenic detrusor overactivity (NDO) in pediatric patients 5 years of age and older
March 2022	Annual review and reference update. Per SME, removed requirement “no dual therapy with a CGRP antagonist for migraine prevention”
September 2022	Added “for all indications” to no dual therapy requirement and changed the indentation so requirement did not appear nested under a single diagnosis for clarity
December 2022	Annual review
March 2023	Annual review and reference update
December 2023	Annual review. Per SME, added option for migraine patients to try an injectable migraine prophylactic therapy considered to be appropriate by the requesting physician
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.