AbobotulinumtoxinA (Dysport®)

NDC CODE(S) 00299-5962-XX DYSPORT 300UNIT VIAL (EA) (GALDERMA LABORA)
15054-0500-XX DYSPORT 500UNIT Solution Reconstituted (IPSEN BIOPHARMACEUTICALS)
15054-0530-XX DYSPORT 300UNIT Solution Reconstituted (IPSEN BIOPHARMACEUTICALS)

DESCRIPTION

Botulinum toxin, produced by the bacterium Clostridium botulinum, is one of the most potent naturally occurring neurotoxins known. It induces chemodenervation by first binding to acceptors on motor nerve terminals. It then enters the terminals and blocks the release of acetylcholine and other neurotransmitters at the neuromuscular junction. This renders smooth and striated muscles incapable of contraction. Acetylcholine also mediates the sympathetic innervation of the sweat glands, explaining how botulinum toxin disrupts the cholinergic outflow to the skin and halts glandular secretion.

The minute amount of toxin used clinically produces only partial, localized chemical denervation with transient results. Over time, axons generate temporary sprouts which release acetylcholine and the original nerve terminal is eventually re-established, ending the toxin's therapeutic activity.

Seven antigenic-specific serotypes of botulinum toxin have been identified, types A, B, C-1, D, E, F and G, but only botulinum toxin types A and B are commercially available. These commercial preparations of the two serotypes (three of serotype A and one of serotype B) vary widely in potency and dosage. They have been given different names to reinforce these differences and to prevent medication errors. It is emphasized that the use and dosage of different formulations of botulinum toxin is not interchangeable.

This policy addresses only the type A formulation abobotulinumtoxinA marketed as Dysport®.

POLICY

- AbobotulinumtoxinA for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Anal fissure, chronic
  - Blepharospasms
  - Cervical dystonia
  - Hemifacial spasms
  - Hyperhidrosis
  - Overactive bladder
  - Sialorrhea
  - Spasticity, Upper and Lower Limbs
  - Urinary Incontinence
  - Ventral Hernia
- AbobotulinumtoxinA for the prevention of chronic migraines is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- AbobotulinumtoxinA for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age (unless otherwise noted); **AND**

Universal Criteria

- Patient does not have a hypersensitivity to any botulinum toxin product; **AND**
- Patient does not have a hypersensitivity to cow's milk protein; **AND**
- Patient does not have an active infection at the proposed injection site; **AND**
- Patient evaluated for any disorders which may contribute to respiratory or swallowing difficulty; **AND**
- Patient is not on concurrent treatment with another botulinum toxin (i.e., incobotulinumtoxinA, onabotulinumtoxinA, rimabotulinumtoxinB, etc.)

Cervical Dystonia

- Patient has a history of recurrent involuntary contraction of one or more muscles in the neck; **AND**
  - Patient has sustained head tilt; OR
  - Patient has abnormal posturing with limited range of motion in the neck

Spastic Conditions

- Patient has one of the following:
  - Upper/Lower Limb Spasticity in adults (i.e., spasticity post-stroke, traumatic brain or spinal cord injuries)
  - ~~o~~ Upper/Lower Limb Spasticity in pediatric patients at least 2 years of age
  - Spasticity of the lower limbs due to Multiple Sclerosis or Schilder's Disease

Blepharospasms

Prophylaxis for Chronic Migraines

- Not used in combination with prophylactic calcitonin gene-related peptide (CGRP) inhibitors (e.g., eptinezumab, erenumab, galcanezumab, fremanezumab, etc.) *(NOTE: This does not include CGRP inhibitors used for acute treatment [e.g., ubrogepant])*; **AND**
- Patient is utilizing prophylactic intervention modalities (i.e. pharmacotherapy, behavioral therapy, or physical therapy, etc.); **AND**
- Patient has 15 or more headache (tension-type-like and/or migraine-like) days per month for at least 3 months; **AND**
  - Patient has had at least five attacks with features consistent with migraine (with and/or without aura)§; AND
  - On at least 8 days per month for at least 3 months:
    - Headaches have characteristics and symptoms consistent with migraine§; **OR**
    - Patient suspected migraines are relieved by a triptan or ergot derivative medication; **AND**
- Patient has failed at least an 8-week trial of any two oral medications for the prevention of migraines (see list of migraine-prophylactic medications below for examples)

Sialorrhea associated with neurological disorders

- Patient has a history of troublesome sialorrhea for at least a 3-month period; **AND**
  - Patient has Parkinson's disease; **OR**
  - Patient has severe developmental delays; **OR**
  - Patient has Cerebral Palsy

Chronic Anal Fissure

- Other causes of disease have been ruled out (e.g., Crohn's Disease, etc.); **AND**
- Patient has failed on non-pharmacologic supportive measures (i.e., sitz baths, psyllium fiber, bulking agents, etc.); **AND**
- Patient has tried and failed a ≥ 1 month trial of conventional pharmacologic therapy (e.g. oral/topical nifedipine, diltiazem, and/or topical nitroglycerin, bethanechol, etc.)

Incontinence due to neurogenic detrusor overactivity

- Patient has detrusor overactivity associated with a neurologic condition (i.e., spinal cord injury, multiple sclerosis, etc.) that is confirmed by urodynamic testing; **AND**
- Patient has failed a 1 month or longer trial of two medications from either the antimuscarinic (i.e., darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine or trospium) or beta-adrenergic (i.e., mirabegron) classes.

Overactive Bladder (OAB)

- Patient has symptoms of urge urinary incontinence, urgency, and frequency; **AND**
- Patient has failed a 1 month or longer trial of two medications from either the antimuscarinic (i.e., darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine or trospium) or beta-adrenergic (i.e., mirabegron) classes.

Severe Primary Axillary Hyperhidrosis

- Patient has tried and failed ≥ 1 month trial of a topical agent (e.g., aluminum chloride, glycopyrronium, etc.); **AND**
  - Patient has a history of medical complications such as skin infections or significant functional impairments; **OR**
  - Patient has had a significant burden of disease or impact to activities of daily living due to condition (e.g., impairment in work performance/productivity, frequent change of clothing, difficulty in relationships and/or social gatherings, etc.)

Hemifacial Spasms

Ventral Hernia

- Patient has a large ventral hernia with loss of domain or contaminated ventral hernia; **AND**
- Used preoperatively in patients scheduled to receive abdominal wall reconstruction (AWR)

Migraine-Prophylaxis Oral Medications (list not all-inclusive)
Migraine without aura – Recurrent, lasting 4 to 72 hours • Antidepressants (e.g., amitriptyline, fluoxetine, nortriptyline, etc.) • Beta blockers (e.g., propranolol, metoprolol, nadolol, timolol, atenolol, pindolol, etc.) • Angiotensin converting enzyme inhibitors/angiotensin II receptor blockers (ex. lisinopril, candesartan, etc.) • Anti-epileptics (e.g., divalproex, valproate, topiramate, etc.) • Calcium channels blockers (e.g., verapamil, etc.)
Migraine Features

Migraine without aura
• At least five attacks have the following:
  ○ Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
  ○ Headache has at least two of the following characteristics:
  ▫ Unilateral location

- Pulsating quality
- Moderate or severe pain intensity
- Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs); AND

- During headache at least one of the following:
  - Nausea and/or vomiting
  - Photophobia and phonophobia

Migraine with aura

- At least two attacks have the following:
  - One or more of the following fully reversible aura symptoms:
    - Visual
    - Sensory
    - Speech and/or language
    - Motor
    - Brainstem
    - Retinal; **AND**
  - o At least three of the following characteristics:
    - At least one aura symptom spreads gradually over ≥5 minutes
    - Two or more symptoms occur in succession
    - Each individual aura symptom lasts 5 to 60 minutes
    - At least one aura symptom is unilateral
    - At least one aura symptom is positive (e.g., scintillations and pins and needles)
    - The aura is accompanied, or followed within 60 minutes, by headache

RENEWAL CRITERIA

- Patient continues to meet universal and indication specific criteria as identified in the Initial Approval Criteria; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: symptoms of a toxin spread effect (e.g., asthenia, diplopia, ptosis, dysphagia, dysphonia, dysarthria, breathing difficulties, etc.); **AND**
- Disease response as evidenced by the following:

Blepharospasms

- Improvement of severity and/or frequency of eyelid spasms

Cervical Dystonia

- Improvement in the severity and frequency of pain; **AND**
- Improvement of abnormal head positioning

Upper/Lower Limb Spasticity

- Decrease in tone and/or resistance, of affected areas, based on a validated measuring tool (e.g., Ashworth scale, Physician Global Assessment, Clinical Global Impression [CGI], etc.)

Severe Primary Axillary Hyperhidrosis

- Significant reduction in spontaneous axillary sweat production; **AND**
- Patient has a significant improvement in activities of daily living

Prophylaxis for Chronic Migraines

- Significant decrease in the number, frequency, and/or intensity of headaches; **AND**
- Improvement in function; **AND**
- Patient continues to utilize prophylactic intervention modalities (i.e., pharmacotherapy, behavioral therapy, physical therapy, etc.)

Sialorrhea associated with neurological disorders

- Significant decrease in saliva production

Incontinence due to detrusor overactivity

- Significant improvements in weekly frequency of incontinence episodes; **AND**
- Patient's post-void residual (PVR) periodically assessed as medically appropriate

Overactive Bladder (OAB)

- Significant improvement in daily frequency of urinary incontinence or micturition episodes and/or volume voided per micturition; **AND**
- Patient's post-void residual (PVR) periodically assessed as medically appropriate

Hemifacial Spasms

- Decrease in frequency and/or severity of spasm, or a decrease in tone and/or improvement in asymmetry to the affected side of the face

Chronic Anal Fissure

- Complete healing of anal fissure; **OR**
- Symptomatic improvement of persistent fissures

Ventral Hernias

- May not be renewed

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Cervical Dystonia	Initial dose: 500 units divided among the affected muscles. Re-treatment: 250-1000 units every 12 -16 weeks or longer as necessary
Upper Limb Spasticity	**Adults:** 500 -1000 units divided among the affected muscles every 12 -16 weeks or longer, as necessary. *Maximum recommended total dose per treatment session (upper and lower limb combined) in adults is 1500 units.* **Pediatrics:** Up to 8-16 units/kg per limb every 12 weeks. Maximum dose per treatment session for upper limb spasticity is 16 units/kg or 640 units, whichever is lower.

	Maximum recommended total dose per treatment session for spasticity in pediatric patients is 30 units/kg or 1000 units, whichever is lower.
Chronic Migraine Prophylaxis	Up to 240 units divided among the affected muscles every 12 weeks
Sialorrhea	Up to 450 units divided among the affected muscles every 12 weeks
Chronic Anal Fissure	Up to 150 units divided among the affected muscles every 12 weeks
Lower Limb Spasticity	Adults Up to 1500 units divided among the affected muscles every 12 weeks. *Maximum recommended total dose per treatment session (upper and lower limb combined) in adults is 1500 units*. Pediatrics Up to 10-15 units/kg divided among gastrocnemius-soleus complex muscles, per limb, every 12 weeks. Maximum dose per treatment session for lower limb spasticity is 15 units/kg for unilateral lower limb injections, 30 units/kg for bilateral lower limb injections, or 1000 units, whichever is lower. *Maximum recommended total dose per treatment session for spasticity in pediatric patients is 30 units/kg or 1000 units, whichever is lower.*
Blepharospasms	Up to 120 units per affected eye every 12 weeks
Neurogenic Detrusor Overactivity/Overactive Bladder (OAB)	Up to 750 units divided among the affected muscles every 12 weeks
Severe Primary Axillary Hyperhidrosis	Up to 200 units per axilla not more often than every 12 weeks
Hemifacial Spasms	Up to 220 units per treatment session based on sites and severity of the spasm. Subsequent injections administered upon recurrence of spasm, every 12 weeks, if needed.
Ventral Hernia	500 units divided among abdominal muscles, injected 2-4 weeks prior to AWR surgery. *May not be renewed.*

LENGTH OF AUTHORIZATION

- Coverage will be provided for six months and may be renewed.
- Preoperative use in Ventral Hernia may NOT be renewed.

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

Indication	Billable Units	Per # days
Cervical Dystonia	200	84
Chronic Migraine Prophylaxis	60	84
Sialorrhea	100	84
Chronic Anal Fissure	60	84
Blepharospasms	60	84
Upper Limb Spasticity	200	84
Upper Limb Spasticity (Pediatric)	160	84
Lower Limb Spasticity	300	84
Lower Limb Spasticity (Pediatric)	200	84
Neurogenic detrusor overactivity/OAB	160	84
Severe Primary Axillary Hyperhidrosis	100	84

Hemifacial Spasms	60	84
Ventral Hernia	500	N/A

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Dysport [package insert]. Wrexham, UK; Ipsen Biopharm Ltd; July 2020. Accessed April 2021.
2. 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: 86:1-9
3. Chankrachang S, Arayawichanont A, Poungvarin N, et al. Prophylactic botulinum type A toxin complex (DYSPORT®) for migraine without aura. Headache 2011; 51(1):52-63.
4. Mancini F, Zangaglia R, Cristina S, et al. Double-blind, placebo-controlled study to evaluate the efficacy and safety of botulinum toxin type A in the treatment of drooling in parkinsonism. Move Disord, 2003; 18(6): 685-688
5. Pal PK, Calne DB, Calne S, Tsui JK. Botulinum toxin A as treatment for drooling saliva in PD. Neurology 2000; 54:244–247.
6. Brisinda G, Albanese A, Cadeddu F, et al. Botulinum neurotoxin to treat chronic anal fissure: results of a randomized 'Botox vs. DYSPORT®' controlled trial. Aliment Pharmacol Ther. 2004; 19:695-701.
7. Brisinda G, Cadeddu F, Brandara F, Marniga G, and Maria G. Randomized clinical trial comparing botulinum toxin injections with 0.2 percent nitroglycerin ointment for chronic anal fissure. Br J Surg. 2007; 94:162-167.
8. Jost W.H. and Schrank B. Chronic anal fissures treated with botulinum toxin injections: a dose-finding study with DYSPORT®. Colorectal Disease. 1999; 1:26-28.
9. Truong D, Comella C, Fernandez HH, et al. Efficacy and safety of purified botulinum toxin type A (Dysport®) for the treatment of benign essential blepharospasm: A randomized, placebo-controlled, phase II trial. Parkinsonism & Related Disorders Volume 14, Issue 5, July 2008, Pages 407–414. doi:10.1016/j.parkreldis.2007.11.003.

10. Bentivoglio AR, Fasano A, Ialongo T, et al. Fifteen-Year Experience in Treating Blepharospasm with Botox or Dysport: Same Toxin, Two Drugs. Neurotoxicity Research April 2009, Volume 15, Issue 3, pp 224-231. DOI 10.1007/s12640-009-9023-3
11. Ching-Piao Tsai1, Ming-Chang Chiu2, Der-Jen Yen1, Yuh-Cherng Guo1, Chih-Lun Yuan1, and Tzu-Chi Lee. Quantitative Assessment of Efficacy of Dysport Botulinum Toxin Type A) in the Treatment of Idiopathic Blepharospasm and Hemifacial Spasm. Acta Neurologica Taiwanica Vol 14 No 2 June 2005
12. Hyman N, Barnes M, Bhakta B, et al. Botulinum toxin (Dysport) treatment of hip adductor spasticity in multiple sclerosis: a prospective, randomised, double blind, placebo controlled, dose ranging study. J Neurol Neurosurg Psychiatry 2000; 68:707–712.
13. Pittock SJ, Moore AP, Hardiman O, et al. A double-blind randomised placebo-controlled evaluation of three doses of botulinum toxin type A (Dysport) in the treatment of spastic equinovarus deformity after stroke. Cerebrovasc Dis 2003; 15:289–300.
14. Gusev YI, Banach M, Simonow A, et al. Efficacy and safety of botulinum type A toxin in adductor spasticity due to multiple sclerosis. J Musculoskel Pain 2008; 16:175-188.
15. Ravindra P, Jackson BL, Parkinson RJ. Botulinum toxin type A for the treatment of nonneurogenic overactive bladder: does using onabotulinumtoxinA (Botox®) or abobotulinumtoxinA (Dysport®) make a difference? BJU International Volume 112, Issue 1, pages 94–99, July 2013. DOI: 10.1111/bju.12028
16. Frohme C, Varga Z, Olbert P, Schrader AJ, Hofmann R, Hegele A. [Effects of botulinum toxin type A in the single and repeated treatment of overactive bladder. A prospective analysis]. Der Urologe. Ausg. A[2010, 49(5):639-644] DOI:10.1007/s00120-009-2208-9
17. Abeywickrama L, Arunkalaivanan A, Quinlan M. Repeated botulinum toxin type A (Dysport®) injections for women with intractable detrusor overactivity: a prospective outcome study. International Urogynecology Journal. May 2014, Volume 25, Issue 5, pp 601-605
18. Montaser-Kouhsari L, Zartab H, Fanian F, et al. Comparison of intradermal injection with iontophoresis of abobotulinum toxin A for the treatment of primary axillary hyperhidrosis: A randomized, controlled trial. Journal of Dermatological Treatment. Volume 25, Issue 4, 2014. DOI: 10.3109/09546634.2012.739679.
19. Heckmann M, Ceballos-Baumann AO, Plewig G. Botulinum toxin A for axillary hyperhidrosis (excessive sweating). N Engl J Med 2001; 344:488-493.
20. Jitpimolmard S, Tiamkao S, & Laopaiboon M: Long term results of botulinum toxin type A (Dysport) in the treatment of hemifacial spasm: a report of 175 cases. J Neurol Neurosurg Psychiatry 1998; 64(6):751-757.
21. Van Den Bergh P, Francart J, Mourin S, et al: Five-year experience in the treatment of focal movement disorders with low-dose Dysport botulinum toxin. Muscle Nerve 1995; 18(7):720-729.
22. The International Classification of Headache Disorders, 3rd edition (beta version).Headache Classification Committee of the International Headache Society (IHS) Cephalalgia. 2013 Jul;33(9):629-808.
23. Gormley EA, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: American Urological Association (AUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) guideline. April 2019.
24. Schwedt TJ. Chronic Migraine. BMJ. 2014;348:g1416.
25. Modi S, Lowder DM. Medications for migraine prophylaxis. Am Fam Physician. 2006 Jan 1; 73(1):72-8.
26. Pringheim T, Davenport W, Mackie G, et al. Canadian Headache Society guideline for migraine prophylaxis. Can Jneurol Sci. 2012 Mar; 39(2 Suppl 2):S1-S9.
27. The International Classification of Headache Disorders, 3rd edition (beta version).Headache Classification Committee of the International Headache Society (IHS) Cephalalgia. 2013 Jul;33(9):629-808.
28. 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: 86:1-9
29. Glaser DA, Hebert AA, Nast A, et al. Topical glycopyrronium tosylate for the treatment of primary axillary hyperhidrosis: Results from the ATMOS-1 and ATMOS-2 phase 3 randomized controlled trials. J Am Acad Dermatol. 2019;80(1):128. Epub 2018 Jul 10

30. American Headache Society. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache. 2019 Jan;59(1):1-18. doi: 10.1111/head.13456. Epub 2018 Dec 10.
31. Haider A, Solish N. Focal hyperhidrosis: diagnosis and management. CMAJ. 2005;172(1):69-75.
32. Nawrocki S, Cha J. The Etiology, Diagnosis and Management of Hyperhidrosis: A Comprehensive Review. Part II. Therapeutic Options. J Am Acad Dermatol. 2019 Jan 30. pii: S0190-9622(19)30167-7.
33. American Society for Gastrointestinal Endoscopy (ASGE): Standards of practice for the role of endoscopy in patients with anorectal disorders. Gastro Endo. Volume 72, No. 6 : 2010
34. Wald A, Bharucha AE, Cosman BC, et al. American Gastroenterological Association. American Gastroenterological Association medical position statement: Diagnosis and care of patients with anal fissure. Gastroenterology. 2003;124(1):233.
35. Stewart DB, Gaertner W, Glasgow S, et al. Clinical Practice Guideline for the Management of Anal Fissures. Dis Colon Rectum 2017; 60: 7–14.
36. Kuo HC, Chen SL, Chou CL, et al. Taiwanese Continence Society clinical guidelines for diagnosis and management of neurogenic lower urinary tract dysfunction. Urological Science, Volume 25, Issue 2, 2014, pp. 35-41
37. Motz BM, Schlosser KA, Heniford BT. Chemical Components Separation: Concepts, Evidence, and Outcomes. Plast Reconstr Surg. 2018 Sep;142(3 Suppl):58S-63S. doi: 10.1097/PRS.0000000000004856.
38. Elstner KE, Read JW, Saunders J, et al. Selective muscle botulinum toxin A component paralysis in complex ventral hernia repair. Hernia. 2019 Apr 4. doi: 10.1007/s10029-019-01939-3.
39. The International Classification of Headache Disorders, 3rd edition (beta version).Headache Classification Committee of the International Headache Society (IHS) Cephalalgia. 2018 Jan;38(1):1-211.
40. Lexi-Comp Online. (2021, February). AHFS DI. *AbobotulinumtoxinA.* Retrieved April 28, 2021 from Lexi-Comp Online with AHFS.
41. MICROMEDEX Healthcare Series. Drugdex Drug Evaluations. (2020, December). *AbobotulinumtoxinA*. Retrieved April 28, 2021 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 8/31/2021

ID_MRx