Reference number
2247-A

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. EXCLUSIONS

Coverage will not be provided for cosmetic use.

III. CRITERIA FOR INITIAL APPROVAL

A. Blepharospasm

Authorization of 12 months may be granted for treatment of blepharospasm, including blepharospasm associated with dystonia and benign essential blepharospasm.

B. Cervical dystonia

Authorization of 12 months may be granted for the treatment of adults with cervical dystonia (e.g., torticollis) when there is abnormal placement of the head with limited range of motion in the neck.

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) three 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:
    i. Antidepressants (e.g., amitriptyline, venlafaxine)
    ii. Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium)
    iii. 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).

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 anticholinergic medications (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trospium], Ditropan XL [oxybutynin]).

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. Member is unresponsive or unable to tolerate oral pharmacotherapy prescribed for excessive sweating (e.g., anticholinergics, beta-blockers, or benzodiazepines); and
2. Significant disruption of professional and/or social life has occurred because of excessive sweating; and
3. Topical aluminum chloride or other extra-strength antiperspirants are ineffective or result in a severe rash.

F. Strabismus

Authorization of 12 months may be granted for treatment of strabismus when interference with normal visual system development is likely to occur and spontaneous recovery is unlikely.

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 either as a primary diagnosis or as a symptom of a condition causing limb spasticity.

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 an anticholinergic medication (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trospium], Ditropan XL [oxybutynin]).

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.

IV. CONTINUATION OF THERAPY

A. All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria for all approvable conditions other than chronic migraine prophylaxis.

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.

V. REFERENCES

1. Botox [package insert]. Madison, NJ: Allergan USA, Inc; February 2021.
2. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at http://www.micromedexsolutions.com. Accessed August 3, 2021.
3. AHFS Drug Information. http://online.lexi.com/lco. Accessed August 3, 2021.
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: 3nd 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.