Clinical Policy: OnabotulinumtoxinA (Botox)
Reference Number: ERX.SPMN.216
Effective Date: 01/17
Last Review Date:

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that onabotulinumtoxinA (Botox®) is medically necessary when one of the following criteria are met:

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I. Initial Approval Criteria

A. Overactive Bladder or Urinary Incontinence (must meet all):
   1. Prescribed by or in consultation with a neurologist or urologist;
   2. Diagnosis of one of the following:
      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, multiple sclerosis);
   3. Botox will be administered as an intradetrusor injection;
   4. Prescribed dose of Botox does not exceed:
      a. 100 units for overactive bladder; or
      b. 200 units for incontinence due to detrusor over activity associated with a neurologic condition;
   5. Member has tried and failed behavioral therapy (e.g., bladder training, pelvic floor muscle training, and fluid management) for at least 8 weeks;
   6. Member has tried and failed, or is intolerant or contraindicated to, at least 2 anticholinergic or oral beta-3 agonist medications (e.g., oxybutynin chloride, tolterodine tartrate; mirabegron) at the maximum tolerated dose for at least 30 days.

   Approval duration: 12 weeks (single treatment session)

B. Chronic Migraines (must meet all):
   1. Prescribed by or in consultation with a neurologist;
   2. Diagnosis of chronic migraine (≥ 15 days per month with headache lasting 4 hours a day or longer);
   3. Botox will be administered as an intramuscular injection;
   4. Prescribed dose of Botox does not exceed 155 units per single treatment session;
   5. Member has tried and failed, or is intolerant or contraindicated to, at least 2 oral migraine preventative therapies, each for at least 8 weeks (e.g., antiepileptic drugs: divalproex sodium, sodium valproate, topiramate; beta-blockers: metoprolol, propranolol, timolol; antidepressants: amitriptyline, venlafaxine).

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

C. Cervical Dystonia or Limb Spasticity (must meet all):
   1. Prescribed by or in consultation with a neurologist, orthopedist, or physiatrist;
   2. Diagnosis of one of the following:
      a. Cervical dystonia and both i and ii:
         i. Diagnosis is confirmed by involuntary tonic or clonic contractions in the neck and shoulder muscles (e.g., splenius, sternocleidomastoid, levator scapulae, scalene, trapezius, posterior cervical) that result in sustained abnormal postures of the head, neck, and shoulders, and/or overlying spasms that produce tremor-like movements with directional quality;
ii. Member is experiencing pain and functional impairment;
   b. Upper or lower limb spasticity and either i or ii:
      i. For upper limb spasticity, intent of treatment is 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);
      ii. For lower limb spasticity, intent of treatment is to decrease the severity of
         increased muscle tone in ankle and toe flexors (gastrocnemius, soleus, tibialis
         posterior, flexor hallucis longus, and flexor digitorum longus);
 3. Botox will be administered as an intramuscular injection;
 4. Prescribed dose of Botox does not exceed 400 units per single treatment session.

Approval duration: 12 weeks (single treatment session)

D. Primary Axillary Hyperhidrosis (must meet all):
   1. Prescribed by or in consultation with a neurologist or dermatologist;
   2. 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);
   3. Botox will be administered as an intradermal injection;
   4. Prescribed dose of Botox does not exceed 50 units per axilla;
   5. Member has tried and failed 6 months of topical aluminum chloride.

Approval duration: 12 weeks (single treatment session)

E. Blepharospasm or Strabismus (must meet all):
   1. Prescribed by or in consultation with a neurologist or ophthalmologist;
   2. Diagnosis of one of the following:
      a. Blepharospasm associated with dystonia, including benign essential
         blepharospasm or VII nerve disorders;
      b. Strabismus;
   3. Member has had significant disability in daily, functional activities due to
      interference with vision;
   4. Botox will be administered as an intramuscular injection;
   5. Prescribed dose of Botox does not exceed:
      a. 5 units per site for blepharospasm (maximum 200 units total dose in a 30-day
         period); or
      b. 25 units per muscle for strabismus.

Approval duration: 12 weeks (single treatment session)

F. Chronic Anal Fissures – Off Label Use (must meet all):
   1. Prescribed by or in consultation with a gastroenterologist or colorectal surgeon;
   2. Age ≥ 18 years;
3. Diagnosis of chronic anal fissures;
4. Prescribed dose of Botox does not exceed 100 units;
5. Member has tried and failed, or is intolerant or contraindicated to, at least 2 months of conventional therapy (e.g., high fiber diet and adequate fluids, bulk fiber supplements, stool softeners, warm sitz baths, nitroglycerin 0.2% ointment).

Approval duration: 12 weeks (single treatment session)

G. Cerebral Palsy – Off Label Use (must meet all):
1. Prescribed by or in consultation with a neurologist;
2. Age \( \geq 2 \) years;
3. Diagnosis of spasticity associated with cerebral palsy with focal increased muscle tone that interferes with function or is likely to lead to joint contracture with growth;
4. Prescribed dose of Botox does not exceed 400 units.

Approval duration: 12 weeks (single treatment session)

H. Dystonias – Off Label Use (must meet all):
1. Prescribed by or in consultation with a neurologist, orthopedist, or physiatrist;
2. Diagnosis of dystonias (e.g., idiopathic torsion dystonia, myoclonus dystonia, oromandibular dystonia);
3. Prescribed dose of Botox does not exceed 400 units per single treatment session or indication-specific maximum if applicable, whichever is lower:
   a. 25 units per muscle for oromandibular dystonia;
4. Member has tried and failed, or is intolerant or contraindicated to, carbidopa/levodopa and trihexyphenidyl.

Approval duration: 12 weeks (single treatment session)

I. Esophageal Achalasia – Off Label Use (must meet all):
1. Prescribed by or in consultation with a gastroenterologist;
2. Age \( \geq 18 \) years;
3. Diagnosis of esophageal achalasia;
4. Prescribed dose of Botox does not exceed 100 units;
5. Member is not a good candidate for pneumatic dilation or myotomy.

Approval duration: 24 weeks (single treatment session)

J. Laryngeal Spasm or Spasmodic Dysphonia – Off Label Use (must meet all):
1. Prescribed by or in consultation with a neurologist or otolaryngologist;
2. Age \( \geq 18 \) years;
3. Diagnosis of adductor laryngeal dystonia (spasmodic dysphonia);
4. Prescribed dose of Botox does not exceed 3 units.

Approval duration: 12 weeks (single treatment session)
K. Hirschsprung’s Disease – Off Label Use (must meet all):
   1. Prescribed by or in consultation with a gastroenterologist;
   2. Diagnosis of one of the following:
      a. Hirschsprung’s disease and Botox will be used for constipation due to increased internal anal sphincter tone after surgery;
      b. Ultra-short segment Hirschsprung’s disease;
      c. Internal anal sphincter achalasia associated with Hirschsprung’s disease;
   3. Prescribed dose of Botox does not exceed 100 units;
   4. Member has tried and failed, or is intolerant or contraindicated to, high fiber diet, adequate fluids, stool softeners, and laxatives for at least 2 months.

Approval duration: 12 weeks (single treatment session)

L. Spastic Conditions – Off Label Use (must meet all):
   1. Prescribed by or in consultation with a neurologist, orthopedist, or physiatrist;
   2. Diagnosis of spastic condition (e.g., spasticity associated with stroke, spinal cord injury, or traumatic brain injury; hereditary spastic paraplegia);
   3. Prescribed dose of Botox does not exceed 400 units;
   4. Member has tried and failed, or is intolerant or contraindicated to, at least 2 conventional therapies (e.g., baclofen, benzodiazepines, dantrolene sodium, tizanidine, physical therapy).

Approval duration: 12 weeks (single treatment session)

M. Other diagnoses/indications:
   1. Refer to ERX.SPMN.16 - Global Biopharm Policy if requested indication is non-cosmetic.

II. Continued Approval
   A. Overactive Bladder, Urinary Incontinence, Cervical Dystonia, Limb Spasticity, Primary Axillary Hyperhidrosis, Blepharospasm, Strabismus, Chronic Anal Fissures, Cerebral Palsy, Dystonias, Laryngeal Spasm, Hirschsprung’s Disease, and Spastic Conditions (must meet all):
      1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
      2. Prescribed dose of Botox does not exceed 400 units total over the last 3 months and indication-specific maximum if applicable:
         a. 100 units for treatment of overactive bladder, chronic anal fissures, or Hirschsprung’s disease;
         b. 200 units for treatment of incontinence due to detrusor over activity associated with a neurologic condition;
         c. 155 units per single treatment session for chronic migraines;
         d. 400 units per single treatment session for cervical dystonia or limb spasticity, spastic conditions, or cerebral palsy;
         e. 50 units per axilla for treatment of primary axillary hyperhidrosis;
OnabotulinumtoxinA

f. 5 units per site for treatment of blepharospasm (maximum 200 units total dose in a 30-day period);
g. 25 units per muscle for treatment of strabismus;
h. 3 units for treatment of laryngeal spasm/spasmodic dysphonia;
i. 25 units per muscle for treatment of oromandibular dystonia;

3. It has been at least 12 weeks since the last injection of Botox;
4. Member is responding positively to therapy.

Approval duration: 12 weeks (single treatment session)

B. Chronic Migraine (must meet all):
1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Prescribed dose of Botox does not exceed 155 units per single treatment session;
3. It has been at least 12 weeks since the last injection of Botox;
4. Member has experienced and maintained a 30% reduction in monthly headache frequency from baseline after 2 or more Botox treatment sessions.

Approval duration: 12 weeks (single treatment session)

C. Esophageal Achalasia (must meet all):
1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Prescribed dose of Botox does not exceed 100 units;
3. It has been at least 24 weeks since the last injection of Botox;
4. Member is responding positively to therapy.

Approval duration: 24 weeks (single treatment session)

D. Other diagnoses/indications (must meet either 1 or 2):
1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
2. Refer to ERX.SPMN.16 - Global Biopharm Policy if requested indication is non-cosmetic.

Background
Description/Mechanism of Action:
OnabotulinumtoxinA is a purified botulinum toxin type A produced from fermentation of Clostridium botulinum. It blocks neuromuscular transmission by binding to acceptor sites on motor or sympathetic nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. This inhibition occurs as the neurotoxin cleaves SNAP-25, a protein integral to the successful docking and release of acetylcholine from vesicles situated within nerve endings.
FDA Approved Indication(s):
Botox is an acetylcholine release inhibitor and neuromuscular blocking agent/intramuscular, intradermal, and intradetrusor injection 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., SCI, MS) 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 with topical agents
- Treatment of strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and above

Limitations of use:

- Safety and effectiveness 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.
C LINICAL POLICY
OnabotulinumtoxinA

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<td>J0585</td>
<td>Injection, onabotulinumtoxinA, 1 unit</td>
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<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
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<tr>
<td>Policy created.</td>
<td>12/16</td>
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References

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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