POLICY: Botulinum Toxin – Dysport® (abobotulinumtoxinA for injection – Ipsen)

DATE REVIEWED: 06/03/2020

OVERVIEW

Dysport® (abobotulinumtoxinA), is indicated for the following:

- Treatment of cervical dystonia in adults;
- Treatment of upper and lower limb spasticity in adults;
- Treatment of upper limb spasticity in pediatric patients ≥ 2 years of age, excluding spasticity caused by cerebral palsy; and
- Treatment of lower limb spasticity in pediatric patients ≥ 2 years of age.[1]

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 (anal sphincter):** 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 ACG clinical guideline for the management of benign anorectal disorders (2014) recommends the use of botulinum toxin therapy or surgical internal anal sphincterotomy in patients who do not respond to conservative or topical pharmacologic agents, such as a calcium channel blockers or nitrates.[9]
- **Blepharospasm:** Dysport has demonstrated efficacy in clinical trials in patients with blepharospasm.[12,13] AAN guidelines (2016) support the use of Dysport for blepharospasm with a Level C recommendation ("possibly effective").[14]
- **Frey's Syndrome (gustatory sweating):** Botulinum toxin A has been successfully used to treat gustatory sweating. Dysport demonstrated efficacy in two small trials in a total of 53 patients with gustatory sweating.[15] American Academy of Neurology (AAN) guidelines state that botulinum toxin is possibly effective and may be considered for this use (Level C).[16]
- **Hyperhidrosis, Primary Axillary:** Topical antiperspirants (e.g., topical aluminum chloride) or Qbrexza are the recommended first-line therapy for the treatment of primary axillary hyperhidrosis.[17-20] The efficacy of Dysport for axillary hyperhidrosis was demonstrated in one randomized, double-blind, multicenter study in patients (n = 145) unresponsive to topical therapy

with aluminum chloride (10% or 20%).[21] A significant ($P < 0.001$) decrease in sweat production vs. placebo occurred 2 weeks post-injection and was maintained 24 weeks post-injection.

- **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 amytrophic lateral sclerosis (ALS).[22-24] Data with Dysport come from two small controlled trials.[22,23] AAN guidelines state that botulinum toxin is probably safe and effective and should be considered (Level B).[16]
- **Spasticity, Other Than Lower and Upper Limb (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis, hemifacial spasm):** Oral medications have a long history in spasticity treatment (e.g., baclofen, benzodiazepines, tizanidine, dantrolene, phenytoin, or gabapentin) yet they have dose-limiting side effects and limited diffusion across the blood brain barrier.[25] Several randomized, controlled trials have evaluated the efficacy of Dysport in spasticity of various etiologies in both upper and lower limbs.[11,25-27] Other randomized, controlled trials evaluated botulinum toxin A for the management of upper limb spasticity in children with cerebral palsy and showed significant improvement in spasticity/tone, range of motion, and functional gains after botulinum toxin A injections.[28] Treatment with botulinum toxin A in hemifacial spasm appears to remain effective over long-term use of several years (4 to 10 years); most cases do not require a dosage increase.[29] In an observational study, patients (n = 133) with hemifacial spasm and reinnervation synkinesias were exclusively treated with either Dysport or Botox for 6 years; Botox and Dysport were similarly effective and the therapeutic effect was stable throughout the observation period.[30]

Dosing Considerations

Definitive dosing has not been established for off-label uses of botulinum toxins, including Dysport. Recommendations for maximum dosing and frequency for Dysport are based on a suggested relative conversion of 3:1 between Dysport and Botox units.**Error! Bookmark not defined.** 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 not to exceed a total dose of 400 units in a 3-month interval.[2]

- **Blepharospasm:** A maximum dose of 120 units of Dysport, not more frequently than once every 12 weeks, has been suggested.[31,32]
- **Hyperhidrosis, Primary Axillary:** A maximum dose of 200 units per axilla, not more frequently than once every 12 weeks, is supported in compendia.[32]
- **Sialorrhea, Chronic:** Xeomin is indicated for this use at a dose of 100 units (50 units per side), administered not more frequently than once every 16 weeks.[4]
- **Spasticity, Other Than Lower and Upper Limb (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis, hemifacial spasm):** A maximum dose of 220 units of Dysport is supported for hemifacial spasm.[31]

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). Requests for doses outside the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). 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.

Medical benefit coverage is not recommended for cosmetic conditions.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

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

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, Lower Limb. Approve for 1 year.
(Note: For other forms of spasticity that do not fit this condition of approval, see Other Uses with Supportive Evidence, Spasticity.)

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

A) For adults (≥ 18 years of age) with lower limb spasticity (or combined lower and upper limb spasticity): Approve up to a maximum dose of 1,500 units, administered not more frequently than once every 12 weeks.

B) For pediatric patients (< 18 years of age) with lower limb spasticity: Approve up to 15 units/kg for unilateral lower limb injections (not to exceed 1,000 units) or 30 units/kg for bilateral lower limb injections (not to exceed 1,000 units), administered not more frequently than once every 12 weeks.

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3. Spasticity, Upper Limb. Approve for 1 year.
(Note: For other forms of spasticity that do not fit this condition of approval, see Other Uses with Supportive Evidence, Spasticity.)

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

A) For adults (≥ 18 years of age): Approve up to a maximum dose of 1,000 units, administered not more frequently than once every 12 weeks.

B) For pediatric patients (< 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

4. Anal Fissure (anal sphincter). Approve for 1 year.

Dosing. Approve up to a maximum dose of 1,200 units, administered not more frequently than once every 3 months.

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5. Blepharospasm. 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. Frey's Syndrome (gustatory sweating). Approve for 1 year.

Dosing. Approve up to a maximum dose of 1,200 units, administered not more frequently than once every 3 months.

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7. Hyperhidrosis, Primary Axillary. Approve for 1 year if the patient has tried at least one topical agent (e.g., topical aluminum chloride, Qbrexza™ [glycopyrronium cloth 2.4% for topical use]).

Dosing. Approve up to a maximum dose of 200 units per axilla, administered not more frequently than once every 12 weeks.

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8. Sialorrhea, Chronic. Approve for 1 year.

Dosing. Approve up to a maximum dose of 300 units (150 units per side), administered not more frequently than once every 16 weeks.

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9. Spasticity, Other Than Lower and Upper Limb (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis, hemifacial spasm). Approve for 1 year.
(Note: For lower limb spasticity and upper limb spasticity, see FDA-Approved Indications criteria #2 and #3 [above]).

Dosing. Approve the following regimens (A or B):
A) For hemifacial spasm: Approve up to a maximum dose of 220 units, administered not more frequently than once every 3 months.[34]
B) For other forms of spasticity: Approve up to a maximum dose of 1,200 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 (e.g., facial rhytides, frown lines, glabellar wrinkling, horizontal neck rhytides, mid and lower face and neck rejuvenation, platsymal bands, 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. Fibromyalgia. Limited data are available with Botox. No data are available with Dysport at this time.

3. Ophthalmic Disorders, Other Than Blepharospasm (e.g., esotropia, exotropia, nystagmus, facial nerve paresis). More data are needed to define the place of therapy of Dysport in the treatment of ophthalmic disorders. Botulinum toxin A has been successful in improving or treating many ophthalmic disorders. Retrospective reviews conclude that botulinum toxin A may have a role in the treatment of exotropia.[33,34] Dysport improved visual acuity in patients with acquired symptomatic nystagmus from multiple sclerosis or brain-stem hemorrhage in one case series (n = 12).[35] Data from an uncontrolled study have shown Dysport to be beneficial in the treatment of fourth nerve palsy.[36]

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

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HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New policy	--	8/08/2018
Selected revision	Dosing updated throughout policy to simplify maximum approved dosing regimens.	12/05/2018
Early annual revision	**Cervical Dystonia:** Clarification note that cervical dystonia is also known as spasmodic or cervical torticollis. **Spasticity, Lower Limb** and **Spasticity, Upper Limb:** Approval conditions reworded and reorganized. Previously, these were grouped as "Spasticity, Adult" and "Spasticity, Pediatric". Clarification note to refer to Spasticity, Other Than Lower and Upper Limb for other forms of spasticity. **Spasticity, Other Than Lower and Upper Limb (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis, hemifacial spasm):** "Other than lower and upper limb" added to clarify this covers uses other than the FDA-approved indications. Also, "e.g." changed to "i.e.".	05/08/2019
Annual revision	**FDA-Approved Indications:** • "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. **Other Uses with Supportive Evidence:** • "Salivary Hypersecretion" updated to "Sialorrhea, Chronic."	06/03/2020