Medicare Advantage (MA) Medical Utilization Review Policy

Policy:	**Botulinum Toxin – Dysport Utilization Management Medical Policy** • Dysport® (abobotulinumtoxinA injection – Ipsen)
Date	02/23/2023
Applicable Lines of Business:	Medicare Advantage – Medical
Applicable States:	NGS, J6: Wisconsin, Minnesota, Illinois NGS, JK: New York, Connecticut, Massachusetts, Maine, New Hampshire, Rhode Island, Vermont

OVERVIEW

Dysport (abobotulinumtoxinA), is indicated for the following uses:[1]

- **Cervical dystonia** in adults.
- **Spasticity** in patients ≥ 2 years of age.

Toxin distribution varies between the commercially available botulinum toxin A products, Botox® (onabotulinumtoxinA), Xeomin® (incobotulinumtoxinA), and Dysport.[1-4] It has been postulated that differences in albumin concentration control diffusion of toxin from the injection site (Botox contains 500 mcg of albumin, while Dysport contains 125 mcg of albumin and Xeomin contains 1 mg of albumin). In addition, the labels for the botulinum toxin type A products (Botox, Dysport, and Xeomin) state that there is a lack of interchangeability between the products for various reasons, including differences in the units of biological activity.[1,2,4] Studies have attempted to establish a conversion ratio between botulinum toxin products, with variable results. In general, conversion ratios of 1:1 for Botox to Xeomin, 1:3 for Botox to Dysport, and 1:50 to 1:100 for Botox to Myobloc have been suggested.[5,6]

Other Uses with Supportive Evidence

Botulinum toxins, including Dysport, have been studied in a variety of indications outside of FDA-approved uses. Literature is available to support use of Dysport in the following conditions:

- **Anal Fissure:** There is an extensive amount of data from open-label studies; randomized, placebo-controlled trials; and randomized, comparative trials supporting the efficacy of botulinum toxin A in the treatment of anal fissures.[7-9] Injection of botulinum toxin allows healing in approximately 60% to 80% of anal fissures.[10] There is no consensus on the dose, site of injection, or number of injections. Botulinum toxin A has been shown to be more effective than topical nitroglycerin but less effective than surgery in inducing and maintaining fissure healing.[11] The American College of Gastroenterology 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).[9]
- **Blepharospasm:** Dysport has demonstrated efficacy in clinical trials in patients with blepharospasm.[12,13] American Academy of Neurology (AAN) guidelines (2016, reaffirmed 2022) support the use of Dysport for blepharospasm with a Level C recommendation ("possibly effective").[14]
- **Hemifacial Spasm:** Per the AAN, botulinum toxin (formulation not specified) may be considered in hemifacial spasm (Level C).[19] Data with Botox and Dysport are cited in the recommendations regarding hemifacial spasm.
- **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.[16-18] Data with Dysport come

from two small controlled trials.[16,17] AAN guidelines state that botulinum toxin is probably safe and effective and should be considered (Level B).[15]

Dosing Considerations

Definitive dosing has not been established for off-label uses of botulinum toxins, including Dysport. Specific dosing considerations by indication are noted below. For other indications addressed in this policy, specific dosing guidance is not available. In these cases, dosing is based on the Botox prescribing information, which states that in a 3-month interval, adults should not exceed a total dose of 400 units, and pediatric patients should not exceed a total dose of the lesser of 10 units/kg or 340 units in a 3-month interval.[2] Recommendations for maximum dosing and frequency for Dysport are based on a suggested relative conversion of 3:1 between Dysport and Botox units.[6] Additionally, the maximum dose supported for a patient < 18 years of age in Dysport labeling is 30 units/kg (not to exceed 1,000 units).[1] Specific considerations by indication are noted below.

- **Blepharospasm:** A maximum dose of 120 units of Dysport, not more frequently than once every 12 weeks, has been suggested.[20,21]
- **Sialorrhea, Chronic:** Xeomin is indicated for this use.[4] Per Xeomin labeling, the maximum recommended dose for adults is 100 units (50 units per side) and for pediatric patients is 75 units (37.5 units per side), administered not more frequently than once every 16 weeks.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Dysport. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication(s). All approvals are provided for 1 year in duration. In cases where the dosing interval is provided in months, 1 month is equal to 30 days.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

1. **Cervical Dystonia.**
   (Note: Cervical dystonia is also known as spasmodic or cervical torticollis.)

Criteria. Approve for 1 year.

Dosing. Approve up to a maximum dose of 1,000 units, administered not more frequently than once every 12 weeks.

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2. Spasticity, Limb.

Note: For other forms of spasticity that do not fit this condition of approval, see Other Uses with Supportive Evidence, Spasticity.

Criteria. Approve for 1 year.

Dosing. Approve the following regimens (A or B):

A) Lower limb spasticity (or combined upper and lower limb spasticity): Approve one of the following regimens (i or ii):
- **i.** Patient is ≥ 18 years of age: Approve up to a maximum dose of 1,500 units, administered not more frequently than once every 12 weeks.
- **ii.** Patient is < 18 years of age: Approve up to a maximum dose of 30 units/kg (not to exceed 1,000 units), administered not more frequently than once every 12 weeks.

B) Upper limb spasticity: Approve one of the following regimens (i or ii):
- **i.** Patient is ≥ 18 years of age: Approve up to a maximum dose of 1,000 units, administered not more frequently than once every 12 weeks.
- **ii.** Patient is < 18 years of age: Approve up to a maximum dose of 16 units/kg (not to exceed 640 units), administered not more frequently than once every 12 weeks.

Other Uses with Supportive Evidence

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3. Anal Fissure.

Criteria. Approve for 1 year.

Dosing. Approve one of the following regimens (A or B):

A) Patient is ≥ 18 years of age: Approve up to a maximum dose of 1,200 units, administered not more frequently than once every 3 months.

B) Patient is < 18 years of age: Approve up to a maximum dose of 30 units/kg (not to exceed 1,000 units), administered not more frequently than once every 3 months.

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4. Achalasia.

Criteria.[22] Approve for 1 year if the patient meets ONE of the following criteria (A, B, C, D, E, or F):

A) Patient has not responded satisfactorily to at least one conventional therapy; OR

B) Patient is at high risk of complication from pneumatic dilation or surgical myotomy; OR

C) Patient had treatment failure with pneumatic dilation or surgical myotomy; OR

D) Patient had perforation from pneumatic dilation; OR

E) Patient has an epiphrenic diverticulum or hiatal hernia; OR

F) Patient has esophageal varices.

Dosing.[20] Dosing is 50-unit (up to 400 units total dose) injections to each quadrant of the lower esophageal sphincter 1 month before pneumatic dilatation

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5. Blepharospasm.

Criteria. Approve for 1 year.

Dosing. Approve up to a maximum dose of 120 units, administered not more frequently than once every 12 weeks.

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6. Sialorrhea, Chronic.

Criteria. Approve for 1 year.

Dosing. Approve one of the following regimens (A or B):
A) Patient is ≥ 18 years of age: Approve up to a maximum dose of 300 units (150 units per side), administered not more frequently than once every 16 weeks.
B) Patient is < 18 years of age: Approve up to a maximum dose of 225 units (112.5 units per side), administered not more frequently than once every 16 weeks.

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7. Spasticity, other than Limb (e.g., spasticity secondary to spastic hemiplegia,[22] hemiparesis,[22] hemifacial spasm).
Note: For limb spasticity, refer to FDA-Approved Indications above.

Criteria. Approve for 1 year.

Dosing. Approve the following regimens (A or B):
A) Patient is ≥ 18 years of age: Approve up to a maximum dose of 1,200 units, administered not more frequently than once every 3 months.
B) Patient is < 18 years of age: Approve up to a maximum dose of 30 units/kg (not to exceed 1,000 units), administered not more frequently than once every 3 months.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Dysport has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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 under the Medicare benefit.[37]

2. 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. Dysport® injection [prescribing information]. Cambridge, MA and Fort Worth, TX: Ipsen/Galderma; July 2020.
2. Botox® injection [prescribing information]. Madison, NJ: Allergan; August 2022.
3. Smith CP, Chancellor MB. Emerging role of botulinum toxin in the management of voiding dysfunction. *J Urol*. 2004;17(6 Pt 1):2128-2137.
4. Xeomin® injection [prescribing information]. Raleigh, NC: Merz; August 2021.
5. Walker TJ, Dayan SH. Comparison and overview of currently available neurotoxins. *J Clin Aesthet Dermatol.* 2014;7(2):31-39.
6. Scaglione F. Conversion ratio between Botox®, Dysport®, and Xeomin® in clinical practice. *Toxins (Basel)*. 2016;8(3):65.
7. Brisinda G, Bentivoglio AR, Maria G, et al. Treatment with botulinum neurotoxin of gastrointestinal smooth muscles and sphincters spasms. *Mov Disord*. 2004;19(Suppl 8):S146-S156.
8. Friedenberg F, Gollamudi S, Parkman HP. The use of botulinum toxin for the treatment of gastrointestinal motility disorders. *Dig Dis Sci*. 2004;49(2):165-175.
9. 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.
10. Bansal C, Omlin KJ, Hayes CM, et al. Novel cutaneous uses for botulinum toxin type A. *J Cosmet Dermatol*. 2006;5(3):268-272.
11. Cheng CM, Chen JS, Patel RP. Unlabeled uses of botulinum toxins: A review, part 2. *Am J Health Syst Pharm*. 2006;63(3):225-232.
12. Truong D, Comella C, Fernandez HH, et al.; Dysport Benign Essential Blepharospasm Study Group. 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 Relat Disord*. 2008;14(5):407-14.
13. Kollewe K, Mohammadi B, Köhler S, et al. Blepharospasm: long-term treatment with either Botox®, Xeomin® or Dysport®. *J Neural Transm*. 2015;122(3):427-31.
14. 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.
15. Naumann M, So Y, Argoff AE, 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;70:1707-1714.
16. Bhidayasiri R, Truong DD. Expanding use of botulinum toxin. *J Neurol Sci*. 2005;235(1-2):1-9.
17. Tan EK. Botulinum toxin treatment of sialorrhea: comparing different therapeutic preparations. *Eur J Neurol.* 2006;13 (Suppl 1):60-64.
18. Sheffield JK, Jakovic J. Botulinum toxin in the treatment of tremors, dystonias, sialorrhea and other symptoms associated with Parkinson's disease. *Expert Rev Neurotherapeutics.* 2007;7(6):637-647.
19. 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.
20. Micromedex®. IBM Corporation. Available at: http://www.micromedexsolutions.com Accessed on January 9, 2023. Search terms: Dysport.
21. Clinical Pharmacology [database online]. Tampa, FL: Elsevier, Inc.; 2022. Available at: https://www.clinicalkey.com/pharmacology/. Accessed on January 9, 2023. Search terms: Dysport.
22. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Determination: Botulinum Toxins (LCD L33646) (Original effective date 10/1/2015; revision effective date 05/01/2021). Accessed on February 21, 2023.
23. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Article: Billing and Coding: Botulinum Toxins (A52848) (Original effective date 10/1/2015; revision effective date 1/5/2023). Accessed on February 21, 2023.

HISTORY

Type of Revision	Summary of Changes	Date
Policy created	New Medicare Advantage Medical Policy	07/11/2018
Policy revision	Statement added to dosing to allow for approval of doses that are below the recommended maximum daily dose for each indication.	n/a
Policy revision	Removed the following criterion: "For all approvable indications, failure of two definitive, consecutive, treatment sessions involving a muscle or group of muscles could preclude further coverage of the serotype/product used in the treatment for a period of one year after the second session. It may be reasonable, however, to attempt treatment with a different serotype." L33646 provides this verbiage and it has since been interpreted as optional criterion	n/a

	because of the 'could' language. Not required to issue approval or denial but can be used when considering an appeal.	
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Determination L33646 and Botulinum Toxin - Dyspot Utilization Review Policy.	08/28/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Policy revision	• "Cervical Dystonia (torticollis)" updated to "Cervical Dystonia (spasmodic torticollis)". • Pediatric dosing added for "Spasticity, Upper Limb" in accordance with updated FDA labeling. • Clarified "adults" as ≥ 18 years of age and "pediatric patients" as < 18 years of age for lower and upper limb spasticity dosing. • Removed spastic conditions of smooth muscle from conditions not recommended for approval	06/09/2020
Policy revision	**Cervical Dystonia:** The phrase "spasmodic torticollis" was removed from the approval condition. **Spasticity, Limb:** The approval conditions of "Spasticity, Lower Limb" and "Spasticity, Upper Limb" were rolled together into this approval condition. **Coverage was added for the following indications:** Anal Fissure, Hyperhidrosis, Gustatory, Chronic Sialorrhea, Spasticity, other than Limb **Hyperhidrosis, Gustatory:** The approval condition was reworded to as listed; previous this was titled "Frey's Syndrome (gustatory sweating)". A Note was added that gustatory hyperhidrosis is also referred to as Frey's Syndrome. **Hyperhidrosis, Primary Axillary:** Examples of topical agents were moved to a Note. **Cosmetic Uses:** Examples were removed from the Condition Not Recommended for Approval into a Note. **Dosing:** In "Spasticity, Lower Limb" pediatric dosing, clarification was added that this dosing also applies to combined lower and upper limb spasticity. Reference to unilateral vs. bilateral lower limb injections was removed, and the maximum dose of 15 units/kg for unilateral lower limb injections was removed. In dosing for "Sialorrhea, Chronic", dosing was updated to reflect the maximum dose of 225 units (112.5 units per side) for a patient < 18 years of age (extrapolated from Xeomin labeling). In the following Other Uses with Supportive Evidence, the dosing was updated such that the maximum dose for patients < 18 years of age is the lesser of 30 units/kg or 1,000 units in 3 months (adult maximum dosing remains unchanged at 1,200 units in 3 months): Anal Fissure; Hyperhidrosis, Gustatory; and Spasticity, other than Limb. Under the condition of Spasticity, other than Limb, the dosing specific to hemifacial spasm was	08/17/2021

	removed from the policy; the same dosing is now applied to hemifacial spasm as for other forms of Spasticity, other than Limb.	
Policy revision	**Hyperhidrosis, Gustatory:** This Other Use with Supportive Evidence was removed from the policy. **Hyperhidrosis, Primary Axillary:** This Other Use with Supportive Evidence was removed from the policy. **Spasticity other than limb:** removed examples of cerebral palsy, brain injury, spinal cord injury, multiple sclerosis. Added examples of spastic hemiplegia, hemiparesis.	02/23/2023