Botulinum Toxins
Botox®, Dysport®, Myobloc®, Xeomin®

FDA Indications and Usage[1,2,3,4]

	Cervical dystonia	Overactive bladder (non-neurogenic)	Urinary incontinence secondary to detrusor overactivity (neurogenic)	Chronic migraine prophylaxis	Blepharospasm	Strabismus	Upper limb spasticity	Axillary hyperhidrosis, severe
Botox *onabotulinumtoxin A*	≥18 years	≥18 years	≥18 years	≥18 years	≥12 years	≥12 years	≥18 years	≥18 years
Xeomin *incbotulinumtoxin A*	≥18 years				≥18 years *treatment-experienced with Botox*			
Dysport *abobotulinumtoxin A*	≥18 years						≥18 years	
Myobloc *rimabotulinumtoxin B*	≥18 years							

Dosage Form/Strength:

Botox: 100 unit and 200 unit powder for injection
Dysport: 300 unit and 500 unit powder for injection
Myobloc: 2500 units/0.5mL, 5000 units/1mL, 10000 units/2mL vial
Xeomin: 50 unit, 100 unit, 200 unit powder for injection

Black Box Warning[1,2,3,4]

WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have an underlying condition that would predispose them to these symptoms. In unapproved uses, including spasticity in children, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and spasticity and at lower doses.

Warnings and Precautions:

Botulinum Toxin Products are not interchangeable. Botulinum toxin units of biological activity are unique to each product.

Indication	Approval Criteria[1,2,3,4]	Denial Criteria	Maximum Quantity[1,2,3,4]
Overactive bladder (OAB)[1,5]	• Age ≥18 years old; **AND** • Documented moderate to severe symptoms of urge urinary incontinence, urgency, and frequency; **AND** • Documented behavioral therapy trials • Documented trial of at least 2 different pharmacologic treatments for at least 60 days with documentation of inadequate response **OR** a justifiable contraindication to oral anti-muscarinics or oral beta-3 adrenergic receptor agonists (e.g. oxybutynin, tolterodine, or mirabegron) ; **AND** • Product requested is **Botox**.	• Patients unable/unwilling to perform self-catheterization if necessary during treatment course • Dose exceeds FDA recommendations for indication • Cumulative Botox dose exceeds 400 units within a 3 month period from all procedures	**Botox:** • No more than 100 Units per 12 weeks
Urinary incontinence due to detrusor overactivity associated with a neurologic condition[1,6]	• Age ≥18 years old; **AND** • Documented neurologic condition [e.g. multiple sclerosis, spinal cord injury]; **AND** • Documented symptoms of detrusor over-activity; **AND** • Documented trial of at least 2 different pharmacologic treatments for at least 60 days with documentation of inadequate response or a justifiable contraindication to oral anti-muscarinics or oral beta-3 adrenergic receptor agonists (e.g. oxybutynin, tolterodine, or mirabegron) ; **AND** • Product requested is **Botox**	• Dose exceeds FDA recommendations for indication • Cumulative Botox dose exceeds 400 units within a 3 month period from all procedures	**Botox:** • No more than 200 Units per 12 weeks

Indication	Approval Criteria[1,2,3,4]	Denial Criteria	Maximum Quantity[1,2,3,4]
Chronic Migraine, headache prophylaxis[1, 7, 8, 9, 10]	• ≥18 yrs of age; **AND** • Headache on ≥15 days per month with headache lasting 4 hours a day or longer (chronic/transformed migraine); **AND** • Patient is on a medication regimen for migraine prophylaxis per the American Academy of Neurology (AAN) clinical practice guidelines; **AND** • Prescriber is a neurologist; **AND** • Product requested is **Botox**. • *Renewal Authorization:* ▪ Headache frequency has decreased by at least 2 headache days from baseline in the previous month	• Episodic migraine (<15 days per month) • Headache attributable to another disorder, including medication overuse • Dose exceeds FDA recommendations for indication • Cumulative Botox dose exceeds 400 units within a 3 month period from all procedures • For renewal authorizations beyond the second treatment, headache frequency has not decreased from baseline by at least 2 headache days per month.	**Botox:** • No more than 155 units per 12 weeks
Upper limb spasticity[1,2]	• ≥18 yrs of age; **AND** • The patient is being treated for upper limb spasticity; **AND** • Spasticity refractory to oral medication; **AND** • Product requested is **Botox, Dysport, or Xeomin**.	• Dose exceeds FDA recommendations for indication • Cumulative Botox dose exceeds 400 units, OR Dysport dose exceeds 1000 units, OR Xeomin dose exceeds 400 units within a 3 month period from all procedures	**Botox:** • No more than 400 cumulative units per 12 weeks **Dysport:** • No more than 1000 cumulative units per 12 weeks **Xeomin:** • No more than 400 units per 12 weeks
Axillary hyperhidrosis, severe[1]	• Age ≥17 years old; **AND** • Patient is being treated for severe axillary hyperhidrosis that has been inadequately managed by topical agents; **AND** • HDSS (Hyperhidrosis Disease Severity Scale) score is ≥ 3; **AND** • Product requested is **Botox**.	• Dose exceeds FDA recommendations for indication • Cumulative Botox dose exceeds 400 units within a 3 month period from all procedures	**Botox:** • No more than 50 units per axilla per 12 weeks

Indication	Approval Criteria[1,2,3,4]	Denial Criteria	Maximum Quantity[1,2,3,4]
Cervical dystonia[1,2,3,4]	• ≥18 yrs of age; **AND** • Diagnosis of cervical dystonia; **AND** • Purpose of treatment is to reduce the severity of abnormal head position and neck pain.	• Dose exceeds FDA recommendations for indication or maximum cumulative dose over a 12 week period	**Botox:** • Maximum cumulative dose of no more than 300 units within a 3 month (12 week) period **Dysport:** • Maximum dose initial – No more than 500 units per 12 weeks • Subsequent maximum dose – no more than 250 units more than previous dose up to a maximum of 1000 units per 12 weeks **Myobloc:** • No more than 5,000 units within a 12 week period • No more than 10,000 units within a 16 week period **Xeomin:** • No more than 120 units per 12 weeks
Strabismus[1]	• Patient is ≥12 years old; **AND** • Patient is being treated for strabismus; **AND** • Product requested is **Botox**.	• Initial or subsequent dose exceeds FDA recommendations for indication • Subsequent dose more than two times the previous dose or exceeds 25 units • Cumulative Botox dose exceeds 400 units within a 3 month period from all procedures	**Botox:** • No more than 25 units for any one muscle per 12 weeks

Indication	Approval Criteria[1,2,3,4]	Denial Criteria	Maximum Quantity[1,2,3,4]
Blepharospasm associated with dystonia[1,4]	• Age ≥12 years old (Botox) or ≥18 years old (Xeomin); **AND** • Patient is unable to open their eyelid(s) or is functionally blind due to dystonia; **AND** • Medication is ordered by a neurologist or ophthalmologist; **AND** • If treatment-naïve and age ≥18 years old, product requested is **Xeomin** • If treatment experienced, prescriber may choose to use **Xeomin** or **Botox** in Botox-treatment-experienced individuals.	• Initial or subsequent dose exceeds FDA recommendations for indication • Cumulative Botox dose exceeds 400 units OR Xeomin dose exceeds 400 units within a 3 month period from all procedures	**Botox:** • No more than 200 cumulative units in 30 day period; no more than 400 units per 12 weeks **Xeomin:** • No more than 35 units per eye per 12 weeks
Non-FDA Approved Indications[11]	• All requests for non-FDA approved medical (non-cosmetic) indications must be submitted with supporting medical literature demonstrating safety and efficacy in the representative population. • A letter of medical necessity must be included with each request and shall include previous therapies trialed. • International Classification of Diseases (ICD) Code must be included in the request and coded to the highest level of specificity. • Each request will be reviewed on a case-by-case basis. • The current version of the *CMS Local coverage determination (LCD) for Botulinum toxin type A & type B (L28555)* document will be used in the evaluation of the request.		

Additional Denial Criteria

- The medication is being used for cosmetic purposes, including treatment of glabellar lines.
- International Classification of Diseases (ICD) Code is absent from prior authorization request.

Length of Authorization

- Coverage may be approved for up to 6 months.
- Re-authorization requires documentation of clinical response and progress.

References

[1] Botox® package insert. Irvine, CA; Allergan, Inc., January 2016. http://www.allergan.com/assets/pdf/botox_pi.pdf

[2] Dysport® package insert. Wrexham, UK; Ipsen Biopharm Ltd, July 2015. http://www.dysport.com/pdf/Dysport%20Full%20Prescribing%20Information.pdf

[3] Myobloc® package insert. South San Francisco, CA; Solstice Neurosciences, Inc.; May 2010. http://www.myobloc.com/hp_about/PI_5-19-10.pdf

[4] Xeomin® package insert. Greensboro, NC; Merz Pharmaceuticals, LLC., December 2015. http://www.xeomin.com/wp-content/uploads/xeomin-full-prescribing-information.pdf

[5] Diagnosis & treatment algorithm: AUA/SUFU guideline on non-neurogenic overactive bladder in adults. *http://www.auanet.org/common/pdf/education/clinical- guidance/Overactive-Bladder-Algorithm.pdf*.

[6] Pannek J, Stöhrer M, Blok B, *et al*. Guidelines on neurogenic lower urinary tract dysfunction. European Association of Urology. 2011. Available at: *http://www.uroweb.org/gls/pdf/17_Neurogenic%20LUTS.pdf*. Accessed Nov 4, 2014.

[7] Beithon J, Gallenberg M, Johnson K, *et al*. Institute for Clinical Systems Improvement. Diagnosis and Treatment of Headache. Health care guideline, diagnosis and treatment of headache. Available at: *https://www.icsi.org/_asset/qwrzng/headache.pdf*. Accessed Nov 4, 2014.

[8] Loder E, Burch R, Rizzoli P. The 2012 AHS/AAN guidelines for prevention of episodic migraine: a summary and comparison with other recent clinical practice guidelines. *Headache*. 2012;52:930-945. Available at: *http://www.headachejournal.org/SpringboardWebApp/userfiles/headache/file/AHS- AAN%20Guidelines.pdf*. Accessed Nov 7, 2014.

[9] Shamliyan TA, Kane RL, Taylor FR. Migraine in Adults: Preventive Pharmacologic Treatments. Comparative Effectiveness Review No. 103. (Prepared by the University of Minnesota Evidence-based Practice Center under Contract No. 290-2007-10064-I) AHRQ Publication No. 13-EHC068-EF. Rockville, MD: Agency for Healthcare Research and Quality; April 2013. Available at: *www.effectivehealthcare.ahrq.gov/reports/final.cfm*. Accessed Nov 4, 2014.

[10] Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2000 Sep 26;55(6):754-62.

[11] CMS Local coverage determination (LCD): Botulinum toxin type A & type B (L28555). Available at: http://www.cms.gov/medicare-coverage-database/details/lcd- details.aspx?LCDId=28555&ContrId=268&ver=78&ContrVer=1&Date=11%2f07%2f2014&DocID=L28555&bc=iAAAAAgAAAAAAA%3d%3d&. Accessed Nov 7, 2014.