PRIOR AUTHORIZATION POLICY

POLICY: Botulinum Toxins – Botox Prior Authorization Policy
- Botox® (onabotulinumtoxinA injection – Allergan)

REVIEW DATE: 01/11/2023

OVERVIEW

Botox, a botulinum toxin, is indicated for the following uses:[1]

- **Blepharospasm** associated with dystonia, including benign essential blepharospasm or seventh nerve disorders, and strabismus in patients ≥ 12 years of age.
- **Cervical dystonia,** in adults to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.
- **Hyperhidrosis, severe primary axillary**, which is inadequately managed with topical agents.
- **Migraine headache prophylaxis (prevention),** in adults with chronic migraine (≥ 15 days per month with headache lasting 4 hours per day or longer).
- **Overactive bladder** with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have inadequate response to or are intolerant of an anticholinergic medication.
- **Spasticity** in patients ≥ 2 years of age.
- **Urinary incontinence due to detrusor overactivity** associated with a neurological condition (e.g., spinal cord injury, multiple sclerosis) in adults who have an inadequate response to or are intolerant of an anticholinergic medication.
- **Neurogenic detrusor overactivity** in pediatric patients ≥ 5 years of age who have had an inadequate response to or are intolerant of an anticholinergic medication.

In addition, botulinum toxin type A has been used to treat a multitude of disorders characterized by abnormal muscle contraction.[2] The benefit of this drug has also been demonstrated in the treatment of gastrointestinal, genitourinary, ocular, and autonomic nervous system disorders.[2,3] Of note, with regard to the indication of migraine headache prophylaxis, an updated assessment of the preventive and acute treatment of migraine by the American Headache Society (2018) notes that several medications are cited as having established or probable efficacy in migraine prevention, including antiepileptic medications, beta-blockers, antidepressants, and Botox.

Other Uses with Supportive Evidence

Botox has been studied in a variety of indications outside of FDA-approved uses. Literature is available to support use of Botox in the following conditions:

- **Achalasia:** The American College of Gastroenterology (ACG) clinical guideline for the diagnosis and management of achalasia (2020) recommends the use of botulinum toxin therapy as first-line therapy for patients with achalasia who are unfit for definitive therapies.[5]
- **Anal Fissures:** The ACG clinical guideline for the management of benign anorectal disorders (2021) suggests that botulinum toxin A injections may be attempted for patients in whom calcium channel blockers fail or as an alternative option to calcium channel blockers (conditional recommendation; quality of evidence low).[6]
- **Chronic Facial Pain/Pain Associated with Temporomandibular Dysfunction:** Data from several open-label studies, as well as one randomized, placebo-controlled trial, support the efficacy of Botox in the treatment of chronic facial pain/chronic facial pain associated with hyperactivity of the masticatory muscles.[7-10]

- **Chronic Low Back Pain:** In one 8-week, randomized, double-blind, placebo-controlled trial in 31 patients with chronic low back pain (no causative factor identified in the majority of patients; of disc disease in 6 patients, discectomy in 3 patients, and trauma in 4 patients), Botox in addition to their current pharmacologic treatment regimen resulted in significantly greater improvement in pain relief and degree of disability compared with placebo.[11] A 14-month, open-label, prospective study evaluated the short- and long-term effects of paraspinal muscle injections of Botox in 75 patients with refractory chronic low back pain. A total of 53% and 52% of patients reported significant pain relief at 3 weeks and 2 months, respectively.[12]
- **Dystonia, other than Cervical:** Guidelines from the American Academy of Neurology (AAN) support use of botulinum toxins in focal dystonias of the upper extremity (should be considered; Level B recommendation).[13] Botulinum toxin A is the most widely accepted treatment for spasmodic dysphonia, a focal laryngeal dystonia, viewed as the treatment of choice by the American Academy of Otolaryngology-Head and Neck Surgery.[14] Per the guideline, clinicians should offer, or refer to a clinician who can offer, botulinum toxin injections for treatment of dysphonia caused by spasmodic dysphonia and other types of laryngeal dystonia. AAN guidelines note that botulinum toxin is probably effective and should be considered for adductor type laryngeal dystonia (Level B).[13]
- **Essential Tremor:** According to the clinical practice parameter on essential tremor by the AAN, propranolol and primidone are first-line therapy in the treatment of essential tremor.[15] Second-line medication options include alprazolam, atenolol, sotalol, gabapentin, and topiramate. Botulinum toxin A may also reduce tremor. The guidelines recommend that botulinum toxin A may be considered in medically refractory cases of limb, head, and voice tremor associated with essential tremor (Level C for limb, head, and voice tremor).
- **Hemifacial Spasm:** Per the AAN, botulinum toxin (formulation not specified) may be considered in hemifacial spasm (Level C).[13] Data with Botox and Dysport® (abobotulinumtoxin A injection) are cited in the recommendations regarding hemifacial spasm.
- **Hyperhidrosis, Gustatory:** AAN guidelines state that botulinum toxin may be considered for this use (Level C). Botox is recommended as a first-line option for gustatory sweating by the International Hyperhidrosis Society.[16,17]
- **Hyperhidrosis, Palmar/Plantar and Facial:** The efficacy of Botox is well-established in the treatment of primary focal/palmar hyperhidrosis based on data from both randomized, double-blind, placebo-controlled studies and open-label studies.[3,18,19] Guidelines from the International Hyperhidrosis Society support use of Botox in patients who have failed to respond to topical therapy.[16,20,21] AAN guidelines state that botulinum toxins are probably safe and effective and should be considered for palmar hyperhidrosis (plantar and facial hyperhidrosis are not addressed in the AAN guideline).[17]
- **Myofascial Pain:** Data from several retrospective reviews and open-label trials support the efficacy of Botox in the treatment of myofascial pain syndromes associated with various muscle groups.[7,22] In one randomized, controlled trial in 40 patients with chronic myofascial pain of various forms, Botox resulted in a significantly greater reduction in pain score from baseline compared with intramuscularly administered methylprednisolone at 30 days and 60 days post injection.[23] Another double-blind, randomized, placebo-controlled study involving 30 patients showed no difference in spontaneous and evoked pain reduction between Botox and isotonic saline.[24]
- **Ophthalmic Disorders, other than Blepharospasm or Strabismus:** Botulinum toxin A has been successful in improving or treating many ophthalmic disorders. One retrospective review (n = 54) concluded that Botox may have a role in the treatment of esotropia in patients > 18 months of age.[25] Botox improved visual acuity in case reports and one small, open-label study in patients with acquired symptomatic nystagmus from multiple sclerosis or brain-stem hemorrhage.[26,27] Data from uncontrolled studies have shown Botox to be beneficial in the treatment of sixth nerve palsy.[28,29]

- **Plantar Fasciitis:** In one randomized, double-blind study (n = 36), botulinum toxin A exhibited more rapid and sustained improvement over the duration of the study as compared with patients who received steroid injections.[30] The clinical consensus statement on the diagnosis and treatment of heel pain (developed by the American College of Foot and Ankle Surgeons) published in 2010 list botulinum toxin injection as a Tier 2 option (Grade I); Tier 1 treatment options include: padding and strapping of the foot (Grade B), therapeutic orthotic insoles (Grade B), oral anti-inflammatory agents (Grade I), corticosteroid injections (Grade B), and Achilles and plantar fascia stretching (Grade B) [Grade B recommendations are supported by fair evidence, Grade I recommendations indicate there is insufficient evidence to make a recommendation].[31]
- **Sialorrhea, Chronic:** Botulinum toxin A has been studied in the treatment of sialorrhea associated with Parkinson's Disease, parkinsonian syndromes, cerebral palsy, head and neck carcinoma, neurodegenerative disease, stroke, and amyotrophic lateral sclerosis.[3] A review of the literature on medical treatment of sialorrhea found that Botox is probably effective for the treatment of this condition (level B evidence).[32] AAN guidelines note that botulinum toxin is probably safe and effective and should be considered (Level B).[17]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Botox. All approvals are provided for the duration noted below. Previous therapy is required to be verified by a clinician in the Coverage Review Department when noted in the criteria as **[verification of therapies required]**.

Prior Authorization and prescription benefit coverage are not recommended for Botox Cosmetic.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Botox is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Blepharospasm Associated with Dystonia or Strabismus**. Approve for 1 year.

2. **Cervical Dystonia.** Approve for 1 year.
   Note: Cervical dystonia is also known as spasmodic or cervical torticollis.

3. **Hyperhidrosis, Primary Axillary.** Approve for 1 year if the patient has tried at least one topical agent.
   Note: Examples of topical agents include topical aluminum chloride, Qbrexza (glycopyrronium cloth 2.4% for topical use).

4. **Migraine Headache Prevention.** Approve for 1 year if the patient meets the following criteria (A, B, C, D, and E):
   A) Patient has ≥ 15 migraine headache days per month with headache lasting 4 hours per day or longer (prior to initiation of Botox therapy); AND
   B) Patient has tried at least two standard prophylactic (preventative) pharmacologic therapies, each from a different pharmacologic class **[verification of therapies required]**; AND
   Note: Examples of standard prophylactic (preventative) pharmacologic therapies include angiotensin receptor blocker, angiotensin converting enzyme inhibitor, anticonvulsant, beta-blocker, calcium channel blocker, tricyclic antidepressant, other antidepressant.

C) Patient meets ONE of the following (i, ii, or iii):
- **i.** Patient has had inadequate efficacy to both of those standard prophylactic (preventive) pharmacologic therapies, according to the prescriber; OR
- **ii.** Patient has experienced adverse event(s) severe enough to warrant discontinuation of both of those standard prophylactic (preventive) pharmacologic therapies, according to the prescriber; OR
- **iii.** Patient has had inadequate efficacy to one standard prophylactic (preventive) pharmacologic therapy and has experienced adverse event(s) severe enough to warrant discontinuation to another standard prophylactic (preventive) pharmacologic therapy, according to the prescriber; AND

D) Botox is being prescribed by or after consultation with a neurologist or headache specialist; AND

E) If the patient is currently taking Botox for migraine headache prevention, the patient has had a significant clinical benefit from the medication as determined by the prescriber.
Note: Examples of significant clinical benefit include a reduction in the overall number of migraine days per month or a reduction in number of severe migraine days per month from the time that Botox was initiated.

5. **Overactive Bladder with Symptoms of Urge Urinary Incontinence, Urgency, and Frequency.** Approve for 1 year if the patient has tried at least one other pharmacologic therapy.
Note: Examples of other pharmacologic therapies include a beta-3 adrenergic agonist or an anticholinergic medication. For treatment of urinary incontinence associated with a neurological condition, refer to FDA-Approved Indications below.

6. **Spasticity, Limb**. Approve for 1 year.

7. **Urinary Incontinence Associated with a Neurological Condition.** Approve for 1 year if the patient has tried at least one other pharmacologic therapy.
Note: Examples of neurological conditions include spinal cord injury, multiple sclerosis, or spina bifida. Examples of other pharmacologic therapies include a beta-3 adrenergic agonist or an anticholinergic medication. For treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency, see FDA-Approved Indications above.

Other Uses with Supportive Evidence

8. **Achalasia**. Approve for 1 year.

9. **Anal Fissure.** Approve for 1 year.

10. **Chronic Facial Pain/Pain Associated with Temporomandibular Dysfunction.** Approve for 1 year.

11. **Chronic Low Back Pain.** Approve for 1 year if the patient meets the following criteria (A and B):
A) Patient has tried at least two other pharmacologic therapies; AND
Note: Examples of pharmacologic therapies include nonsteroidal anti-inflammatory drugs (NSAIDs), antispasmodics, muscle relaxants, opioids, or antidepressants.
B) Botox is being used as part of a multimodal therapeutic pain management program.

12. **Dystonia, other than Cervical.** Approve for 1 year.
Note: Examples of dystonias include focal dystonias, tardive dystonia, anismus, or laryngeal dystonia/spasmodic dysphonia. For cervical dystonia, refer to FDA-Approved Indications above.

13. **Essential Tremor.** Approve for 1 year if the patient has tried at least one other pharmacologic therapy.

Note: Examples of pharmacologic therapies for essential tremor include primidone, propranolol, benzodiazepines, gabapentin, or topiramate.

14. **Hemifacial Spasm.** Approve for 1 year.

15. **Hyperhidrosis, Gustatory.** Approve for 1 year.
    Note: Gustatory hyperhidrosis is also referred to as Frey's Syndrome.

16. **Hyperhidrosis, Palmar/Plantar and Facial.** Approve for 1 year if the patient has tried at least one topical agent (e.g., aluminum chloride).

17. **Myofascial Pain.** Approve for 1 year.

18. **Ophthalmic Disorders, other than Blepharospasm or Strabismus.** Approve for 1 year.
    Note: Examples of ophthalmic disorders include esotropia, exotropia, nystagmus, or facial nerve paresis. For blepharospasm associated with dystonia or strabismus, refer to FDA-Approved Indications above.

19. **Plantar Fasciitis.** Approve for 1 year if the patient has tried two other treatment modalities.
    Note: Examples of other treatment modalities include padding and strapping of the foot, therapeutic orthotic insoles, oral anti-inflammatory drugs, corticosteroid injections, or stretching.

20. **Sialorrhea, Chronic.** Approve for 1 year.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Botox is not recommended in the following situations:

1. **Cosmetic Uses.** Note: Examples of cosmetic uses include facial rhytides, frown lines, glabellar wrinkling, horizontal neck rhytides, mid and lower face and neck rejuvenation, platsymal bands, or rejuvenation of the periorbital region. Cosmetic use is not recommended for coverage as this indication is excluded from coverage in a typical medical benefit.

2. **Gastroparesis.** The ACG issued clinical guidelines on the management of gastroparesis (2013).[35] ACG does not recommend the use of botulinum toxin injected into the pylorus as a treatment for gastroparesis. This is based on two double-blind, placebo-controlled studies which did show some improvement in gastric emptying, but no improvement in symptoms compared with placebo.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Botox® injection [prescribing information]. Madison, NJ: Allergan; August 2022.
2. Micromedex®. IBM Corporation. Available at: http://www.micromedexsolutions.com Accessed on January 9, 2023. Search terms: Botox.
3. Bhidayasiri R, Truong DD. Expanding use of botulinum toxin. *J Neurol Sci*. 2005;235(1-2):1-9.
4. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. *Headache*. 2019;59:1-18.
5. Vaezi MF, Pandolfino JE, Yadlapati RH, et al. ACG Clinical Guidelines: diagnosis and management of achalasia. *Am J Gastroenterol*. 2020 Sep;115(9):1393-1411.
6. Wald A, Bharucha AE, Limketkai B, et al. ACG Clinical Guidelines: Management of Benign Anorectal Disorders. *Am J Gastroenterol*. 2021 Oct 1;116(10):1987-2008.
7. Lang AM. Botulinum toxin type A therapy in chronic pain disorders. *Arch Phys Med Rehabil.* 2003;84(3 Suppl 1):S69-73.
8. von Lindern JJ, Niederhagen B, Berge S, Appel T. Type A botulinum toxin in the treatment of chronic facial pain associated with masticatory hyperactivity. *J Oral Maxillofac Surg*. 2003;61(7):774-778.
9. Borodic GE, Acquadro MA. The use of botulinum toxin for the treatment of chronic facial pain. *J Pain.* 2002;3(1)21-27.
10. Freund B, Schwartz M, Symington JM. Botulinum toxin: new treatment for temporomandibular disorders. *Br J Oral Maxillofac Surg*. 2000;38(5):466-471.
11. Foster L, Clapp L, Erickson M, Jabbari B. Botulinum toxin A and chronic low back pain: a randomized, double-blind study. *Neurology*. 2001;56:1290-1293.
12. Jabbari B, Ney J, Sichani A, et al. Treatment of refractory, chronic low back pain with botulinum neurotoxin A: an open-label, pilot study. *Pain Med*. 2006;7(3):260-264.
13. Simpson DM, Blitzer A, Brashear A, et al. Assessment: botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2008;70:1699-1706.
14. Stachler RJ, Francis DO, Schwartz SR, et al. Clinical practice guideline: hoarseness (dysphonia). *Otolaryngology – Head and Neck Surgery*. 2018;Supplement:1-42.
15. Zesiewicz TA, Elble R, 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.
16. International Hyperhidrosis Society. Primary focal craniofacial and gustatory hyperhidrosis (Frey's Syndrome). Updated January 15, 2012. Available at: https://sweathelp.org/treatments-hcp/clinical-guidelines/primary-focal-hyperhidrosis/primary-focal-facial-and-gustatory.html. Accessed on January 9, 2023.
17. Naumann M, So Y, Argoff CE, et al. Assessment: botulinum neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review). Report of the therapeutics and technology assessment subcommittee of the American Academy of Neurology. *Neurology.* 2008;70(19):1707-1714.
18. Cheng CM, Chen JS, Patel RP. Unlabeled uses of botulinum toxins: A review, part 1. *Am J Health Syst Pharm.* 2006;63(2): 145–152.
19. Lowe N, Campanati A, Bodokh I, et al. The place of botulinum toxin type A in the treatment of focal hyperhidrosis. *Br J Dermatol.* 2004;151(6):1115-1122.
20. International Hyperhidrosis Society. Primary focal palmar hyperhidrosis. Updated January 15, 2012. Available at: https://sweathelp.org/treatments-hcp/clinical-guidelines/primary-focal-hyperhidrosis/primary-focal-palmar.html. Accessed on January 9, 2023.
21. International Hyperhidrosis Society. Primary focal plantar hyperhidrosis. Updated January 15, 2012. Available at: https://sweathelp.org/treatments-hcp/clinical-guidelines/primary-focal-hyperhidrosis/primary-focal-plantar.html. Accessed on January 9, 2023.
22. Porta M, Maggioni G. Botulinum toxin (BoNT) and back pain. *J Neurol.* 2004;251(Suppl 1):1/15-1/18.
23. Porta M. A comparative trial of botulinum toxin type A and methylprednisolone for the treatment of myofascial pain syndrome and pain from chronic muscle spasm. *Pain.* 2000;85:101-105.
24. Qerama E, Fuglsang-Frederiksen, Kasch H, et al. A double-blind, controlled study of botulinum toxin A in chronic myofascial pain. *Neurology.* 2006;67(2):241-245.
25. Ruiz MF, Moreno M, Sanchez-Garrido CM, et al. Botulinum treatment of infantile esotropia with abduction nystagmus. *J Ped Ophthal Strabismus.* 2000;37:196-205.
26. Repka MX, Savino PJ, Reinecke RD. Treatment of acquired nystagmus with botulinum neurotoxin A. *Arch Ophthalmol.* 1994;112(10):1320-1324.
27. Leigh RJ, Tomsak RL, Grant MP, et al. Effectiveness of botulinum toxin administered to abolish acquired nystagmus. *Ann Neurol.* 1992;32(5):633-642.
28. Kao LY, Chao AN. Subtenon injection of botulinum toxin for treatment of traumatic sixth nerve palsy. *J Pediatr Ophthalmol Strabismus*. 2003;40(1):27-30.
29. Hung HL, Kao LY, Sun MH. Botulinum toxin treatment for acute traumatic complete sixth nerve palsy. *Eye.* 2005;19(3):337-341.
30. Elizondo-Rodriguez J, Araujo-Lopez Y, Moreno-Gonzalez JA, et al. A comparison of botulinum toxin A and intralesional steroids for the treatment of plantar fasciitis: a randomized, double-blinded study. *Foot Ankle Int*. 2013;34(1):8-14.

31. Thomas JL, Christensen JC, Kravitz SR, et al. The diagnosis and treatment of heel pain: a clinical practice guideline – revision 2010. *J Foot Ankle Surg.* 2010;49:S1-S19.
32. Lakraj AA, Moghimi N, Jabbari B. Sialorrhea: anatomy, pathophysiology and treatment with emphasis on the role of botulinum toxin. *Toxins*. 2013;5:1010-1031.
33. Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache. Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2016;86:1818-1826.
34. Camilleri M, Parkman HP, Shafi MA, et al. Clinical guideline: management of gastroparesis. *Am J Gastroenterol.* 2013;108(1):18-38.