

**PHARMACY PRIOR AUTHORIZATION
Clinical Guideline Botulinum toxins**

Botox® (onabotulinumtoxinA), Dysport™ (abobotulinumtoxinA), Xeomin® (incobotulinumtoxinA) and Myobloc® (rimabotulinumtoxinB)

FDA Indications (non-cosmetic uses)				
Indication	Dysport (abobotulinumtoxin A)	Botox (onabotulinumtoxin A)	Xeomin (incobotulinumtoxin A)	Myobloc (rimabotulinumtoxin B)
Cervical Dystonia	X	X	X	X
Blepharospasm	Off-label use*	X	X	
Upper limb spasticity		X		
Severe primary Axillary Hyperhidrosis	Off-label use*	X		
Migraine prophylaxis		X		
Hemifacial spasm	Off-label use*			
Strabismus		X		
Focal spasticity in pediatric patients with cerebral palsy with concurrent equinus gait (tiptoeing)		Off-label use*		
Classical Achalasia		Off-label use*		
Second line treatment for neurogenic bladder		X		
Sialorrhea		Off-label use*		Off-label use*

*Off-label use based on peer-reviewed clinical studies

Dosage Forms
Dysport: 300 unit and 500 unit powder for intramuscular, intradermal and subcutaneous



injection

Botox: 100 unit and 200 unit powder for intradermal or intramuscular injection

Xeomin: 50 unit and 100 unit powder for intramuscular injection

Myobloc: 2500 unit/0.5 mL, 5000 unit/mL, 10,000 unit/2 mL solution for intramuscular injection

Dosage

• Dysport

- **Cervical dystonia (muscle spasm causing abnormal head position and neck pain):** 500 units given intramuscularly as a divided dose among the affected muscles every 12-16 weeks
- **Blepharospasm* (eyelid muscle spasm):** The recommended initial dose in the UK is 120 units SC per eye: 20 units SC made medially and 40 units SC made laterally into the junction between the preseptal and orbital parts of both the upper and lower orbicularis oculi muscles of each eye. Injections may be repeated every 12 weeks.
- **Hemifacial spasm*:** 120 units SC to the affected eye: 20 units SC made medially and 40 units SC made laterally into the junction between the preseptal and orbital parts of both the upper and lower orbicularis oculi muscles of the affected eye every 12 weeks.
- **Severe primary axillary hyperhidrosis (excessive sweating)*:** 100 units intradermally per axilla; may be increased to up to 200 units per axilla if desired response is not achieved. The maximum effect may be expected within two weeks after injection. Injections may be repeated if needed, but not more often than every 12 weeks.

• Botox

- **Cervical dystonia (muscle spasm causing abnormal head position and neck pain):** mean dose in phase III studies was 236 U IM (range 198 U to 300 U) divided among the affected muscles. Dosing in initial and sequential treatment sessions should be tailored to the individual patient based on head and neck position, localization of pain, muscle hypertrophy, patient response, and adverse event history. Patients without prior use of botulinum toxin should be started with a lower initial dose, with subsequent dosing adjusted based on individual response.
- **Migraine prophylaxis:** The recommended dose for treating chronic migraine is 155 units administered intramuscularly (IM) divided across 7 specific head/neck muscle areas (31 different sites) every 12 weeks.
 - Frontalis: 20 units divided in 4 sites
 - Corrugator: 10 units divided into 2 sites
 - Procerus: 5 units in 1 site
 - Occipitalis: 30 units divided in 6 sites
 - Temporalis: 40 units divided in 8 sites
 - Trapezius: 30 units divided in 6 sites
 - Cervical Paraspinal Muscle group: 20 units divided in 4 sites
- **Upper limb spasticity:** Doses in clinical trials ranged from 75 Units to 360 Units and were divided among selected muscles at a given treatment session. The lowest recommended starting dose should be used. Generally, do not administer more than 50



units per site (see specific dose range per muscle below). Repeat doses may be administered when the effect of a previous injection has diminished; however, generally, do not give more often than every 12 weeks. Upon re-injection, the degree and pattern of muscle spasticity may necessitate alterations in the dose of onabotulinumtoxin A and muscles to be injected.

- Biceps Brachii: 100—200 Units divided in 4 sites
 - Flexor Carpi Radialis: 12.5—50 Units in 1 site
 - Flexor Carpi Ulnaris: 12.5—50 Units in 1 site
 - Flexor Digitorum Profundus: 30—50 Units in 1 site
 - Flexor Digitorum Sublimis: 30—50 Units in 1 site
- **Severe primary axillary hyperhidrosis (excessive perspiration):** 50 units per axilla. Repeat injections for hyperhidrosis should be administered when the clinical effect of a previous injection diminishes.
- **Blepharospasm (eyelid muscle spasm):** initial recommended dose is 1.25—2.5 U (0.05—0.1 ml per site) injected at each site. Each treatment lasts approximately 3 months, after which the procedure can be repeated. At repeat treatment sessions, the dose may be increased up to two-fold if the response from the initial treatment is considered insufficient which is usually defined as an effect that does not last longer than two months. Little benefit appears to be obtained from injecting more than 5 U per site. Some tolerance may be observed when the toxin is administered any more frequently than every 3 months, and is rare to have the effect be permanent. The cumulative dose in a 30-day period should not exceed 200 U.
- **Strabismus [misalignment of the eyes due to an imbalance of the eye muscles (e.g., cross-eyed, horizontal or vertical gaze deviation)]:**
- **Vertical muscles, and for horizontal strabismus of less than 20 prism diopters:** Adults and children \geq 12 years, 1.25—2.5 U IM in any one muscle.
 - **Horizontal strabismus of 20 prism diopters to 50 prism diopters:** Adults and children \geq 12 years, 2.5—5 U IM in any one muscle.
 - **Persistent VI nerve palsy of one month or longer duration:** Adults and children \geq 12 years, 1.25—2.5 U IM in the medial rectus muscle.
 - **Subsequent dosing for residual or recurrent strabismus:** Adults and children \geq 12 years, patients should be re-examined 7—14 days after each injection to assess the effect of that dose. Patients experiencing adequate paralysis of the target muscle that require subsequent injections should receive a dose comparable to the initial dose. For patients experiencing incomplete paralysis of the target muscle, subsequent doses may be increased up to two-fold compared to the previously administered dose. Subsequent injections should not be given until the effects of the previous dose have dissipated as evidenced by substantial function in the injected and adjacent muscles. Maximum recommended dose as a single injection for any one muscle is 25 U.\
- **Chronic management of focal spasticity in pediatric patients (2-18 years of age) with cerebral palsy with concurrent equinus gait (tiptoeing)*:** In one study, 155 children aged 2—18 years with cerebral palsy and exhibiting equinus foot deformity



received IM injections of botulinum toxin type A for at least 1 year. A total dose of 4 U/kg IM (maximum dose 200 units per treatment) was administered every 3 months.

- **For the treatment of classical achalasia* (lower esophageal sphincter spasm):** 80 Units injected into the lower esophageal sphincter.
- **For second-line treatment of neurogenic bladder:** Adults: maximum dose is 200 Units injected into the detrusor muscle using 30 injections, sparing the trigone. Children*: Drug was evaluated in children with myelomeningocele and neurogenic bladder. A dose of 12 Units/kg (maximum 300 Units) was injected into the detrusor muscle using 30—50 injections, sparing the trigone.
- **Sialorrhea (excessive drooling) associated with neurological disorders (i.e., Parkinson's disease, amyotrophic lateral sclerosis, cerebral palsy)*:** doses from 10—65 Units have been injected into parotid and submandibular glands; results appear to be best when injections are combined with ultrasonic guidance.

- **Xeomin**

- **Cervical dystonia to decrease the severity of abnormal head position and neck pain in both botulinum toxin-naive and botulinum toxin-experienced patients:** 120 units IM divided and injected into affected muscles (e.g., sternocleidomastoid, levator scapulae, splenius capitis, scalenus, trapezius) is recommended. Dosing more frequent than every 12 weeks is generally not recommended.
- **Blepharospasm in patients who were previously treated with onabotulinumtoxinA (Botox):** 1.25 to 2.5 units/injection. Do not exceed 35 units/eye. Each treatment is expected to last approximately 12 weeks, after which the procedure can be repeated; do not dose more frequently than every 12 weeks.

- **Myobloc**

- **Cervical dystonia (muscle spasm causing abnormal head position and neck pain):** the recommended initial dose of for patients with a prior history of tolerating botulinum toxin injections is 2500 to 5000 U divided among affected muscles. The duration of effect in patients responding to treatment has been observed in studies to be between 12 and 16 weeks at doses of 5000 U or 10,000 U.
- **For the treatment of sialorrhea (excessive drooling) associated with neurological disorders (e.g., Parkinson's disease)*:**
Intramuscular dosage: Sixteen patients with problematic sialorrhea due to Parkinson's disease were randomized between rimabotulinumtoxinB (1000 units injected into each parotid gland and 250 units into each submandibular gland) and pH-matched placebo.

*Off-label use based on peer-reviewed clinical studies

Authorization Guidelines

Prior authorization personnel will review the request for prior authorization and apply the clinical guidelines to assess the medical necessity of the request for a prescription for Dysport, Botox, Xeomin, and Myobloc. If the guidelines are met, the reviewer will prior authorize the prescription. If the guidelines are not met, the prior authorization request will be referred to a physician reviewer for a medical necessity determination. Such a request for prior authorization will be approved when, in the professional judgment of the physician reviewer, the services are medically necessary to meet the



medical needs of the recipient.

For patients who meet all of the following:

- **No hypersensitivity to botulinum toxin preparation or to any of the components in the formulation**
- **Is not being used for cosmetic purposes (benefit exclusion)**
- **Botulinum toxin is prescribed by appropriate specialist per indication (e.g. neurologist, headache specialist)**
- **Xeomin not to be used in Botox-naïve patients.**
- **Not being used during pregnancy; may cause fetal harm**
 - Botulinum toxin is classified in FDA pregnancy risk category C.
- **Used for appropriate indication based on agent used:**
 - **Upper limb spasticity and hemifacial spasm*:**
 - Medical records documenting diagnosis
 - Trial and failure of at least two formulary muscle relaxants including baclofen and tizanidine
 - **Cervical dystonia, blepharospasm, strabismus and achalasia*:** medical records documenting diagnosis
 - **Severe primary axillary hyperhidrosis**
 - Medical records documenting diagnosis, exclusion of secondary causes of hyperhidrosis, and medical complications such as skin maceration with secondary skin infections, **and**
 - Trial and failure of at least two consecutive months of topical aluminum chloride 20%
 - **Chronic management of focal spasticity in pediatric patients (2-18 years of age) with cerebral palsy with concurrent equinus gait (tiptoeing)*:** medical records documenting diagnosis. **Note:** FDA issued an early communication in 2008 about an ongoing safety review regarding Botox and Botox Cosmetic. FDA has received reports of systemic adverse reactions including respiratory compromise and death following the use of botulinum toxins types A and B for both FDA-approved and unapproved uses. The most serious cases had outcomes that included hospitalization and death, and occurred mostly in children treated for cerebral palsy-associated limb spasticity. The pediatric botulism cases occurred in patients less than 16 years old, with reported symptoms ranging from dysphagia to respiratory insufficiency requiring gastric feeding tubes and ventilatory support. Serious outcomes included hospitalization and death. The most commonly reported use of botulinum toxin among these cases was treatment of limb muscle spasticity associated with cerebral palsy. For Botox, doses ranged from 6.25 to 32 Units/kilogram (U/kg) in these cases. For Myobloc, reported doses were from 388 to 625 U/kg. The FDA will communicate to the public its conclusions, resulting recommendations, and any regulatory actions after the review of the data are completed.
 - **Migraine prophylaxis:**



- Requires clinical notes documenting chronic migraine diagnosis, **and**
 - Documented frequency of more than 15 migraine headaches in a 30 day period with each headache lasting 4 hours or longer, **and**
 - Documented failure or intolerance to 2 different classes of formulary medications used for migraine prophylaxis: e.g. beta-blocker, calcium channel blocker, anticonvulsant, tricyclic antidepressants
- **For second-line treatment of neurogenic bladder:**
- Medical records documenting diagnosis, **and**
 - Trial and failure of first-line agents, such as oxybutynin and Vesicare
- **Sialorrhea (excessive drooling) associated with neurological disorders (i.e., Parkinson's disease, amyotrophic lateral sclerosis, cerebral palsy)*:**
- Medical records documenting diagnosis, **and**
 - Trial and failure of oral or topical agents (e.g., glycopyrrolate, scopolamine)

* Off-label use

Prior Authorization Requirements

Initial Approval

- 1 treatment
- Dose and injection sites must be clearly documented in clinical notes (i.e., units injected per site)

Renewal

- Up to 4 treatments per 12 month period, spaced at least 3 months apart
- Medical records supporting response to therapy
- Review of Rx history
- Dose and injection sites must be clearly documented in clinical notes (i.e., units injected per site)

Additional Information

Black Box Warning:

WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of BOTOX and 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 at lower doses.

Important limitations:

- The potency units of individual botulinum products are specific to the preparation and assay



method utilized. They are not interchangeable with other preparations of botulinum toxin products and therefore, cannot be compared to or converted into units of any other botulinum toxin products.

- Safety and efficacy have not been shown for treatment of lower limb spasticity
- Not for use in joints affected by a fixed contracture
- Not for use in presence of active infection at proposed injection sites
- Patients being treated for cervical dystonia who have smaller neck muscle mass and patients who require bilateral injections into the sternocleidomastoid muscles are at greater risk of dysphagia. Limiting the dose injected into the sternocleidomastoid muscle may decrease the occurrence of dysphagia.
- Reduced blinking from injection of botulinum toxin products in the orbicularis muscle can lead to corneal exposure, persistent epithelial defect and corneal ulceration, especially in patients with VII nerve disorder.
- Dysport contains human albumin and carries an extremely remote risk for transmission of viral diseases.

References

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