**SCOPE:**
Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

**APPLIES TO:**
Commercial
Medicaid

**POLICY CRITERIA:**

**COVERED USES:**
All Food and Drug Administration (FDA) approved and selected medically accepted indications not otherwise excluded from the benefit, as outlined below.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

**CRITERIA:**
OnabotulinumtoxinA (Botox®) may be covered for the following indications when criteria are met:
1. Chronic migraine headaches in adults when all of the following is met:
   a. Documentation of at least 15 headache days per month with headaches lasting 4 hours or longer
   b. Documentation of trial and failure, intolerance, or contraindication to at least TWO of the following classes used for migraine prevention. Trial and
failure is defined as inadequate response following a minimum three (3) months of consistent use.
   i. Antidepressants (e.g., amitriptyline, venlafaxine)
   ii. Beta-blockers (e.g., metoprolol, propranolol, timolol)
   iii. Antiepileptics (e.g., divalproex, valproate, topiramate)

   c. Combination therapy with Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists (e.g., Aimovig®, Emgality®, Ajovy®) is considered investigational and is not covered

2. Upper and lower limb spasticity in patients at least 2 years of age
3. Cervical dystonia in adults
4. Strabismus and blepharospasm associated with dystonia in patients at least 12 years of age
5. Severe axillary hyperhidrosis in adults after documented trial and failure, intolerance or contraindication to topical agents
   a. Note: The safety and effectiveness of onabotulinumtoxinA for hyperhidrosis in other body areas have not been established.
6. Overactive bladder in adults with:
   a. Symptoms of urge urinary incontinence, urgency, and frequency
   b. Documented trial and failure, intolerance, or contraindication to at least one month of anticholinergic medication (e.g., oxybutynin, tolterodine)
7. Urinary incontinence in adults:
   a. Due to detrusor over activity related to a neurologic condition (e.g., spinal cord injury, multiple sclerosis)
   b. Documented trial and failure, intolerance, or contraindication at least one month of anticholinergic medication (e.g., oxybutynin, tolterodine)
8. Excessive salivation due to advanced Parkinson’s disease
9. Hemifacial spasm
10. Chronic anal fissure when all of the following is met:
    a. Prescribed by, or in consultation with, a gastroenterologist or colorectal surgeon
    b. Documentation of trial and failure, intolerance, or contraindication to at least 6 weeks of therapy with either topical nitrates or topical calcium channel blockers
    c. One of the following:
       i. Documentation that the patient is not a good candidate for surgery or appropriate medical rationale is provided for avoiding surgery
       ii. Botox® is to be used in conjunction with fissurotomy
    d. The use of Botox® in combination with sphincterotomy or anal advancement flap is considered experimental and investigational and will not be covered
AbobotulinumtoxinA (Dysport®) may be covered for the following indications:
1. Spasticity in adults
2. Cervical dystonia in adults
3. Upper and lower limb spasticity in patients at least 2 years of age
4. Blepharospasm in adults

IncobotulinumtoxinA (Xeomin®) may be covered for the following indications:
1. Chronic sialorrhea in adult patients
2. Upper limb spasticity in patients at least 2 years of age
3. Cervical dystonia in adults
4. Blepharospasm in adults

RimabotulinumtoxinB (Myobloc®) may be covered for the following indications:
1. Cervical dystonia in adults
2. Chronic sialorrhea in adult patients

EXCLUSION CRITERIA:
- When the above criteria are not met, botulinum toxin is considered investigational and not covered.
- Botulinum toxin is considered cosmetic and is not covered for the treatment of glabellar lines and/or fine wrinkles on the face.
  - PrabotulinumtoxinA (Jeuveau®) will not be covered as it is only FDA approved for the treatment of glabellar lines and/or fine wrinkles on the face.

REQUIRED MEDICAL INFORMATION:
For initiation of treatment, a prior authorization form and relevant chart notes documenting medical rationale are required and for continuation of therapy, ongoing documentation of successful response to the medication may be necessary.

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS: N/A

COVERAGE DURATION:
Initial authorization and reauthorization will be approved for one year

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber’s medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.
Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
Botulinum toxin injections are used to treat various focal muscle spastic disorders and excessive muscle contractions such as dystonias, spasms, twitches, etc. These drugs produce a presynaptic neuromuscular blockade by preventing the release of acetylcholine from the nerve endings. The resulting chemical denervation of muscle produces local paresis or paralysis and allows individual muscles to be weakened selectively. Botulinum toxins have the advantage of being potent neuromuscular blocking agents with good selectivity and duration of action.

Botulinum toxins types A and B are neurotoxins produced by Clostridium Botulinum. Botulinum Toxin Type A and Botulinum Toxin Type B have many similarities and as experience has been gained, medical consensus has gradually developed that the two toxins have similar, but not identical, properties. Each botulinum toxin product is pharmacologically and clinically distinct, and therefore, not interchangeable with any other botulinum toxin product. As a result, approved indications for the two toxins differ.

The rationale for treatment is to create temporary paralysis of sufficient depth and duration that the injected muscles become slightly atrophied and stretched. The antagonist muscle shortens simultaneously taking up the slack created by agonist paralysis. After several weeks enervation to the injected muscle returns. The safety and efficacy of long term use of Botox, Myobloc, Dysport or Xeomin is unknown.

FDA APPROVED INDICATIONS:
Botox® (onabotulinumtoxinA)
- Bladder Dysfunction
- Chronic Migraine
- Adult upper and lower limb spasticity
- Pediatric upper limb spasticity (2 to 17 years of age)
- Pediatric lower limb spasticity (2 to 17 years of age), excluding spasticity caused by cerebral palsy
- Cervical dystonia
- Primary axillary hyperhidrosis
  - Limitations of use:
- Safety and effectiveness for hyperhidrosis in other body areas have not been established. Weakness of hand muscles and blepharoptosis may occur in patients who receive treatment 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 have not been established for the treatment of axillary hyperhidrosis in pediatric patients under age 18
  - Blepharospasm and strabismus

**Dysport® (abebotulinumtoxinA)**
- Glabellar Lines
- Cervical dystonia
- Spasticity in adults
- Lower limb spasticity in pediatric patients 2 years of age and older
- Upper limb spasticity in pediatric patients 2 years of age and older, excluding spasticity caused by cerebral palsy

**Myobloc® (rimabotulinumtoxinB)**
- Cervical dystonia
- Chronic sialorrhea in adults

**Xeomin® (incobotulinumtoxinA)**
- Chronic Sialorrhea in adult patients
- Glabellar Lines
- Cervical dystonia in adult patients
- Upper limb spasticity in adult patients
- Upper limb spasticity in pediatric patients 2 to 17 years of age, excluding spasticity caused by cerebral palsy
- Blepharospasm in adult patients

**Jeuveau® (prabotulinumtoxinA-xvfs)**
- Glabellar Lines

**POSITION STATEMENT:**
The safety and efficacy of long term use of Botox, Myobloc, Dysport or Xeomin is unknown.
The policy criteria was developed based on medically accepted indications for the specific products. Medically accepted refers to FDA approved or generally recognized as efficacious by certain drug compendia references (e.g., DrugDex, AHFS).

**Migraine Headache Prophylaxis**

The 2018 American Headache Society (AHS) Consensus Statement uses the International Classification of Headache Disorders definition of chronic migraines as follows:

A. Migraine-like or tension-type-like headache on ≥15 days/month for >3 months that fulfill criteria B and C
B. Occurring in a patient who has had at least 5 attacks fulfilling criteria B-D for migraine without aura and/or criteria B and C for migraine with aura
C. On ≥8 days/month for >3 months, fulfilling any of the following:
   1. Criteria C and D for migraine without aura
   2. Criteria B and C for migraine with aura
   3. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative

E. Not better accounted for by another diagnosis

Furthermore, the AHS recommends initiation of prophylactic treatment when any of the following occurs:

- Attacks significantly interfere with patients’ daily routines despite acute treatment
- Frequent attacks (≥4 monthly headache days)
- Contraindication to, failure, or overuse of acute treatments, with overuse defined as:
  - 10 or more days per month for ergot derivatives, triptans, opioids, combination analgesics, and a combination of drugs from different classes that are not individually overused
  - 15 or more days per month for non-opioid analgesics, acetaminophen, and nonsteroidal anti-inflammatory drugs

- Adverse events with acute treatments
- Patient preference

Treatments with established efficacy for migraine prophylaxis include antiepileptic drugs (i.e., divalproex sodium, valproate sodium, topiramate), beta-blockers (i.e., metoprolol, propranolol, and timolol), triptans (i.e., frovatriptan for short-term prevention of menstrual migraines), onabotulinumtoxinA, and calcitonin gene-related peptide (CGRP) receptor antagonists [i.e., erenumab (Aimovig®), fremanezumab (Ajovy®), and galcanezumab (Emgality®)].
CGRP receptor antagonists are a newer class of medications indicated for migraine prophylaxis. The clinical trials for these agents excluded patients that were currently using botulinum toxin. There is currently no clinical information to support use of combination therapy. The AHS statement includes recommendations that adding on injectable CGRP therapy to oral preventive therapies is appropriate given the lack of drug-drug interactions.

**Chronic Anal Fissure**

The [2014 American College of Gastroenterology guidelines](#) outline the diagnosis and management of chronic anal fissure. They define anal fissure as an “ulcer-like, longitudinal tear in the midline of the anal canal” and define chronic as lasting more than 8-12 weeks with edema and fibrosis.

Treatment typically consists of topical agents targeting the relief of spasms, such as topical nitrates, such as 0.2% nitroglycerin ointment applied twice for 6-8 weeks, and topical calcium channel blockers (CCBs), such as 2% diltiazem applied twice daily for 6–8 weeks. While these therapies are minimally invasive and typically inexpensive, the rate of healing are considered only marginally better than placebo for nitrates, to have “insufficient data to conclude whether [topical CCBs] are superior to placebo.” Botulinum toxin has healing rates superior than placebo (60-80%) and patients may be retreated on relapse with similar healing rates. Patients considered medical refractory to these treatments should be referred for surgical evaluation. Lateral internal sphincterotomy (LIS) is preferred over manual anal dilation due to better outcomes and less incontinence adverse effects. However, there is still a risk of incontinence, so topical and injectable therapies continue to be used, despite better efficacy with LIS. A systematic review found that LIS was statistically significantly better in healing rates and recurrence rates than Botox®

Recommendation: “Gastroenterologists and other providers should refer patients who do not respond to conservative or pharmacologic treatment for local injections of botulinum toxin (strong recommendation, low quality of evidence) or surgical internal anal sphincterotomy (strong recommendation, high quality of evidence).”

**CPT/HCPCS Codes**

<table>
<thead>
<tr>
<th>All Lines of Business Except Medicare</th>
<th>Prior Authorization Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>31513</td>
<td>Laryngoscopy, indirect; with vocal cord injection</td>
</tr>
<tr>
<td>31570</td>
<td>Laryngoscopy, direct, with injection into vocal cord(s), therapeutic</td>
</tr>
<tr>
<td>31571</td>
<td>Laryngoscopy, direct, with injection into vocal cord(s), therapeutic; with operating microscope or telescope</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
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<tr>
<td>31573</td>
<td>Laryngoscopy, flexible; with therapeutic injection(s) (eg, chemodenervation</td>
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<tr>
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<td>agent or corticosteroid, injected percutaneous, transoral, or via endoscope</td>
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<tr>
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<td>channel), unilateral</td>
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<td>Esophagoscopy, rigid, transoral; with directed submucosal injection(s), any</td>
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<td>injection(s), any substance</td>
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<tr>
<td>46505</td>
<td>Chemodenervation of internal anal sphincter</td>
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<td>52287</td>
<td>Cystourethroscopy, with injection(s) for chemodenervation of the bladder</td>
</tr>
<tr>
<td>64611</td>
<td>Chemodenervation of parotid and submandibular salivary glands, bilateral</td>
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<tr>
<td>64612</td>
<td>Chemodenervation of muscle(s); muscle(s) innervated by facial nerve,</td>
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<tr>
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<td>unilateral (eg, for blepharospasm, hemifacial spasm)</td>
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<tr>
<td>64615</td>
<td>Chemodenervation of muscle(s); muscle(s) innervated by facial, trigeminal,</td>
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<td>cervical spinal and accessory nerves, bilateral (eg, for chronic migraine)</td>
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<td>64616</td>
<td>Chemodenervation of muscle(s); neck muscle(s), excluding muscles of the</td>
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<td>larynx, unilateral (eg, for cervical dystonia, spasmodic torticollis)</td>
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<td>Chemodenervation of muscle(s); larynx, unilateral, percutaneous (eg, for</td>
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<td>spasmodic dysphonia), includes guidance by needle electromyography, when</td>
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<td>64642</td>
<td>Chemodenervation of one extremity; 1-4 muscle(s)</td>
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<td>64643</td>
<td>Chemodenervation of one extremity; each additional extremity, 1-4 muscle(s)</td>
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<td>(List separately in addition to code for primary procedure)</td>
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<tr>
<td>64644</td>
<td>Chemodenervation of one extremity; 5 or more muscles</td>
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<tr>
<td>64645</td>
<td>Chemodenervation of one extremity; each additional extremity, 5 or more</td>
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<td>muscles (List separately in addition to code for primary procedure)</td>
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<td>64646</td>
<td>Chemodenervation of trunk muscle(s); 1-5 muscle(s)</td>
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<td>64647</td>
<td>Chemodenervation of trunk muscle(s); 6 or more muscles</td>
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<td>Chemodenervation of eccrine glands; both axillae</td>
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<td>Chemodenervation of eccrine glands; other area(s) (eg, scalp, face, neck),</td>
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<td>Chemodenervation of extraocular muscle</td>
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<td>95873</td>
<td>Electrical stimulation for guidance in conjunction with chemodenervation</td>
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<td>(List separately in addition to code for primary procedure)</td>
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<td>(List separately in addition to code for primary procedure)</td>
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<td>J0586</td>
<td>Injection, abobotulinumtoxina, 5 units</td>
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<tr>
<td>J0587</td>
<td>Injection, rimabotulinumtoxinb, 100 units</td>
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<tr>
<td>J0588</td>
<td>Injection, incobotulinumtoxin a, 1 unit</td>
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<tr>
<td>J3590</td>
<td>Injection, prabotulinumtoxin a (dump code)</td>
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<tr>
<td>S2340</td>
<td>Chemodenervation of abductor muscle(s) of vocal cord</td>
</tr>
<tr>
<td>S2341</td>
<td>Chemodenervation of adductor muscle(s) of vocal cord</td>
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</table>
Unlisted Codes
All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then prior-authorization is required.

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<thead>
<tr>
<th>Code</th>
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<td>43499</td>
<td>Unlisted procedure, esophagus</td>
</tr>
<tr>
<td>64999</td>
<td>Unlisted procedure, nervous system</td>
</tr>
</tbody>
</table>

REFERENCE/RESOURCES:
2. Dysport package insert.
5. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically.
8. Shao WJ Li GC, Zhang ZK. Systematic review and meta-analysis of randomized controlled trials comparing botulinum toxin injection with lateral internal sphincterotomy for chronic anal fissure Int J Colorectal Dis. 2009 Sep;24(9):995-1000.