Clinical Policy: OnabotulinumtoxinA (Botox)
Reference Number: ERX.SPA.192
Effective Date: 01.11.17
Last Review Date: 05.19

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)

Botox is indicated for:
- Treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication
- Treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) in adults who have an inadequate response to or are intolerant of an anticholinergic medication
- Prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer)
- Treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), finger flexors (flexor digitorum profundus and flexor digitorum sublimis), and thumb flexors (adductor pollicis and flexor pollicis longus)
- Treatment of lower limb spasticity in adult patients to decrease the severity of increased muscle tone in ankle and toe flexors (gastrocnemius, soleus, tibialis posterior, flexor hallucis longus, and flexor digitorum longus)
- Treatment of adults with cervical dystonia, to reduce the severity of abnormal head position and neck pain associated with cervical dystonia
- Treatment of severe primary axillary hyperhidrosis that is inadequately managed by topical agents
- Treatment of strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients ≥12 years of age

Limitation(s) of use:
- Safety and effectiveness of Botox have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) in seven placebo-controlled studies.
- Safety and effectiveness of Botox have not been established for the treatment of other upper or lower limb muscle groups. Safety and effectiveness of Botox have not been established for the treatment of spasticity in pediatric patients under age 18 years. Botox has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture. Treatment with Botox is not intended to substitute for usual standard of care rehabilitation regimens.
- The safety and effectiveness of Botox for hyperhidrosis in other body areas have not been established. Weakness of hand muscles and blepharoptosis may occur in patients who receive Botox for palmar hyperhidrosis and facial hyperhidrosis, respectively. Patients should be evaluated for potential causes of secondary hyperhidrosis (e.g., hyperthyroidism) to avoid symptomatic treatment of hyperhidrosis without the diagnosis and/or treatment of the underlying disease. Safety and effectiveness of Botox have not been established for the treatment of axillary hyperhidrosis in pediatric patients under age 18.

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.
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. Cervical Dystonia (must meet all):
      1. Diagnosis of CD (see Appendix D);
      2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;
      3. Age ≥ 16 years;
      4. 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, shoulder or head;
      5. Contraction are causing pain and functional impairment;
      6. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
      7. Dose does not exceed 400 units per treatment session.
      Approval duration: 12 weeks (single treatment session)

   B. Blepharospasm (a focal dystonia) or Strabismus (must meet all):
      1. Diagnosis of (a or b):
         a. Blepharospasm (i.e., abnormal contraction of eyelid muscles);
         b. Strabismus (i.e., misalignment of the eyes);
      2. Prescribed by or in consultation with a neurologist or ophthalmologist;
      3. Age ≥ 12 years;
      4. Member has significant disability in daily functional activities due to interference with vision;
      5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
      6. Dose does not exceed (a or b):
         a. Blepharospasm: 5 units per site per treatment session (maximum of 200 units total in a 30-day period);
         b. Strabismus: 25 units per muscle per treatment session.
      Approval duration: 12 weeks (single treatment session)

   C. Other Dystonias (off-label) (must meet all):
      1. Diagnosis of dystonia (see definitions and types in Appendices D and E);
      2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;
      3. Failure of carbidopa/levodopa or trihexyphenidyl unless contraindicated or clinically significant adverse effects are experienced;
      4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
      5. Dose does not exceed 400 units per single treatment with the following exceptions:
         a. Oromandibular dystonia: 25 units per muscle per treatment session;
         b. Laryngeal dystonia (spasmodic dysphonia): 3 units per treatment session.
      Approval duration: 12 weeks (single treatment session)

   D. Upper and Lower Limb Spasticity (must meet all):
      1. Diagnosis of upper or lower limb spasticity;
      2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;
      3. Age ≥ 18 years;
      4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
      5. Dose does not exceed 400 units per treatment session.
      Approval duration: 12 weeks (single treatment session)
E. Spasticity Associated with Cerebral Palsy (off-label) (must meet all):
1. Diagnosis of spasticity associated with cerebral palsy (CP);
2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;
3. Age ≥ 2 years;
4. Focal increased muscle tone interferes with function or is likely to lead to joint contracture with growth;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed 400 units per treatment session.
**Approval duration: 12 weeks (single treatment session)**

F. Chronic Migraine (must meet all):
1. Diagnosis of chronic migraine (≥ 15 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 oral migraine preventative therapies, each used for at least 8 weeks (e.g., antiepileptic drugs: divalproex sodium, sodium valproate, topiramate; beta-blockers: metoprolol, propranolol, timolol; antidepressants: amitriptyline, venlafaxine), unless contraindicated or clinically significant adverse effects are experienced;
5. Botox is not prescribed concurrently with injectable CGRP inhibitors (e.g., Aimovig™, Ajovy™, Emgality™);
6. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
7. Dose does not exceed 200 units per treatment session.
**Approval duration: 24 weeks (two 12-week treatment sessions)**

G. Primary Axillary Hyperhidrosis (must meet all):
1. Diagnosis of severe primary axillary hyperhidrosis (e.g., resulting in medical complications such as skin maceration and infection or significant disruption of professional/social life);
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. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed 50 units per axilla per treatment session.
**Approval duration: 12 weeks (single treatment session)**

H. Overactive Bladder and Urinary Incontinence (must meet all):
1. Diagnosis of (a or b):
   a. Overactive bladder with symptoms of urge urinary incontinence, urgency and frequency;
   b. Urinary incontinence due to detrusor over activity associated with a neurologic condition (e.g., spinal cord injury, MS);
2. Prescribed by or in consultation with a neurologist or urologist;
3. Age ≥ 18 years;
4. Failure of at least two anticholinergic agents and one oral beta-3 agonist medication (e.g., oxybutynin chloride, tolterodine tartrate; mirabegron), each used for at least 30 days, unless contraindicated or clinically significant adverse effects are experienced;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed (a or b):
   a. Overactive bladder: 100 units per treatment session;
   b. Urinary incontinence: 200 units per treatment session.
Approval duration: 12 weeks (single treatment session)

I. **Esophageal Achalasia (off-label) (must meet all):**
   1. Diagnosis of esophageal achalasia (i.e., failure of relaxation of the lower esophageal sphincter accompanied by loss of peristalsis in the distal esophagus);
   2. Prescribed by or in consultation with a gastroenterologist;
   3. Age ≥ 18 years;
   4. Member is not a good candidate for pneumatic dilation or myotomy (e.g., high surgical risk due to age, comorbidities);
   5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
   6. Dose does not exceed 100 units.

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. Member is responding positively to therapy;
   3. If member has received 2 or more Botox treatment sessions, member has experienced and maintained a 30% reduction in monthly migraine headache frequency from baseline;
   4. It has been at least 12 weeks since the last injection of Botox;
   5. Botox is not prescribed concurrently with injectable CGRP inhibitors (e.g., Aimovig, Ajovy, Emgality);
6. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
7. If request is for a dose increase, new dose does not exceed 200 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. It has been at least 24 weeks since the last injection of Botox;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
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. It has been at least 12 weeks since the last injection of Botox;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
5. Botox administration has not exceeded 400 units over the last 3 months;
6. If request is for a dose increase, new dose does not exceed indication-specific maximum if applicable:
   a. Dystonias:
      i. CD, upper/lower limb spasticity, CP: 400 units per treatment session;
      ii. Blepharospasm: 5 units per site per treatment session (maximum of 200 units total in a 30-day period);
      iii. Strabismus: 25 units per muscle per treatment session;
      iv. Oromandibular dystonia: 25 units per muscle per treatment session;
      v. Laryngeal dystonia (spasmodic dysphonia): 3 units per treatment session;
   b. Primary axillary hyperhidrosis: 50 units per axilla per treatment session;
   c. Overactive bladder, HD, IAS achalasia, chronic anal fissures: 100 units per treatment session;
   d. Urinary incontinence: 200 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).

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CD: cervical dystonia
CP: cerebral palsy
FDA: Food and Drug Administration
HD: Hirschsprung’s disease
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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbidopa/levodopa (Sinemet®, Duopa®, Rytary®)</td>
<td>Other Dystonias (see appendices C and D) 25 mg/100 mg PO QD, and increase by 1 tablet every 3 to 5 days.</td>
<td>1,200 mg/day of levodopa</td>
</tr>
<tr>
<td>trihexyphenidyl</td>
<td>Other Dystonias (see appendices C and D) 30 mg PO QD</td>
<td>30 mg/day</td>
</tr>
<tr>
<td>lactulose</td>
<td>Hirschsprung’s Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure 15-30 ml PO QD</td>
<td>60 mL/day</td>
</tr>
<tr>
<td>Senokot® (sennosides)</td>
<td>Hirschsprung’s Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure Two 8.6 mg tabs PO QD-BID</td>
<td>34.4 mg/day</td>
</tr>
<tr>
<td>Metamucil® (psyllium)</td>
<td>Chronic anal fissure One rounded tsp in 8 oz liquid PO up to TID</td>
<td>3 doses/day</td>
</tr>
<tr>
<td>Dulcolax® (bisacodyl)</td>
<td>Hirschsprung’s Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure 5 to 15 mg PO or 10 mg PR QD</td>
<td>30 mg/day</td>
</tr>
<tr>
<td>FiberCon® (calcium polycarbophil)</td>
<td>Chronic anal fissure Two 625 mg tabs PO QD-QID</td>
<td>5000 mg/day</td>
</tr>
<tr>
<td>Citrucel® (Methylcellulose)</td>
<td>Chronic anal fissure Caplet: 2 caplets up to 6 times daily Powder: 2 grams in 8 oz of cold water by mouth up to 3 times daily</td>
<td>12 caplets/day or 6 grams/day</td>
</tr>
<tr>
<td>MiraLax® (polyethylene glycol 3350)</td>
<td>Hirschsprung’s Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure 17 grams of polyethylene glycol 3350 in 4-8 oz water by mouth once daily</td>
<td>17 grams/day</td>
</tr>
<tr>
<td>Colace® (docusate sodium)</td>
<td>Hirschsprung’s Disease, Internal Anal Sphincter Achalasia, Chronic anal fissure 50-200 mg PO QD-QID</td>
<td>200 mg/day</td>
</tr>
<tr>
<td>nitroglycerin 0.2% ointment (Rectiv®)</td>
<td>Chronic anal fissure 15 to 30 mg (2.5 to 5 cm as squeezed from the tube, about 1 to 2 inches), applied topically to the skin every 8 hours while awake and at bedtime; frequency of application 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 reapply 6 hours later</td>
<td>75 mg (12.5 cm as squeezed from the tube)/day</td>
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<tr>
<td>oxybutynin (Ditropan®/XL, Gelnique®)</td>
<td>Overactive Bladder Immediate-release tablets: 5 mg orally two to three times daily Extended-release tablets: 5-10 mg orally once daily</td>
<td>Immediate-release: 20 mg/day  Extended-release: 30 mg/day</td>
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<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/Maximum Dose</td>
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<tr>
<td>tolterodine tartrate (Detrol®/LA)</td>
<td><strong>Overactive Bladder</strong>&lt;br&gt;Immediate-release tablets: 2 mg orally twice daily&lt;br&gt;Extended-release tablets: 4 mg orally once daily</td>
<td>4 mg/day</td>
</tr>
<tr>
<td>Myrbetriq® (mirabegron)</td>
<td><strong>Overactive Bladder</strong>&lt;br&gt;25 mg orally once daily</td>
<td>50 mg/day</td>
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<tr>
<td>Anticonvulsants such as:</td>
<td><strong>Chronic Migraines</strong>&lt;br&gt;Refer to prescribing information</td>
<td>Refer to prescribing information</td>
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<tr>
<td>divalproex (Depakote®),</td>
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<td>topiramate (Topamax®)</td>
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<td>Beta blockers such as:</td>
<td><strong>Chronic Migraines</strong>&lt;br&gt;Refer to prescribing information</td>
<td>Refer to prescribing information</td>
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<tr>
<td>propranolol (Inderal®),</td>
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<td>metoprolol (Lopressor®),</td>
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<td>timolol</td>
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<tr>
<td>Antidepressants/tricyclic</td>
<td><strong>Chronic Migraines</strong>&lt;br&gt;Refer to prescribing information</td>
<td>Refer to prescribing information</td>
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<tr>
<td>antidepressants such as:</td>
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<td>amitriptyline (Elavil®),</td>
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<td>venlafaxine (Effexor®)</td>
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<tr>
<td>Non-steroidal anti-inflammatory</td>
<td><strong>Chronic Migraines</strong>&lt;br&gt;Refer to prescribing information</td>
<td>Refer to prescribing information</td>
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<td>drugs (NSAIDs) such as:</td>
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<td>fenoprofen (Nalfon®),</td>
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<td>ibuprofen (Motrin®),</td>
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<td>ketoprofen (Orudis®),</td>
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<td>naproxen (Naprosyn®)</td>
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<tr>
<td>Drysol® (aluminum chloride)</td>
<td><strong>Primary Axillary Hyperhidrosis</strong>&lt;br&gt;Apply topically once daily</td>
<td>One application/day</td>
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</table>

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: Definition and Classification of Dystonia**
- Dystonia is defined as a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both.
  - Dystonic movements are typically patterned and twisting, and may be tremulous.
  - Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation.
- Dystonia is classified along two axes:
  - Clinical characteristics: Age at onset, body distribution, temporal pattern, associated features (additional movement disorders or neurological features) - the clinical characteristics fall into several specific dystonia syndromes that help to guide diagnosis and treatment;
  - Etiology: Nervous system pathology, inheritance.

**Appendix E: Descriptions and Examples of Dystonia Syndromes**
## Clinical Policy

### OnabotulinumtoxinA

<table>
<thead>
<tr>
<th>Category</th>
<th>Subcategory</th>
<th>Description and Examples</th>
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<tbody>
<tr>
<td>Isolated dystonias</td>
<td>Early-onset generalized isolated dystonia</td>
<td>Dystonia with focal-onset in childhood often progresses to generalized involvement. Cases may be sporadic, familial, genetically defined or without known cause.</td>
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<tr>
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<td>• Early-onset generalized dystonia (DYT-TOR1A)</td>
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<td>• Adolescent-onset dystonia of mixed type (DYT-THAP1)</td>
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<td></td>
<td>Adult-onset focal or segmental isolated dystonia</td>
<td>Usually begins after age 30 years. Most are sporadic without identifiable cause. Rarely progress to generalized dystonia but can extend to contiguous body regions.</td>
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<td></td>
<td>• Adult-onset segmental dystonia (DYT-GNAL)</td>
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<td></td>
<td>• Cervical dystonia</td>
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<td></td>
<td></td>
<td>• Blepharospasm</td>
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<td>• Writer’s cramp</td>
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<td>• Oroanibular dystonia</td>
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<td></td>
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<td>• Laryngeal dystonia (spasmodic dysphonia)</td>
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<td>• Limb dystonia</td>
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<tr>
<td>Combined dystonias</td>
<td>Dystonia-parkinsonism</td>
<td>Disorders that combine dystonia and parkinsonian features. May be accompanied by pyramidal tract involvement or nonmotor features including cognitive decline. Many are inherited.</td>
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<td>• Dopa-responsive dystonia (DYT-GCH1, DYT-TH, and DYT-SPR)</td>
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<td>• Wilson disease</td>
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<td>• Early-onset parkinsonism (PARK-PARKIN)</td>
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<td></td>
<td>• Conditions associated with neurodegeneration with brain iron accumulation</td>
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<tr>
<td>Myoclonus- dystonia</td>
<td>Disorders in which there is a combination of dystonia and myoclonus. Dystonia may be mild and myoclonus generally predominates.</td>
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<td></td>
<td></td>
<td>• Myoclonus-dystonia (DYT-SGCE)</td>
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<tr>
<td>Paroxysmal dyskinesia with dystonia</td>
<td>Disorders characterized by episodes of spontaneous or induced dyskinesia with dystonia.</td>
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<tr>
<td></td>
<td></td>
<td>• Paroxysmal nonkinesigenic dyskinesia (DYT-MR1)</td>
</tr>
</tbody>
</table>

*Table adapted with permission from: Comella C. Classification and evaluation of dystonia. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available at www.uptodate.com. Accessed on June 22, 2017.*

### Appendix F: General Information

- The potency units of botulinum toxin products are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of one product cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method.
- Safety and effectiveness have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) and is a Class III recommendation in Micromedex.
- Indication specific dosage and administration recommendations should be followed for Botox. When initiating treatment, the lowest recommended dose should be used. In treating adult patients for one or more indications, the maximum cumulative dose should not exceed 400 units, in a 3 month interval.
- For detrusor overactivity associated with a neurologic condition there was no additional benefit of Botox 300 units over 200 units.
- Safety and effectiveness have not been uniformly established for the treatment of temporomandibular disorders (TMD). Use of botulinum toxin for this indication is a Class IIb recommendation in Micromedex based on a single study from 1999. A review of two clinical studies (from 2002 and 2011) (15 and 21 patients) found no significant differences in pain reduction between botulinum toxin and placebo. Other small studies (from 2005 - Italy and 2008 - Turkey) have been performed and showed improvement in objective measures of pain (20 patients and 26 patients). The most common total dose of BTX-A used in the studies was 25u for each temporalis muscle and 50u for each masseter muscle. The studies did not repeat the dosing, but measured efficacy at 16 weeks post dose. The 2003 Guidelines for diagnosis and
management of disorders involving the temporomandibular joint and related musculoskeletal structures mention Botox as a possible treatment option for temporomandibular joint (TMJ) based on its mechanism of action and the pathophysiology of TMD.

- TMD “gold standard” treatment continues to be: 1) TMJ intraoral orthotic; 2) Muscle relaxants by mouth; and 3) Home muscle relaxation exercises/techniques.

- Limb spasticity may be caused by heredity spastic paraplegia, multiple sclerosis or other demyelinating diseases of the central nervous system, spastic hemiplegia, infantile cerebral palsy, and stroke.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Average Duration of Effect</th>
<th>Average Dose</th>
<th>Maximum dose per Treatment Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blepharospasm</td>
<td>12.5 weeks</td>
<td>5 units per site</td>
<td>200 units total in a 30-day period</td>
</tr>
<tr>
<td>Strabismus</td>
<td>6-8 weeks to 6-12 months</td>
<td>2.5 to 5 units per muscle (max 25 units)</td>
<td>25 units</td>
</tr>
<tr>
<td>Cervical dystonia</td>
<td>4 weeks to 3 months</td>
<td>200 to 300 units divided among affected muscles</td>
<td>400 units</td>
</tr>
<tr>
<td>Oromandibular dystonia*</td>
<td>10 to 14 weeks</td>
<td>25 to 50 units per masseter muscle, 5 to 40 units per temporalis</td>
<td>100 units</td>
</tr>
<tr>
<td>Spasmodic dysphonia*</td>
<td>3-6 months</td>
<td>0.031 to 10 units per vocal cord. 5 to 30 units in abductor muscle</td>
<td>400 units</td>
</tr>
<tr>
<td>Overactive bladder</td>
<td>12 weeks</td>
<td>Total dose 100 Units, as 0.5 mL (5 Units) injections across 20 sites into the detrusor. Repeat doses should be 12 weeks apart</td>
<td>400 units</td>
</tr>
<tr>
<td>Spastic muscle contracture of pediatric cerebral palsy*</td>
<td>1-6 months</td>
<td>3 to 6 units/kg (maximum 12 units/kg). total dose 82 to 220 units divided among affected muscles</td>
<td>100 units</td>
</tr>
<tr>
<td>Childhood myoclonus following failure of Baclofen, benzodiazepines, and antiseizure medications*</td>
<td>4-8 months</td>
<td>8 to 80 units/kg</td>
<td>400 units</td>
</tr>
<tr>
<td>Chronic anal fissure*</td>
<td>Single injection</td>
<td>20 units both sides</td>
<td>80 units/kg</td>
</tr>
<tr>
<td>Internal anal sphincter achalasia*</td>
<td>Single treatment. Patient may require repeat treatment</td>
<td>15 units to 25 units in each quadrant or up to 50 units on either side of IAS</td>
<td>100 units</td>
</tr>
<tr>
<td>Axillary Hyperhidrosis</td>
<td>4-12 months</td>
<td>50 units per axilla</td>
<td>100 units</td>
</tr>
<tr>
<td>Migraines</td>
<td>3-4 months</td>
<td>155 to 195 total units given in 5 to 40 units/site</td>
<td>200 units</td>
</tr>
<tr>
<td>Neurogenic bladder</td>
<td>8-12 months</td>
<td>200 units given in multiple sites</td>
<td>200 units</td>
</tr>
<tr>
<td>Upper limb spasticity</td>
<td>12 weeks</td>
<td>12.5 to 50 units in one site</td>
<td>400 units</td>
</tr>
</tbody>
</table>

*Off label

VI. Product Availability

Vial of powder for solution for injection: 100 units, 200 units
VII. References

Dystonias, Spasticity, Chronic Migraine

Primary Axillary Hyperhidrosis, Overactive Bladder, Urinary Incontinence

Esophageal Achalasia

Hirschsprung’s Disease, Internal Anal Sphincter Achalasia

**Chronic Anal Fissures**


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created</td>
<td>12.01.16</td>
<td>01.17</td>
</tr>
<tr>
<td>4Q17 Annual Review</td>
<td>10.08.17</td>
<td>11.17</td>
</tr>
<tr>
<td>- Converted to new template.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Added age limits where appropriate.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Removed requirement to document mode of administration.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Removed requirements that cannot be verified objectively and/or are under the purview of the prescriber (e.g., trial of behavioral therapy for overactive bladder, disability due to vision interference for blepharospasm, candidacy for pneumatic dilation or myotomy for esophageal achalasia).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.</td>
<td>02.20.18</td>
<td>05.18</td>
</tr>
<tr>
<td>2Q 2019 annual review: added requirement that Botox is not prescribed concurrently with injectable CGRP inhibitors; references reviewed and updated.</td>
<td>01.15.19</td>
<td>05.19</td>
</tr>
</tbody>
</table>

**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.

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