Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCNEU029.1223	**NEUROMUSCULAR DRUGS** **BOTULINUM TOXIN** See Appendix A for medications covered by policy
Effective Date: 2/1/2024	**Review/Revised Date**: 05/19, 08/19, 12/19, 03/20, 05/20, 07/20, 09/20, 11/20, 01/21, 05/21, 07/21, 07/22, 07/23, 12/23 (BS)
Original Effective Date: 09/19	**P&T Committee Meeting Date**: 06/19, 08/19, 10/19, 12/19, 02/20, 06/20, 08/20, 12/20, 02/21, 06/21, 08/21, 08/22, 08/23, 12/23
Approved by: Oregon Region Pharmacy and Therapeutics Committee Page 1 of 12	

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 when all applicable indication-specific criteria below are met. The Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefit provides comprehensive and preventive health care services for children and adolescents up to their 21st birthday who are enrolled in Medicaid. Management of unfunded conditions falls under this benefit when they impact the ability to grow, develop or participate in school and the applicable indication-specific criteria below are met.

REQUIRED MEDICAL INFORMATION:
For initial authorization, must meet specific criteria outlined below for each botulinum toxin product:

1. OnabotulinumtoxinA (Botox®) may be covered for the following indications when criteria are met:
    a. Chronic migraine headaches in adults when all the following is met:

i. Documentation of at least 15 headache days per month with headaches lasting four hours or longer
ii. 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 months of consistent use.
    1) Antidepressants (e.g., amitriptyline, venlafaxine)
    2) Beta-blockers (e.g., metoprolol, propranolol, timolol)
    3) Antiepileptic's (e.g., divalproex, valproate, topiramate)
iii. For patients established on a Calcitonin Gene Related Peptide (CGRP) receptor antagonist for migraine prophylaxis, combination therapy with Botox® may be considered medically necessary if the following criteria are met:
    1) The patient has been established on, and adherent to, CGRP prophylaxis therapy (e.g., Aimovig®, Emgality®, Ajovy®) for at least six months and has a documented improvement in frequency and/or severity of migraine headaches
    2) Patient continues to have at least 15 headache days per month with headaches lasting four hours or longer, despite use of CGRP prophylaxis monotherapy

b. Spasticity in patients at least two years of age
c. Cervical dystonia in adults
d. Strabismus and blepharospasm associated with dystonia in patients at least 12 years of age
e. Severe axillary hyperhidrosis in adults after documented trial and failure, intolerance or contraindication to topical agents. Note for commercial only: aluminum chloride hexahydrate (Drysol®) is on formulary.
    i. Note: The safety and effectiveness of onabotulinumtoxinA for hyperhidrosis in other body areas have not been established.
f. Overactive bladder in adults with:
    i. Symptoms of urge urinary incontinence, urgency, and frequency
    ii. Documented at least one month trial and failure, intolerance, or contraindication to an anticholinergic medication (e.g., oxybutynin, tolterodine) or beta-3 adrenoceptor agonist (e.g., mirabegron)
g. Urinary incontinence in patients at least five years of age:
    i. Due to detrusor over activity related to a neurologic condition (e.g., spinal cord injury, multiple sclerosis)
    ii. Documented at least one month trial and failure, intolerance, or contraindication to an anticholinergic medication (e.g., oxybutynin, tolterodine) or beta-3 adrenoceptor agonist (e.g., mirabegron)
h. Excessive salivation due to advanced Parkinson's disease

i. Hemifacial spasm
j. Chronic anal fissure when *all* the following is met:
    i. Prescribed by, or in consultation with, a gastroenterologist or colorectal surgeon
    ii. Documentation of trial and failure, intolerance, or contraindication to at least six weeks of therapy with either topical nitrates or topical calcium channel blockers
    iii. The use of Botox® in combination with sphincterotomy or anal advancement flap is not considered medically necessary and will not be covered
k. Spastic dysphonia (laryngeal dystonia) for adductor type when prescribed by, or in consultation with, a specialist in laryngology
l. Achalasia in patients ineligible for definitive treatments, such as pneumatic dilation, surgical myotomy or peroral endoscopic myotomy (POEM)
    i. The use of Botox® in combination with pneumatic dilation is not considered medically necessary and will not be covered

2. AbobotulinumtoxinA (Dysport®) may covered for the following indications:
    a. Spasticity in patients two years of age and older
    b. Cervical dystonia in adults
    c. Blepharospasm in adults
3. IncobotulinumtoxinA (Xeomin®) may covered for the following indications:
    a. Chronic sialorrhea in patients two years and older
    b. Upper limb spasticity in patients at least two years of age
    c. Cervical dystonia in adults
    d. Blepharospasm in adults
4. RimabotulinumtoxinB (Myobloc®) may covered for the following indications:
    a. Cervical dystonia in adults
    b. Chronic sialorrhea in adult patients
5. DaxibotulinumtoxinA-lanm (Daxxify®) may be covered for the following indications:
    a. Moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adults
    b. Cervical dystonia in adults
6. For indications not listed above, the requested medication must be FDA approved for the intended use or medical rational must be submitted in support of therapy (such as high-quality peer reviewed literature, accepted compendia or evidence-based practice guidelines). Coverage will be considered on a case-by-case basis.

Reauthorization:

1. For onabotulinumtoxinA (Botox®) monotherapy or combination therapy with CGRP agent for prophylaxis of chronic migraine headaches: documentation of a 30% reduction in headache days from baseline.
2. All other reauthorization requests for botulinum toxin products require documentation of successful response to therapy.

EXCLUSION CRITERIA:

- 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.

AGE RESTRICTIONS:
N/A, except where noted

PRESCRIBER RESTRICTIONS:
N/A, except where noted

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

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Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

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 in adults
- Chronic Migraine in adults
    - 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.
- Spasticity in patients two years of age and older
    - Limitations of Use: has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture.
- Cervical dystonia in adults
- Primary axillary hyperhidrosis in adults that is inadequately managed with topical agents
    - 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 associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and older.
- Pediatric Detrusor Overactivity associated with a Neurologic Condition

Dysport® (abebotulinumtoxinA)
- Glabellar Lines
- Cervical dystonia in adults
- Spasticity in patients two years of age and older

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

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

Jeuveau® (prabotulinumtoxinA-xvfs)
- Glabellar Lines

Daxxify® (DaxibotulinumtoxinA-lanm)
- Moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adults
- Cervical dystonia in adults

POSITION STATEMENT:
The safety and efficacy of long-term use of Botox, Myobloc, Dysport, Daxxify 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:

1. Migraine-like or tension-type-like headache on ≥15 days/month for >3 months that fulfill criteria 2 and 3
2. 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†
3. On ≥8 days/month for >3 months, fulfilling any of the following:
    1. Criteria C and D 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
4. Not better accounted for by another diagnosis

Migraine Features

*Migraine without aura	†Migraine with aura
B. Headache attacks lasting 4-72 hr (untreated or unsuccessfully treated) C. Headache has at least two of the following four characteristics: • unilateral location • pulsating quality • moderate or severe pain intensity • aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs) D. During headache at least one of the following: • nausea and/or vomiting • photophobia and phonophobia	B. One or more of the following fully reversible aura symptoms: • visual • sensory • speech and/or language • motor • brainstem • retinal C. At least three of the following six characteristics: • at least one aura symptom spreads gradually over ≥5 minutes • two or more aura symptoms occur in succession • each individual aura symptom lasts 5-60 minutes[1] • at least one aura symptom is unilateral[2] • at least one aura symptom is positive[3] • the aura is accompanied, or followed within 60 minutes, by headache

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 the prophylaxis CGRP 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 2021 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[7].

Treatment typically consists of topical agents targeting the relief of spams, such as topical nitrates (e.g., 0.2% nitroglycerin ointment applied twice for 6-8 weeks), and topical calcium channel blockers (e.g., 2% diltiazem applied twice daily for 6–8 weeks). While these therapies are minimally invasive and typically inexpensive, the rate of healing is considered only marginally better than placebo for nitrates and there is "insufficient data to conclude whether [topical CCBs] are superior to placebo."[7] Botulinum toxin has healing rates superior to placebo (60-80%) and

patients may be retreated on relapse with similar healing rates. There is no consensus protocol for dosing of botulinum toxin or injection technique. 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.

American College of Gastroenterology treatment recommendations for chronic anal fissures[7]:

- Local application of a calcium channel blocker should be the initial medical treatment (strong recommendation, low quality of evidence)
- Botulinum toxin A injections may be attempted in patients whom CCB fails or as an alternative option to CCB (conditional recommendation, low quality of evidence)
- LIS is the surgical treatment of choice for chronic anal fissures that do not heal with nonsurgical measures (strong recommendation, high quality of evidence)

The American Society of Colon and Rectal Surgeons Guidelines recommendations for chronic anal fissures[11]:

- May be treated with topical nitrates, although headache symptoms may limit their efficacy (strong recommendation, moderate-quality evidence)
- Compared with topical nitrates, the use of calcium channel blockers for chronic anal fissures has a similar efficacy, with a superior side-effect profile, and can be used as first-line treatment (strong recommendation, moderate-quality)
- Botulinum toxin has similar results compared with topical therapies as first-line therapy and modest improvement in healing rates as second-line therapy following failed treatment with topical therapies (strong recommendation, moderate-quality evidence)
- Lateral internal sphincterotomy (LIS) may be offered in selected pharmacologically naive patients with chronic anal fissure (strong recommendation, high-quality evidence)
- LIS is the treatment of choice in selected patients without baseline fecal incontinence [FI] (strong recommendation, high-quality evidence)
- The addition of an anocutaneous flap to botulinum toxin injection or to LIS may decrease postoperative pain and allow for primary wound healing (weak recommendation, low-quality evidence)
- Short-term outcomes of repeat LIS or botulinum injection for recurrent anal fissure have shown good healing rates with a low risk of FI, but the data are limited and require further study (weak recommendation, low-quality evidence)

Achalasia
Achalasia is a rare mobility disorder of the esophagus and can lead to gastrointestinal issues such as progressive dysphagia to solids and liquids, heartburn, chest pain, regurgitation, and varying degrees of weight loss or nutritional deficiencies. The American College of Gastroenterology (ACG) Clinical Guidelines: Diagnosis and Management of Achalasia recommends botulinum toxin as first-line therapy for patients with achalasia that are unfit for definitive therapies [i.e., pneumatic dilation, surgical myotomy or peroral endoscopic myotomy (POEM)].

The Medicaid Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefit was introduced in 1967 as a part of the Social Security Act Amendments. The goal of the EPSDT benefit is to ensure that children under the age of 21 who are enrolled in Medicaid receive appropriate preventative, dental, mental health, and developmental specialty services. The EPSDT standard requires states to cover all medically necessary and medically appropriate treatment for children and adolescents on Medicaid, including medications, regardless of what services states provide to adults. Under EPSDT, the Prioritized List is a guidance tool for assessment of coverage. Medically appropriate and medically necessary services are defined in Oregon Administrative Rule (OAR) 410-120-000.

CPT/HCPCS Codes

All Lines of Business Except Medicare	
Prior Authorization Required	
31513	Laryngoscopy, indirect; with vocal cord injection
31570	Laryngoscopy, direct, with injection into vocal cord(s), therapeutic
31571	Laryngoscopy, direct, with injection into vocal cord(s), therapeutic; with operating microscope or telescope
31573	Laryngoscopy, flexible; with therapeutic injection(s) (eg, chemodenervation agent or corticosteroid, injected percutaneous, transoral, or via endoscope channel), unilateral
43192	Esophagoscopy, rigid, transoral; with directed submucosal injection(s), any substance
43201	Esophagoscopy, flexible, transoral; with directed submucosal injection(s), any substance
43236	Esophagogastroduodenoscopy, flexible, transoral; with directed submucosal injection(s), any substance
46505	Chemodenervation of internal anal sphincter
52287	Cystourethroscopy, with injection(s) for chemodenervation of the bladder
64611	Chemodenervation of parotid and submandibular salivary glands, bilateral
64612	Chemodenervation of muscle(s); muscle(s) innervated by facial nerve, unilateral (eg, for blepharospasm, hemifacial spasm)
64615	Chemodenervation of muscle(s); muscle(s) innervated by facial, trigeminal,

	cervical spinal and accessory nerves, bilateral (eg, for chronic migraine)
64616	Chemodenervation of muscle(s); neck muscle(s), excluding muscles of the larynx, unilateral (eg, for cervical dystonia, spasmodic torticollis)
64617	Chemodenervation of muscle(s); larynx, unilateral, percutaneous (eg, for spasmodic dysphonia), includes guidance by needle electromyography, when performed
64642	Chemodenervation of one extremity; 1-4 muscle(s)
64643	Chemodenervation of one extremity; each additional extremity, 1-4 muscle(s) (List separately in addition to code for primary procedure)
64644	Chemodenervation of one extremity; 5 or more muscles
64645	Chemodenervation of one extremity; each additional extremity, 5 or more muscles (List separately in addition to code for primary procedure)
64646	Chemodenervation of trunk muscle(s); 1-5 muscle(s)
64647	Chemodenervation of trunk muscle(s); 6 or more muscles
64650	Chemodenervation of eccrine glands; both axillae
64653	Chemodenervation of eccrine glands; other area(s) (eg, scalp, face, neck), per day
67345	Chemodenervation of extraocular muscle
95873	Electrical stimulation for guidance in conjunction with chemodenervation (List separately in addition to code for primary procedure)
95874	Needle electromyography for guidance in conjunction with chemodenervation (List separately in addition to code for primary procedure)
J0585	Injection, onabotulinumtoxina, 1 unit
J0586	Injection, abobotulinumtoxina, 5 units
J0587	Injection, rimabotulinumtoxinb, 100 units
J0588	Injection, incobotulinumtoxin a, 1 unit
J0589	Injection, daxibotulinumtoxina-lanm, 1 unit
J3590	Injection, prabotulinumtoxin a (dump code)
S2340	Chemodenervation of abductor muscle(s) of vocal cord
S2341	Chemodenervation of adductor muscle(s) of vocal cord
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.**	
31599	Unlisted procedure, larynx
43499	Unlisted procedure, esophagus
64999	Unlisted procedure, nervous system

REFERENCE/RESOURCES:

1. Botox package insert. Irvine, CA; Allergan Pharmaceuticals; 2022 Aug.
2. Dysport package insert. Galderma Laboratories, L.P; 2023 Jan.
3. Xeomin package insert. Franksville, WI; Maerz Aestethics; 2021 Aug.
4. Myobloc package insert. Louisville, KY; Solstice Neurosciences; 2021 Mar.

5. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically.
6. American Headache Society. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Available at https://headachejournal.onlinelibrary.wiley.com/doi/epdf/10.1111/head.13456 (Accessed May 7, 2020)
7. Wald A, Bharucha AE, Limketkai B, *et al*. ACG Clinical Guidelines: Management of Benign Anorectal Disorders. *Am J Gastroenterol*. 2021 Oct 1;116(10):1987-2008.
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.
9. Sileri P, Stolfi VM, Franceschilli L et al. Conservative and surgical treatment of chronic anal fissure: prospective longer term results. J Gastrointest Surg. 2010 May;14(5):773-80.
10. ACG Clinical Guidelines: Diagnosis and Management of Achalasia, The American Journal of Gastroenterology: September 2020 - Volume 115 - Issue 9 - p 1393-1411 doi: 10.14309/ajg.0000000000000731
11. Davids JS, Hawkins AT, Bhama AR, *et al*. Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Anal Fissures. *Dis Colon Rectum*. 2023 Feb 1;66(2):190-199.

APPENDIX A.

Brand Name	Generic Name
Botox®	onabotulinumtoxinA
Daxxify®	daxibotulinumtoxinA-lanm
Dysport®	abobotulinumtoxinA
Jeuveau®	prabotulinumtoxinA-xvfs
Myobloc®	rimabotulinumtoxinB
Xeomin®	incobotulinumtoxinA