# POLICY Document for BOTOX (onabotulinumtoxin A)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

**Section 1: Preferred Product**
- Policy information specific to preferred medications

**Section 2: Clinical Criteria**
- Policy information specific to the clinical appropriateness for the medication

## Section 1: Preferred Product

### CAREFIRST: EXCEPTIONS CRITERIA
### BOTULINUM TOXINS

### PREFERRED PRODUCTS: DYSPORT, XEOMIN

**Client Requested:** The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

**POLICY**
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

**I. PLAN DESIGN SUMMARY**

This program applies to the botulinum toxins products specified in this policy. Coverage for targeted product is provided based on clinical circumstances that would exclude the use of the preferred products. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

**Table. Botulinum Toxins**

| | Product(s) |
|---|---|
| **Preferred*** | • **Dysport** (abobotulinumtoxinA)<br>• **Xeomin** (incobotulinumtoxinA) |
| **Targeted** | • **Botox** (onabotulinumtoxinA)<br>• **Myobloc** (rimabotulinumtoxinB)<br>• **Daxxify** (daxibotulinumtoxinA) |

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

**II. EXCEPTION CRITERIA**

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for Botox is provided when ANY of the following criteria is met:
A. Request is not for spasticity or cervical dystonia in adult patients, or blepharospasm
B. Member has a documented inadequate response, contraindication, or intolerable adverse event to all preferred products.

Coverage for Myobloc is provided when ANY of the following criteria is met:
A. Member has a documented inadequate response, contraindication, or intolerable adverse event to Xeomin for chronic sialorrhea in patients ≥ 12 years of age
B. Member has a documented inadequate response, contraindication, or intolerable adverse event to Dysport and Xeomin for cervical dystonia in adult patients.

Coverage for Daxxify is provided when ANY of the following criteria is met:
A. Member has a documented inadequate response, contraindication, or intolerable adverse event to Dysport and Xeomin for cervical dystonia in adult patients.

# Section 2: Clinical Criteria

## SPECIALTY GUIDELINE MANAGEMENT

### BOTOX (onabotulinumtoxin A)

**POLICY**

**I. INDICATIONS**

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Treatment of overactive bladder 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 overactivity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) in adults or pediatric patients 5 years of age or older 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 spasticity in patients 2 years of age and older
5. Treatment of cervical dystonia in adults, to reduce the severity of abnormal head position and neck pain
6. Treatment of severe primary axillary hyperhidrosis that is inadequately managed with topical agents. Safety and effectiveness have not been established in patients under age 18.
7. Treatment of strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and older

B. Compendial Uses
1. Achalasia
2. Chronic anal fissures
3. Essential tremor
4. Excessive salivation (ptyalism)

5. Hemifacial spasm
6. Spasmodic dysphonia (laryngeal dystonia)
7. Oromandibular dystonia
8. Myofascial pain syndrome
9. Focal hand dystonia
10. Facial myokymia
11. Hirschsprung disease with internal sphincter achalasia
12. Orofacial tardive dyskinesia
13. Painful bruxism
14. Palatal myoclonus
15. First bite syndrome
16. Palmar or gustatory (Frey's syndrome) hyperhidrosis

All other indications are considered experimental/investigational and not medically necessary.

## II. PRESCRIBER SPECIALTIES

The medication must be prescribed by, or in consultation with one of the following:

A. Blepharospasm, Strabismus: neurologist or ophthalmologist
B. Overactive bladder, urinary incontinence: neurologist, urologist or gynecologist
C. Spasticity, cervical dystonia, hemifacial spasm, myofascial pain syndrome, focal hand dystonia, facial myokymia: neurologist, orthopedist, otolaryngologist or physiatrist
D. Hyperhidrosis: neurologist, internist or dermatologist
E. Migraine prophylaxis, tremor, orofacial tardive dyskinesia: neurologist, pain specialist or physiatrist
F. Chronic anal fissures, achalasia, Hirschsprung disease: gastroenterologist, proctologist or colorectal surgeon
G. Excessive salivation, spasmodic dystonia, oromandibular dystonia, bruxism, palatal myoclonus: neurologist or otolaryngologist
H. First bite syndrome: neurologist or oncologist

## III. EXCLUSIONS

Coverage will not be provided for cosmetic use.

## IV. CRITERIA FOR INITIAL APPROVAL

### A. Blepharospasm

Authorization of 12 months may be granted for treatment of blepharospasm when all of the following are met:

1. Member is 12 years of age or older
2. Member is diagnosed with blepharospasm including blepharospasm associated with dystonia, benign essential blepharospasm or VII nerve disorder.

### B. Cervical dystonia

Authorization of 12 months may be granted for the treatment of adults with cervical dystonia (e.g., torticollis) when all of the following are met:

1. There is abnormal placement of the head with limited range of motion in the neck
2. Member is 18 years of age or older.

### C. Chronic migraine prophylaxis

Authorization of 6 months (two injection cycles) may be granted for treatment of chronic migraine prophylaxis when all of the following criteria are met:

1. Member experiences headaches 15 days or more per month.
2. Member experiences headaches lasting 4 hours or longer on at least 8 days per month.

3. Member completed an adequate trial of (or has a contraindication to) two oral migraine preventative therapies coming from at least 2 of the following classes with a trial of each medication at least 60 days in duration:
   a. Antidepressants (e.g., amitriptyline, venlafaxine)
   b. Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium)
   c. Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol)
4. Member has signs and symptoms consistent with chronic migraine diagnostic criteria as defined by the International Headache Society (IHS).
5. Member is 18 years of age or older

**D. Overactive bladder with urinary incontinence**

Authorization of 12 months may be granted for treatment of overactive bladder with urinary incontinence, urgency, and frequency when all of the following criteria are met:

1. The member has tried and failed behavioral therapy.
2. The member has had an inadequate response or experienced intolerance to two agents from either of the following classes:
   a. Anticholinergic medication (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trospium], Ditropan XL [oxybutynin]).
   b. Beta-3 adrenergic agonist (e.g., Myrbetriq [miraberon], Gemtesa [vibegron]).
3. Member is 18 years of age or older.

**E. Primary axillary, palmar, and gustatory (Frey's syndrome) hyperhidrosis**

Authorization of 12 months may be granted for treatment of primary axillary, palmar, or gustatory (Frey's syndrome) hyperhidrosis when all of the following criteria are met:

1. Significant disruption of professional and/or social life has occurred because of excessive sweating; and
2. Topical aluminum chloride or other extra-strength antiperspirants are ineffective or result in a severe rash.
3. Member is 18 years of age or older.

**F. Strabismus**

Authorization of 12 months may be granted for treatment of strabismus when all of the following are met:

1. Strabismus interference with normal visual system development is likely to occur and spontaneous recovery is unlikely.
2. Member is 12 years of age or older.

Note: Strabismus repair is considered cosmetic in adults with uncorrected congenital strabismus and no binocular fusion.

**G. Upper or lower limb spasticity**

Authorization of 12 months may be granted for treatment of upper or lower limb spasticity when all of the following are met:

1. Member is 2 years of age or older
2. Member has a primary diagnosis of upper or lower limb spasticity or as a symptom of a condition causing limb spasticity (including focal spasticity or equinus gait due to cerebral palsy).

**H. Urinary incontinence associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis)**

Authorization of 12 months may be granted for treatment of urinary incontinence associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) when all of the following criteria are met:

1. The member has tried and failed behavioral therapy
2. The member has had an inadequate response or experienced intolerance to one agent from either of the following classes:
   a. Anticholinergic medication (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trospium], Ditropan XL [oxybutynin]).
   b. Beta-3 adrenergic agonist (e.g., Myrbetriq [miraberon]
3. Member is 5 years of age or older.

**I. Achalasia**
Authorization of 12 months may be granted for treatment of achalasia when the member has tried and failed or is a poor candidate for conventional therapy such as pneumatic dilation and surgical myotomy.

**J. Chronic anal fissures**
Authorization of 12 months may be granted for treatment of chronic anal fissures when the member has not responded to first line therapy such as topical calcium channel blockers or topical nitrates.

**K. Essential tremor**
Authorization of 12 months may be granted for treatment of essential tremor.

**L. Excessive salivation**
Authorization of 12 months may be granted for treatment of excessive salivation (chronic sialorrhea or ptyalism) when the member has been refractory to pharmacotherapy (e.g., anticholinergics).

**M. Hemifacial Spasm**
Authorization of 12 months may be granted for treatment of hemifacial spasm.

**N. Spasmodic dysphonia (laryngeal dystonia)**
Authorization of 12 months may be granted for treatment of spasmodic dysphonia (laryngeal dystonia).

**O. Oromandibular dystonia**
Authorization of 12 months may be granted for treatment of oromandibular dystonia.

**P. Myofascial Pain Syndrome**
Authorization of 12 months may be granted for treatment of myofascial pain syndrome when the member has tried and failed all of the following:
1. Physical therapy
2. Injection of local anesthetics into trigger points
3. Injection of corticosteroids into trigger points

**Q. Focal hand dystonia**
Authorization of 12 months may be granted for the treatment of focal hand dystonias.

**R. Facial myokymia**
Authorization of 12 months may be granted for the treatment of facial myokymia.

**S. Hirschsprung disease with internal sphincter achalasia**
Authorization of 12 months may be granted for the treatment of Hirschsprung's disease with internal sphincter achalasia following endorectal pull through and the member is refractory to laxative therapy.

**T. Orofacial tardive dyskinesia**
Authorization of 12 months may be granted for the treatment of orofacial tardive dyskinesia when conventional therapies have been tried and failed (e.g., benzodiazepines, clozapine, or tetrabenazine).

**U. Painful bruxism**
Authorization of 12 months may be granted for the treatment of painful bruxism when the member has had an inadequate response to a night guard and has had an inadequate response to pharmacologic therapy such as diazepam.

**V. Palatal myoclonus**
Authorization of 12 months may be granted for the treatment of palatal myoclonus when the member has disabling symptoms (e.g., intrusive clicking tinnitus) who had an inadequate response to clonazepam, lamotrigine, carbamazepine or valproate.

**W. First bite syndrome**

Authorization of 12 months may be granted for the treatment of first bite syndrome when the member has failed relief from analgesics, antidepressants or anticonvulsants.

## V. CONTINUATION OF THERAPY

**A.** All members (including new members) requesting authorization for continuation of therapy for approvable conditions other than migraine prophylaxis must meet ALL initial authorization criteria and be experiencing benefit from therapy.

**B.** Authorization of 12 months may be granted for treatment of chronic migraine prophylaxis when the member has achieved or maintained a reduction in monthly headache frequency since starting therapy with Botox.

## VI. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines**.**

Adults: Dosing should not exceed a cumulative dose of 400 units every 84 days
Pediatric (patients less than 18 years of age): Dosing should not exceed the lessor of 10 units/kg or 340 units every 84 days.

## REFERENCES:

### SECTION 1


1. Botox [package insert]. Irvine, CA: Allergan, Inc.; August 2023.
2. Daxxify [package insert]. Newark, CA: Revance Therapeutics, Inc; August 2023.
3. Dysport [package insert]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; September 2023.
4. Myobloc [package insert]. South San Francisco, CA: Solstice Neurosciences, Inc.; March 2021.
5. Xeomin [package insert]. Frankfurt, Germany: Merz Pharmaceuticals GmbH; September 2023.


### SECTION 2


1. Botox [package insert]. Madison, NJ: Allergan USA, Inc; August 2023.
2. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at http://www.micromedexsolutions.com. Accessed August 1, 2023.
3. AHFS Drug Information. http://online.lexi.com/lco. Accessed August 1, 2023.
4. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology*. 2012;78(17):1337-45.
5. Snow V, Weiss K, Wall EM, et al. Pharmacologic management of acute attacks of migraine and prevention of migraine headache. *Ann Intern Med.* 2002;137(10):840-849.
6. Evers S, Afra J, Frese A, et al. EFNS guideline on the drug treatment of migraine--revised report of an EFNS task force. *Eur J Neurol*. 2009;16(9):968-981.
7. Pringsheim T, Davenport W, Mackie G, et al. Canadian Headache Society guideline for migraine prophylaxis. Can J Neurol Sci. 2012;39(2 Suppl 2):S1-59.
8. Zesiewics TA, Elble RJ, Louis ED et al. Evidence-based guideline update: Treatment of essential tremor: Report of the Quality Standards Subcommittee of the American Academy of Neurology: *Neurology* 2011; 77: 1752-1755.
9. Restivo D, Panebianco M, Casabona A et al. Botulinum Toxin A for Sialorrhea Associated with Neurological Disorders: Evaluation of the Relationship between Effect of Treatment and the Number of Glands Treated. *Toxins* 2018;55:1-10.

10. Lakraj AA, Moghimi N, Jabbari B. Sialorrhea: Anatomy, Pathophysiology and Treatment with Emphasis on the Role of Botulinum Toxins. *Toxins* 2013, 5, 1010-1031
11. Zoons E, Dijkgraaf M, Dijk J et al. Botulinum toxin as treatment for focal dystonia: a systematic review of the pharmaco-therapeutic and pharmaco-economic value. *J Neurol* 2012;259: 2519-2526.
12. Conrin L, Karp BI, Alter K et al. Long Term Follow-up Botulinum Toxin Therapy for Focal Hand Dystonia: Outcome at 10 or More Years: Mov Disord. 2011 Mar; 26(4): 750–753.
13. Daele D, Finnegan E, Rodnitzky R et al. Head and Neck Muscle Spasm After Radiotherapy. *Otolaryngol Head and Neck Surg* 2002;128:956-959.
14. Han-Guerts I, Hendrix V, Blaauw I et al. Outcome after Anal Intrasphincteric Botox Injection in Children with Surgically Treated Hirschsprung Disease. *JPGN* 2014; 59: 604-607.
15. Asutay F, Atalay Y, Asutay H, Huseyin Acar A. The Evaluation of the clinical effects of Botulinum Toxin on Nocturnal Bruxism. *Pain Research and Management* 2017;1-5.
16. Gosain A, Frykman PK, Cowles RA, et al. Guidelines for the diagnosis and management of Hirschsprung-associated enterocolitis. Pediatr Surg Int. 2017; 33(5):517–521.
17. Thuruthiath N, Arayamparambil R. Essential palatal myoclonus: A rare cause of objective tinnitus. *J Adv Med Heath Res* 2016;3:1-3.
18. Laccourreye O, Werner A, Garcia D, Malinvaud D, Tran Ba Huy P, Bonfils P. First bite syndrome. *Euro Ann Otolaryngol Head Neck Diseases.* 2013; 130:269-273.
19. Linkov G et al. First bite syndrome: incidence, risk factors, treatment, and outcomes. The Laryngoscope. 2012; 122: 1773-1778.
20. Slotema CW;van Harten PN;Bruggeman R;Hoek HW. Botulinum toxin in the treatment of orofacial tardive dyskinesia: a single blind study. *Prog Neuropsychopharmacol Biol Psychiatry* 2008;32(2):507-509.
21. Odderson IR. Hyperhidrosis treated by botulinum A exotoxin. Dermatol Surg. 1998;24(11):1237-1241.
22. Solomon BA, Hayman R. Botulinum toxin type A therapy for palmar and digital hyperhidrosis. J Am Acad Dermatol. 2000;42(6):1026-1029.
23. Naver H, Swartling C, Aquilonius SM. Palmar and axillary hyperhidrosis treated with botulinum toxin: One-year clinical follow-up. Eur J Neurol. 2000;7(1):55-62.
24. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders: 3rd edition. Cephalalgia. 2018;Vol. 38(1) 1–211.
25. Glader L, Delsing C, Hughes A et al. Sialorrhea in cerebral palsy. American Academy for Cerebral Palsy and Developmental Medicine Care Pathways. https://www.aacpdm.org/publications/care-pathways/sialorrhea. Accessed August 3, 2021.
26. Garuti G, Rao F, Ribuffo V et al. Sialorrhea in patients with ALS: current treatment options. *Degener Neurol Neuromuscul Dis*. 2019; 9: 19–26.
27. Digre KB for the American Headache Society. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache 2019;59:1-18. doi: 10.1111/head.13456.
28. Lightner DJ, Gomelsky A, Souter L, Vasavada SP. Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline Amendment 2019. J Urol 2019; 202:558.
29. Smith C, Pariser D. Primary Focal Hyperhidrosis. Waltham, MA. UpToDate. Last Modified January 2, 2020. https://www.uptodate.com/contents/primary-focal-hyperhidrosis. Accessed August 1, 2023