Clinical Policy: OnabotulinumtoxinA (Botox)

Reference Number: ERX.SPA.192
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Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
OnabotulinumtoxinA (Botox®) is an acetylcholine release inhibitor and a neuromuscular blocking agent.

FDA Approved Indication(s)

Indication	Adults	Pediatrics	Treatment	Prophylaxis
Overactive bladder	X		X	
Urinary incontinence	X		X	
Migraine	X			X
Upper/lower limb spasticity (includes CP)	X	X	X	
Cervical dystonia (focal dystonia)	X	X	X	
Axillary hyperhidrosis	X		X	
Blepharospasm (focal dystonia)	X	X	X	
Strabismus	X	X	X	
Off-Label Uses				
Laryngeal dystonia*	X		X	
Oromandibular dystonia*	X		X	
Upper extremity dystonia*	X	X	X	
Upper extremity essential tremor*	X		X	
Esophageal achalasia	X		X	
HD and IAS achalasia	X	X	X	
Chronic anal fissure	X		X	

Abbreviations: cerebral palsy (CP); Hirschsprung disease (HD), internal anal sphincter (IAS) achalasia.
**See criteria set entitled Focal Dystonia and Essential Tremor*

Botox is indicated for:
- Treatment of:
  - Overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication
  - Urinary incontinence due to detrusor over-activity associated with a neurologic condition [e.g., spinal cord injury (SCI), multiple sclerosis (MS)] in adults who have an inadequate response to or are intolerant of an anticholinergic medication
  - Neurogenic detrusor overactivity (NDO) in pediatric patients 5 years of age and older who have an inadequate response to or are intolerant of anticholinergic medication
  - Spasticity in patients 2 years of age and older
  - Cervical dystonia (CD) in adult patients, to reduce the severity of abnormal head position and neck pain
  - Severe axillary hyperhidrosis that is inadequately managed by topical agents in adult patients
  - Blepharospasm associated with dystonia in patients ≥ 12 years of age
  - Strabismus in patients ≥ 12 years of age
- Prophylaxis of headaches in adult patients with chronic migraine (≥ 15 days per month with headache lasting 4 hours a day or longer)

Limitation(s) of use:
- Safety and effectiveness of Botox have not been established for:
  - Prophylaxis of episodic migraine (14 headache days or fewer per month)
  - Treatment of hyperhidrosis in body areas other than axillary
  - Treatment of axillary hyperhidrosis in pediatric patients under 18 year of age

- Botox has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

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It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Botox is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Overactive Bladder and Urinary Incontinence (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. OAB, and member's history is positive for urinary urgency, frequency, and nocturia with or without incontinence;
   b. Urinary incontinence, and member's history is positive for an associated neurologic condition (e.g., spinal cord injury, spinal dysraphsim, multiple sclerosis);
2. Prescribed by or in consultation with a neurologist or urologist;
3. Age ≥ 5 years;
4. For adult and pediatric patients, failure of a trial of at least two anticholinergic agents *(see Appendix B)*, each used for at least 30 days, unless clinically significant adverse effects are experienced or all are contraindicated;
5. For adult patients, failure of a 30-day trial of one oral beta-3 agonist medication *(see Appendix B)*, unless clinically significant adverse effects are experienced or all are contraindicated;

6. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
7. Treatment plan details number of Units per indication and treatment session;
8. Request meets one of the following (a or b):
   a. OAB: Dose does not exceed 100 Units per treatment session;
   b. Urinary incontinence associated with a neurologic condition:
      i. Weight ≥ 34 kg: dose does not exceed 200 Units per treatment session;
      ii. Weight < 34 kg: dose does not exceed 6 units/kg per treatment session.

Approval duration: 12 weeks (single treatment session)

B. Chronic Migraine (must meet all)**:**

1. Diagnosis of chronic migraine (i.e., ≥ 15 headache days per month for at least 3 months with headache lasting 4 hours a day or longer);
2. Prescribed by or in consultation with a neurologist or pain specialist;
3. Age ≥ 18 years;
4. Failure of at least 2 of the following oral migraine preventative therapies, each for 8 weeks and from different therapeutic classes, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, or c):
   a. Antiepileptics (e.g., divalproex sodium, sodium valproate, topiramate);
   b. Beta-blockers (e.g., metoprolol, propranolol, timolol);
   c. Antidepressants (e.g., amitriptyline, venlafaxine);
5. Member meets all of the following (a, b, and c):
   a. Botox is not prescribed concurrently with injectable calcitonin gene-related peptide (CGRP) inhibitors (e.g., Aimovig®, Ajovy®, Emgality®);
   b. Botox is not prescribed concurrently with other botulinum toxin products;
   c. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan details number of Units per indication and treatment session;
7. Dose does not exceed 155 Units per treatment session.

Approval duration: 24 weeks (two 12-week treatment sessions)

C. Upper and Lower Limb Spasticity *(includes cerebral palsy)* (must meet all)**:**

1. Diagnosis of upper or lower limb spasticity (e.g., associated with paralysis, central nervous system demyelinating diseases such as multiple sclerosis, cerebral palsy, stroke);
2. Prescribed by or in consultation with a neurologist, orthopedist, or physiatrist;
3. Age ≥ 2 years;
4. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
5. Treatment plan details number of Units per indication and treatment session;
6. Request meets one of the following (a or b):
   a. Age ≥ 18 years: Upper and/or lower limb: Dose does not exceed 400 Units per treatment session;
   b. Age 2 through 17 years (i, ii, and iii):
      i. Upper limb: Dose does not exceed the lower of 6 Units/kg body weight or 200 Units per treatment session;
      ii. Lower limb: Dose does not exceed the lower of 8 Units/kg body weight or 300 Units per treatment session;
      iii. If upper and lower limb spasticity are treated in the same treatment session, number of Units per treatment session does not exceed the lower of 10 Units/kg body weight or 340 Units per treatment session.

Approval duration: 12 weeks (single treatment session)

D. Cervical Dystonia *(focal dystonia)* (must meet all):
1. Diagnosis of CD;
2. Prescribed by or in consultation with a neurologist, orthopedist, or physiatrist;
3. Age ≥ 16 years;
4. Member is experiencing involuntary contractions of the neck and shoulder muscles (e.g., splenius capitis, sternocleidomastoid, levator scapulae, scalene, trapezius, semispinalis capitis) resulting in abnormal postures or movements of the neck, shoulders or head;
5. Contractions are causing pain and functional impairment;
6. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
7. Treatment plan details number of Units per indication and treatment session;
8. Request meets one of the following (a or b):
   a. Age ≥ 18 years: Dose does not exceed 100 Units total in the sternocleidomastoid (SCM) muscle and 300 Units per treatment session;
   b. Age 16 through 17 years: Dose does not exceed 100 Units total in the SCM muscle and the lower of 10 Units/kg body weight or 300 Units per treatment session.

Approval duration: 12 weeks (single treatment session)

E. Primary Axillary Hyperhidrosis *(excessive underarm sweating)* (must meet all)**:**
1. Diagnosis of primary axillary hyperhidrosis;
2. Prescribed by or in consultation with a neurologist or dermatologist;
3. Age ≥ 18 years;
4. Failure of a 6-month trial of topical aluminum chloride, unless contraindicated or clinically significant adverse effects are experienced;
5. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan details number of Units per indication and treatment session;
7. Dose does not exceed 100 Units per treatment session.

Approval duration: 12 weeks (single treatment session)

F. Blepharospasm *(focal dystonia - abnormal eyelid muscle contraction)* (must meet all)***:***
1. Diagnosis of blepharospasm;
2. Prescribed by or in consultation with a neurologist or ophthalmologist;
3. Age ≥ 12 years;
4. Member is experiencing significant disability in daily functional activities due to interference with vision;
5. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan details number of Units per indication and treatment session;
7. Dose does not exceed 2.5 Units per muscle, 7.5 Units per eye, and 15 Units per treatment session.

Approval duration: 12 weeks (single treatment session)

G. Strabismus *(eye misalignment)* (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. Vertical strabismus (superior and inferior rectus muscles, superior and inferior oblique muscles);
   b. Horizontal strabismus (medial and lateral rectus muscles) (i or ii):
      i. Horizontal strabismus < 20 prism diopters;
      ii. Horizontal strabismus 20 to 50 prism diopters;

c. Persistent sixth cranial nerve (VI; abducens nerve) palsy of ≥ one month involving the lateral rectus muscle;

2. Prescribed by or in consultation with a neurologist or ophthalmologist;
3. Age ≥ 12 years;
4. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
5. Treatment plan details number of Units per indication and treatment session;
6. Request meets one of the following (a, b, or c):
   a. Vertical strabismus, or horizontal strabismus < 20 prism diopters: Dose does not exceed 2.5 Units per muscle and 5 Units per treatment session;
   b. Horizontal strabismus 20 to 50 prism diopters: Dose does not exceed 5 Units per muscle and 10 Units per treatment session;
   c. VI nerve palsy: Dose does not exceed 2.5 Units per treatment session (limited to treatment of one eye).

Approval duration: 12 weeks (single treatment session)

H. Focal Dystonia and Essential Tremor (off-label) (must meet all):

1. Diagnosis of one of the following (a, b, c, or d):
   a. Laryngeal dystonia;
   b. Oromandibular dystonia (OMD);
   c. Upper extremity (UE) dystonia;
   d. UE essential tremor;
2. Prescribed by or in consultation with a neurologist, ENT specialist, orthopedist, or physiatrist;
3. Age meets one of the following (a or b):
   a. For UE dystonia: Age ≥ 2 years;
   b. For all other indications: Age ≥ 18 years;
4. For UE dystonia: Failure of a trial of carbidopa/levodopa or trihexyphenidyl *(see Appendix B),* unless clinically significant adverse effects are experienced or both are contraindicated;
5. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan details number of Units per indication and treatment session;
7. Request meets one of the following (a or b):
   a. Laryngeal dystonia/OMD: Dose does not exceed 25 Units per treatment session;
   b. UE dystonia, UE essential tremor: Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use and member age (*prescriber must submit supporting evidence; Units per treatment session does not exceed the lower of 10 Units/kg body weight or 340 Units for pediatrics, or 400 Units for adults*).

Approval duration: 12 weeks (single treatment session)

I. Esophageal Achalasia (off-label) (must meet all)**:**

1. Diagnosis of esophageal achalasia;
2. Prescribed by or in consultation with a or gastroenterologist;
3. Age ≥ 18 years;
4. Member is not a candidate for pneumatic dilation or laparoscopic surgical myotomy (e.g., due to age, comorbidity);
5. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan details number of Units per indication and treatment session;
7. Dose does not exceed 100 Units per treatment session.

Approval duration: 12 weeks (single treatment session)

J. Hirschsprung Disease, Internal Anal Sphincter Achalasia (off-label) (must meet all):
1. Diagnosis of one of the following (a or b):
   a. Hirschsprung disease (HD) and (i or ii):
      i. Member has an HD subtype known as ultra-short segment HD;
      ii. Botox is prescribed for constipation post-surgery;
   b. Internal anal sphincter (IAS) achalasia;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 2 years;
4. Failure of a trial of stool softeners and laxatives *(see Appendix B)*, unless clinically adverse effects are experienced or all are contraindicated;
5. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan details number of Units per indication and treatment session;
7. Dose does not exceed 100 Units per treatment session.

Approval duration: 12 weeks (single treatment session)

K. Chronic Anal Fissure (off-label) (must meet all)**:**
1. Diagnosis of chronic anal fissure;
2. Prescribed by or in consultation with a neurologist or gastroenterologist or colorectal surgeon;
3. Age ≥ 18 years;
4. Failure of nitroglycerin ointment and either oral/topical nifedipine or diltiazem *(see Appendix B)*, unless contraindicated or clinically significant adverse effects are experienced;
5. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan details number of Units per indication and treatment session;
7. Dose does not exceed 25 Units per treatment session.

Approval duration: 12 weeks (single treatment session)

L. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Chronic Migraine (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. If receipt of ≥ 2 Botox treatment sessions, member has experienced and maintained a 30% reduction in monthly migraine headache frequency from baseline;
3. Member meets all of the following (a, b, and c):
   a. Botox is not prescribed concurrently with injectable CGRP inhibitors (e.g., Aimovig, Ajovy, Emgality);
   b. Botox is not prescribed concurrently with other botulinum toxin products;
   c. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
4. Treatment plan details number of Units per indication and treatment session;
5. If request is for a dose increase, new dose does not exceed 155 Units per treatment session.

Approval duration: 24 weeks (two 12-week treatment sessions)

B. Esophageal Achalasia (off-label) (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

2. Member is responding positively to therapy;
3. Member meets all of the following (a, b, and c):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
   c. If member has previously received ≥ 2 Botox treatment sessions for esophageal achalasia, it has been at least 24 weeks since the last treatment session;
4. Treatment plan details number of Units per indication and treatment session;
5. If request is for a dose increase, new dose does not exceed 100 Units per treatment session.

Approval duration: 24 weeks (single treatment session)

C. All Other Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member meets both of the following (a and b):
   a. Botox is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
4. Treatment plan details number of Units per indication and treatment session;
5. If request is for a dose increase, request meets one of the following (a through j):
   a. OAB: Dose does not exceed 100 Units per treatment session;
   b. Urinary incontinence associated with a neurologic condition: Dose does not 200 Units per treatment session;
   c. Upper/lower limb spasticity (i or ii):
      i. Age ≥ 18 years: Upper and/or lower limb: Dose not exceed 400 Units per treatment session;
      ii. Age 2 through 17 years (a, b, and c):
         a) Upper limb: Dose does not exceed the lower of 6 Units/kg body weight or 200 Units per treatment session;
         b) Lower limb: Dose does not exceed the lower of 8 Units/kg body weight or 300 Units per treatment session;
         c) If upper and lower limb spasticity are treated in the same treatment session, number of Units per treatment session does not exceed the lower of 10 Units/kg body weight or 340 Units per treatment session;
   d. CD (i or ii):
      i. Age ≥ 18 years: Dose does not exceed 100 Units total in the SCM muscle and 300 Units per treatment session;
      ii. Age 16 through 17 years: Dose does not exceed 100 Units total in the SCM muscle and the lower of 10 Units/kg body weight or 300 Units per treatment session;
   e. Primary axillary hyperhidrosis: Dose does not exceed 100 Units per treatment session;
   f. Blepharospasm: Dose does not exceed 5 Units per muscle, 15 Units per eye, and 30 Units per treatment session;
   g. Strabismus (i or ii):
      i. Vertical and horizontal strabismus: Dose does not exceed the lower of a two-fold increase or 25 Units per muscle and 50 Units per treatment session;
      ii. VI nerve palsy: Dose does not exceed the lower of a two-fold increase or 25 Units per muscle and 25 Units per treatment session;
   h. Focal dystonia and essential tremor (i or ii):
      i. Laryngeal dystonia/OMD: Dose does not exceed 25 Units per treatment session;
      ii. UE dystonia, UE essential tremor: Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use and member age (*prescriber must submit supporting evidence; number of Units per treatment session does not exceed the lower of 10 Units/kg body weight or 340 Units for pediatrics, or 400 Units for adults*);
   i. HD, IAS achalasia: Dose does not exceed 100 Units per treatment session;

j. Chronic anal fissure: Dose does not exceed 25 Units per treatment session.

Approval duration: 12 weeks (single treatment session)

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: 12 weeks (single treatment session); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

B. Cosmetic treatment of hyperfunctional wrinkles of the upper face including glabellar frown lines, deep forehead wrinkles and periorbital wrinkles (crow's feet);

C. Episodic migraine (≤ 14 headache days per month): Safety and efficacy have not been established per the package insert;

D. Total treatment dose per session does not exceed the lower of 10 Units/kg body weight or 340 Units in a 3-month interval for pediatrics and 400 Units for adults.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CD: cervical dystonia
CGRP: calcitonin gene-related peptide
FDA: Food and Drug Administration
HD: Hirschsprung disease
IAS: internal anal sphincter
MS: multiple sclerosis
NDO: neurogenic detrusor overactivity
OAB: overactive bladder
SPI: spinal cord injury
UE: upper extremity

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Overactive bladder, urinary incontinence		
oxybutynin (Ditropan®/XL, Gelnique®) *(anticholinergic agent)*	• Immediate-release tablets (adults and children): 5 mg orally two to three times daily • Extended-release tablets: 5-10 mg orally once daily • Topical gel: Apply contents of one sachet topically once daily	• Immediate-release: 20 mg/day • Extended-release: 30 mg/day • Gel: one sachet/day
tolterodine tartrate (Detrol®/LA) *(anticholinergic agent)*	• Immediate-release tablets: 2 mg orally twice daily • Extended-release tablets: 4 mg orally once daily	4 mg/day
solifenacin (Vesicare®) *(anticholinergic agent)*	• Adults and children weighing more than 60 kg: 5 mg PO once daily • Children weighing between 46 to 60 kg: 4 mg PO once daily • Children weighing between 16 to 45 kg: 3 mg PO once daily • Children weighing between 9 to 15 kg: 2 mg once daily	10 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Myrbetriq® (mirabegron) *(beta-3 agonist)*	25 mg orally once daily	50 mg/day
Chronic migraine		
Examples of oral migraine preventive therapies - • Anticonvulsants: divalproex (Depakote®), topiramate (Topamax®) • Beta blockers: propranolol (Inderal®), metoprolol (Lopressor®), timolol • Antidepressants/tricyclic antidepressants: amitriptyline (Elavil®), venlafaxine (Effexor®)	*Refer to prescribing information for dosing regimens.*	*Refer to prescribing information*
Primary axillary hyperhidrosis		
Drysol® (aluminum chloride)	Apply topically once daily	One application/day
Dystonia		
carbidopa/levodopa (Sinemet®, Duopa®, Rytary®)	25 mg/100 mg PO QD, and increase by 1 tablet every 3 to 5 days.	1,200 mg/day of levodopa
trihexyphenidyl	30 mg PO QD	30 mg/day
HD, IAS achalasia		
Dulcolax® (bisacodyl)	5 to 15 mg PO or 10 mg PR QD	30 mg/day
MiraLax® (Polyethylene glycol 3350)	17 grams of polyethylene glycol 3350 in 4-8 oz water by mouth once daily	17 grams/day
Colace® (Docusate sodium)	50-200 mg PO QD-QID	200 mg/day
Chronic anal fissure		
nitroglycerin 0.2% ointment (Rectiv®)	15 to 30 mg (2.5 to 5 cm as squeezed from the tube, about 1 to 2 inches), applied topically to skin every 8 hours while awake and at bedtime; application frequency may be increased to every 6 hours if needed; alternatively, a regimen providing a 12-hour nitrate-free interval may be used; apply dosage once each morning, then 6 hours later	75 mg (12.5 cm as squeezed from the tube)/day
nifedipine or diltiazem (oral or topical ointment/gel-compounded)	PO: At provider discretion Intra-anal: 0.2% ointment or gel, applied around fissure(s) 2 times daily for 6-8 weeks	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications and Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation
  - Infection at the proposed injection site
  - Intradetrusor injections: urinary tract infection or urinary retention
- Boxed warning(s): distant spread of toxin effect

Appendix D: Botulinum Toxin Product Interchangeability

- Potency Units of Botox are not interchangeable with other botulinum toxin product preparations (e.g., Dysport®, Myobloc®, Xeomin®).

Appendix E: Guideline Support for Botulinum Toxin Use

Indication	Guideline
Focal Dystonia* and Essential Tremor, and Headache	
Blepharospasm, cervical dystonia, adult spasticity, and headache	Academy of Neurology (2016)
Migraine prevention	American Academy of Neurology and the American Headache Society. Neurology (2012)
Laryngeal dystonia	American Academy of Otolaryngology-Head and Neck Surgery Foundation (2018)
Oromandibular dystonia	American Academy of Oral Medicine (2018)
Focal limb dystonia - UE**	American Academy of Neurology (2008)
Essential tremor - UE	American Academy of Neurology (2008)
Sialorrhea	American Academy of Cerebral Palsy and Developmental Medicine (AACPDM, 2018); International Parkinson and Movement Disorder Society (2018)
OAB/urinary incontinence	American Urological Association Society of Urodynamics (2019)
Gastrointestinal Conditions *(see guidelines for required oral medication information)*	
Esophageal achalasia	American College of Gastroenterology (2013)
HD and IAS achalasia	American Pediatric Surgical Association (2017)
Chronic anal fissure	American College of Gastroenterology (2014)

**American Academy of Neurology (AAN) classifies Botox use for hemifacial spasm and motor tics as category C, and notes that data are inadequate to make a recommendation for lower limb dystonia. All other AAN Botox recommendations above are classified as category B - probably effective.*
***Policy criteria requiring failure of oral medication for dystonias are limited to dystonias affecting the limbs (see Cloud and Jinnah, 2010).*

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Average Dose</th><th>Maximum dose per Treatment Session</th></tr>
<tr><td>Adults: OAB</td><td>Up to 5 Units IM per injection across up to 20 injection sites in the detrusor muscle for a total of up to 100 Units per treatment session</td><td rowspan="2">See dosing regimens for maximum dose

Frequency:
• Esophageal acalasia: one treatment session every 24 weeks.
• All other indications: one treatment session every 12 weeks.</td></tr>
<tr><td>Pediatric NDO</td><td>• Weight ≥ 34 kg: 200 units
• Weight < 34 kg: 6 units/kg (see table below)
<table>
<tr><th>Body weight (kg)</th><th>Botox (mL)</th><th>Diluent (mL)</th><th>Final dose of Botox in dosing syringe</th></tr>
<tr><td>12 to > 14 kg</td><td>3.6</td><td>6.4</td><td>72 units</td></tr>
<tr><td>14 to < 16 kg</td><td>4.2</td><td>5.8</td><td>84 units</td></tr>
<tr><td>16 to < 18 kg</td><td>4.8</td><td>5.2</td><td>96 units</td></tr>
<tr><td>18 to < 20 kg</td><td>5.4</td><td>4.6</td><td>108 units</td></tr>
<tr><td>20 to < 22 kg</td><td>6</td><td>4</td><td>120 units</td></tr>
<tr><td>22 to < 24 kg</td><td>6.6</td><td>3.4</td><td>132 units</td></tr>
<tr><td>24 to < 26 kg</td><td>7.2</td><td>2.8</td><td>144 units</td></tr>
<tr><td>26 to < 28 kg</td><td>7.8</td><td>2.2</td><td>156 units</td></tr>
<tr><td>28 to < 30 kg</td><td>8.4</td><td>1.6</td><td>168 units</td></tr>
<tr><td>30 to < 32 kg</td><td>9</td><td>1</td><td>180 units</td></tr>
<tr><td>32 to < 34 kg</td><td>9.6</td><td>0.4</td><td>192 units</td></tr>
</table></td></tr>
</table>

Indication	Average Dose	Maximum dose per Treatment Session
Adults: urinary incontinence associated with neurologic condition	Up to approximately 6.7 Units IM per injection across up to 30 injection sites in the detrusor muscle for a total of up to 200 Units per treatment session	
Adults: chronic migraine	Up to 5 Units IM per injection across up to 7 head/neck muscles for a total of up to 155 Units per treatment session	
Adults: upper and lower limb spasticity	Up to 50 Units IM per injection and up to 400 Units per treatment session	
Pediatrics: upper and limb spasticity	• Upper limb spasticity: Up to the lower of 6 Units/kg or 200 Units IM per treatment session • Lower limb spasticity: Up to the lower of 8 Units/kg or 300 Units IM per treatment session • Upper and lower limb spasticity: Up to the lower of 10 Units/kg or 340 Units IM per treatment session	
Adults: CD	Up to 50 Units IM per injection, 100 Units total in the sternocleidomastoid (SCM) muscle, and 300 Units per treatment session	
Pediatrics: CD	Up to 50 Units IM per injection, 100 Units total in the SCM muscle, and the lower of 10 Units/kg body weight or 300 Units per treatment session	
Adults: axillary hyperhidrosis	Up to 50 Units IM per axilla per treatment session	
Adults and pediatrics: blepharospasm	• Botox naive: Up to 2.5 Units IM per muscle, 7.5 Units per eye, and 15 Units per treatment session • Botox experienced: Up to 5 Units IM per muscle, 15 Units per eye, and 30 Units per treatment session	
Adults and pediatrics: strabismus	• Botox naive: ○ Vertical muscles, or horizontal strabismus < 20 prism diopters: Up to 2.5 Units IM per muscle and 5 Units per treatment session ○ Horizontal strabismus 20 to 50 prism diopters: Up to 5 Units IM per muscle and 10 Units per treatment session ○ VI nerve palsy: 2.5 Units IM in the medial rectus muscle and 2.5 Units per treatment session • Botox experienced: ○ Vertical and horizontal strabismus: Up to the lower of a two-fold increase or 25 Units IM per muscle and 50 Units per treatment session ○ VI nerve palsy: Up to the lower of a two-fold increase or 25 Units IM per muscle and 25 Units per treatment session	
Off-label uses		
Laryngeal dystonia	Up to 25 Units IM per treatment session (*Off-label - Micromedex 2020*)	
UE dystonia UE essential tremor	Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use and member age (prescriber must submit supporting evidence; number of Units per treatment session does not exceed the lower of 10 Units/kg body weight or 340 Units IM for pediatrics, or 400 Units IM for adults)	
OMD	Up to 25 Units IM per treatment session.	

Indication	Average Dose	Maximum dose per Treatment Session
	(Off-label - Hallet 2009)	
Esophageal achalasia	Up to 100 Units IM per treatment session (*Off-label - Vaezi 2013*)	
HD, IAS achalasia	Up to 100 Units IM per treatment session (*Off-label - Langer 2017*)	
Chronic anal fissure	Up to 25 Units IM per treatment session (*Off-label - Micromedex 2020*)	

VI. Product Availability
Vials: 100 Units, 200 Units

VII. References
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14. Wald A, Bharucha AE, Cosman BC, et al. American College of Gastroenterology clinical guideline: Management of benign anorectal disorders. Am J Gastroenterol 2014; 109:1141–1157; doi: 10.1038/ajg.2014.190; published online 15 July 2014.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: added physical medicine and rehabilitation specialist / pain specialist for relevant indications; expanded maximum dose for chronic migraine treatment to 200 units per treatment per 2012 NICE guidelines; removed laryngeal spasm or spasmodic dysphonia (DrugDex IIb); removed spastic conditions; added internal anal sphincter achalasia off-label indication; added provider submission of treatment plan for all indications for initial and continued approval; Hirschsprung's disease and internal anal sphincter Achalasia: removed requirement for dietary and fluid control; CD: lowered age limit from 18 to 16 years; references reviewed and updated.	02.20.18	05.18
2Q 2019 annual review: added requirement that Botox is not prescribed concurrently with injectable CGRP inhibitors; references reviewed and updated.	01.15.19	05.19
RT4: criteria added for newly FDA approved indication for pediatric extension of upper limb spasticity.	07.23.19	
RT4: criteria added for newly FDA approved indication for pediatric extension of lower limb spasticity removed 2% specific strength requirement for nitroglycerin ointment due to availability reasons.	11.06.19	
2Q 2020 annual review: CP criteria incorporated under upper/lower limb spasticity; rehabilitation specialist incorporated under physiatrist; previous (last 12 weeks) or concurrent toxin product use restriction added to all initial/continuation criteria; off-label uses limited to those with guideline-based support (laryngeal dystonia, OMD, UE dystonia/essential tremor, HD, IAD, esophageal achalasia - Appendix E); dosing updated per package insert/off-label literature (Section V); initial approval duration shortened to 12 weeks for esophageal achalasia and CCB trial added for chronic anal fissure per guidelines; same-visit treatment for multiple indications is limited to upper/lower limb spasticity (Section III); references reviewed and updated.	03.02.20	05.20
For chronic migraine, clarified requirement for use of two oral migraine preventative therapies that are from different therapeutic classes. RT4: updated FDA approved indication for spasticity which now includes cerebral palsy for lower limb spasticity in pediatric patients. Per-injection dosing limitation removed to support individualized treatment for the following indications: OAB/urinary incontinence, chronic migraine, UE/LE, CD, primary axillary hyperhidrosis; CD continuation pediatric dosing is corrected to reflect 300 rather than 340 Units; for esophageal achalasia continuation criteria, prior toxin therapy is corrected to reflect 12 rather than 24 weeks with addition of a 24-week treatment session limitation after 2 or more sessions.	07.14.20	11.20
2Q 2021 annual review: treatment plan requirement detailing number of Units per site and treatment session is changed to per indication and treatment session; treatment of multiple indications restriction removed and replaced with total treatment dose limitation (Section III); added duration of trial needed for anal fissure; RT4: added newly FDA-approved diagnosis of pediatric detrusor overactivity; references reviewed and updated.	02.16.21	05.21
2Q 2022 annual review: no significant changes; removed required 2-week trial duration of nitroglycerin and nifedipine/diltiazem for chronic anal fissures to align with approach in Dysport; revised max dose for continued therapy of upper and lower limb spasticity in age 2-17 from 300 to 340 units per treatment session per PI (based on maximum cumulative dose in pediatrics); references reviewed and updated.	02.07.22	05.22

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.