Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-2596

Drug Class Update: Botulinum Toxins

Date of Review: April 2025

Date of Last Review: June 2023
Dates of Literature Search: 01/01/2023 - 01/22/2025
(anal fissures) 01/01/2015 - 01/22/2025

Current Status of PDL Class:
See **Appendix 1**.

Purpose for Class Update:
The purpose of this review is to evaluate new high-quality evidence for botulinum toxins (BoNT) since the previous class update. This review will also identify and review evidence for use in anal fissures, a diagnosis which is currently not funded under the prioritized list which is being re-evaluated by the Health Evidence Review Commission (HERC). Evidence for botulinum toxins in treatment of hyperhidrosis is evaluated separately in the April 2025 Drugs for Hyperhidrosis review.

Plain Language Summary:
- Botulinum toxin is used for many different reasons; however, the Oregon Health Plan only covers botulinum toxin for medical purposes, such as migraine headaches or leaky bladder rather than cosmetic reasons such as minimizing wrinkles. Botulinum toxin is not currently covered for chronic anal fissures, and this review evaluates evidence to determine if botulinum toxin should be covered for this condition.
- Anal fissures are small tears in the anal canal that can cause bleeding and pain. Most of these fissures heal on their own. Sometimes they last longer than 6 weeks and can become “chronic”. Even chronic anal fissures can often heal on their own, but home treatments, such as a sitz bath or taking fiber can help with the discomfort. Fiber can reduce risk of tears coming back after they heal. Sometimes they do not heal and additional medication or surgery is needed to correct the condition.
- The American Society of Colon and Rectal Surgeons says that the following medicines can help treat chronic anal fissures:
    - Creams/gels/ointments containing medicines called nitrates or calcium channel blockers for most patients with chronic anal fissures. Nitrates may cause headaches in many people. Calcium channel blockers work just as well as nitrates, but they are not commercially available in the United States in a form that can be applied to skin.
    - Botulinum toxin injections into the anal sphincter may be appropriate for some patients as the first treatment when anal fissures become chronic, or if the nitrates or calcium channel blockers do not promote healing.
    - Surgery can also help chronic anal fissures as the first treatment or after medicines have not worked. Surgery may be more effective than other treatments.
- New guidelines from the Veterans Affairs (VA) support the current policy for use of botulinum toxins in headache.

- New evidence for use in strabismus (crossed eyes) show that botulinum toxin may be less effective than surgery. Most of those tested were children and additional studies need to be done to verify the benefit of using botulinum toxin for this condition.
- Currently, providers must explain why a patient needs botulinum toxin before the Oregon Health Plan will pay for it. We do not recommend any changes to this policy based on new evidence for headaches or crossed eyes, but we recommend adding coverage of botulinum toxins for chronic anal fissures.

Research Questions

1. Is there new comparative evidence evaluating treatments or preventative therapies using BoNT based on relevant disease states/conditions?
2. Is there new comparative harms data for BoNT treatments (e.g., withdrawals due to adverse events, severe adverse events)?
3. Are there certain sub-populations (based on age, gender, ethnicity, or comorbidities) in which certain BoNT treatments are more effective or cause less harm?

Conclusions:

- There are 2 guidelines, 2 systematic reviews, 2 randomized controlled trials, and 3 new drug indications included in this update. There were no studies specifically in Medicaid patients.
- New guidelines from the United States (US) Department of Veterans Affairs (VA):
    - suggest onabotulinumtoxinA injection for the prevention of chronic migraine (weak recommendation for).[1]
    - suggest against abobotulinumtoxinA or onabotulinumtoxinA injection for the prevention of episodic migraine and against botulinum/neurotoxin injection for the prevention of chronic tension-type headache (weak recommendations against).[1]
    - These recommendations are unchanged from the previous guideline version.[1]
    - There is insufficient evidence to recommend for or against any specific medication over another for the prevention of migraine headache, tension headache, or cluster headache (recommendation neither for nor against).[1] This is a new statement in this guideline update.
- No additional high-quality literature for treatment of migraine with BoNT was found in this update.
- Guidelines from The American Society of Colon and Rectal Surgeons (ASCRS) suggest lateral internal sphincterotomy, topical vasodilators, and botulinum toxins all have a place as first line-therapy for chronic anal fissures, depending upon patient factors (moderate to high-quality evidence).[2]
- One high quality systematic review found a lower, but non-statistically significant, rate of incomplete fissure healing with BoNT (28.6%) compared to topical nitrates (TN) (42.1%) (odds ratio [OR]=0.47; 95% confidence interval [CI] 0.13 to 1.67, p=0.24; 5 studies; n=313) with significant heterogeneity.[3] The same 5 studies report twice as much transient anal incontinence in the BoNT group without heterogeneity (BoNT 10.4% vs. TN 4.4%, OR 2.53; 95% CI 0.98 to 6.57, p=0.06, I^2=0%), though this did not reach statistical significance.[3] Fissure recurrence was reported in all included studies not statistically different between groups (BoNT 18.5% vs. TN 25.1%, OR 0.7; 95% CI 0.39 to 1.25, p=0.22, n=393; I^2=4%).[3]
- There is insufficient evidence for or against combination therapy of BoNT plus topical vasodilators in chronic anal fissures.[2,4,5]
- There is insufficient evidence to recommend a specific dosing protocol for BoNT use in chronic anal fissures.[2]
- One systematic review of strabismus, which primarily included children, found that patients who receive surgery may be more likely to improve or correct strabismus compared with those who treated with BoNT (risk ratio (RR) 0.72, 95% CI 0.53 to 0.99; I^2 = 50%; 4 studies, 242 participants; low-certainty evidence).[6]
- There were 4 new labeled indications approved since last review on 3 different products.[7-9] **Table 1** shows current FDA approved indications.

Recommendations:

- No changes to policy for use in migraine headache, strabismus, or other previously reviewed and funded indications.

Author: Fletcher Date: April 2025

- Update prior authorization (PA) criteria to incorporate coverage of BoNT for chronic anal fissures in eligible populations.
- Evaluate costs in executive session.

Summary of Prior Reviews and Current Policy:

- The botulinum toxins drug class was most recently reviewed in June 2023, with special interest in providing an approval route for unfunded conditions to allow coverage under the Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) program for individuals under 21 years of age. Prior to 2023, BoNT use in migraines was reviewed in May 2019. The original drug class review was conducted in May 2014.
- BoNT indications which are funded include cervical dystonia, spasticity, overactive bladder (including neurogenic detrusor overactivity and urinary incontinence), blepharospasm, migraine headaches, and esophageal stricture.
- Reduction in moderate to severe glabellar lines is a cosmetic indication and not eligible for coverage under the Oregon Medicaid state plan.
- Indications not funded due to lack of evidence include surgical interventions for conditions of the back and spine other than scoliosis (guideline note 37), treatments for benign prostate enlargement with lower urinary tract symptoms (guideline note 145), sialorrhea (line 493), disorders of the sweat glands including axillary and palmar hyperhidrosis (Line 510), and chronic anal fissure (line 519).

Background:

Botulinum toxin works by blocking acetylcholine release at the neuromuscular junction, preventing muscular contraction.[10] Botulinum toxin is available in two serotypes. There are five Food and Drug Administration (FDA) approved BoNT-A products and one BoNT-B product currently available. The different BoNT preparations are not interchangeable and potencies are specific for the different formulations. Botulinum toxins have multiple Food and Drug administration approved indications, as well as off-label indications supported by compendia. A list of approved BoNTs and their indications are listed in **Table 1**. Botulinum toxin lasts for three to six months dependent upon indication. **Table 2** describes requirements for BoNT coverage for OHP Fee-for-Service (FFS) patients as determined by the Health Evidence Review Commission (HERC) and outlined on the Prioritized List of Health Services. Hyperhidrosis and chronic anal fissures are currently unfunded. Evidence for these conditions is being reevaluated in order to inform future coverage criteria and establish definitions for medically appropriate and necessary therapy.

Migraine Headaches

Use of BoNT in migraine headaches has been previously reviewed by the P and T committee. Detailed background information related to different types of headaches can be found in the April 2025 Drug class update on Headache Treatment and Prevention. Updated evidence for use of botulinum toxins in migraine will be included in this document.

Hyperhidrosis

Medication therapy for hyperhidrosis has previously not been a funded use on the Oregon Prioritized list. Background information and a review of evidence for drug therapies, including botulinum toxins, is included in the April 2025 Drugs for Hyperhidrosis review and changes to the PA are incorporated into this document (**Appendix 5**).

Anal Fissures

Medication therapy for anal fissures has previously not been a funded use on the Oregon Prioritized list and is found on line 519. Surgical coverage is being considered by HERC prior to 1/1/27. Evidence supporting pharmacologic therapy for anal fissures has not been previously reviewed by the OHP Pharmacy and Therapeutics (P&T) committee.

Anal fissures, also called fissure in ano, are linear splits or tears that occur in the skin of the distal anal canal and are the most common cause of rectal bleeding.[11] They may cause significant pain during defecation which may last several hours.[2] Anal fissures are generally caused by trauma and irritation of the anal canal, often related to constipation or diarrhea.[11] They extend below the dentate line to the anal verge and can occur as primary or secondary fissures.[11] Secondary fissures are associated with underlying chronic diseases, while primary fissures may result from precipitating factors (e.g. diarrhea) but not chronic diseases.[11] They occur more often in younger and middle age adults with roughly an 11% lifetime incidence.[11] Acute anal fissures typically heal spontaneously.[11] If lasting more than 6 weeks a fissure may become chronic, and will often display 1 or more of the following characteristics of chronicity: hypertrophied anal papilla at the proximal aspect of the fissure, sentinel tag at the distal aspect of the fissure, or exposed internal anal sphincter muscle within the base of the fissure.[2] As many as 40% of chronic anal fissures spontaneously heal.[11]

Treatment for anal fissures initially includes a high fiber diet and conservative treatments aimed at symptom control.[11] These include bulk forming laxatives, sitz baths, topical lidocaine cream (2% and 5%) and topical steroids (e.g., 1% hydrocortisone cream).[11] Topical nitrates or topical calcium channel blockers (e.g., nifedipine or diltiazem,) may be used for treatment.[11] The only commercially available topical vasodilator product the United States (US) is nitroglycerin ointment (RECTIV) which is currently available in the fee-for-service program without prior authorization. Topical nitroglycerin is FDA approved for moderate-severe pain from chronic anal fissures.[11] Botulinum toxins have been studied for treatment of chronic fissures,[11] though they are not FDA approved or supported through official Medicaid compendia (i.e., Micromedex) for treatment of chronic anal fissures. Surgical options include lateral internal sphincterotomy, fissurectomy with or without anal advancement flap anoplasty, and fissurectomy with botulinum toxin and sphincterotomy.[11]

Symptom improvement, reduced fissure persistence, prevention of recurrence, and fissure healing are generally used as efficacy outcomes.[2] Standardized definitions of these endpoints and minimum clinically important differences have not been defined for treatment of chronic anal fissure. Incontinence, often transient, is a potential consequence of some treatments for chronic anal fissure. There are various scoring systems for incontinence and debate regarding which most accurately quantifies incontinence and patient quality of life.[12] One scoring system, the Wexner Fecal Incontinence Questionnaire, assesses presence of solid, liquid, or gas incontinence and behaviors of wearing a pad and lifestyle alteration.[12] Each of these 5 parameters is scored as never (0), rarely (1; <1/month), sometimes (2; ≥ 1/month), usually (3; <1/day), and always (4; ≥1/day) with a score range of 0 to 20 points.[12]

Table 1. FDA Approved Botulinum Products

Generic Name	Brand Name	FDA Indication
OnabotulinumtoxinA	BOTOX[8] BOTOX COSMETIC[13]	• Overactive bladder with symptoms of urge incontinence, urgency and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication • 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 • Treatment of neurogenic detrusor overactivity in pediatric **patients 5 years** of age or older who have an inadequate response to or are intolerant of an anticholinergic medication • Prophylaxis of headache in adults with chronic migraine (15 or more days per month with headache lasting 4 hours a day or longer)

		• Treatment of spasticity in **patients 2 years** of age and older
		• Treatment of cervical dystonia in adults to reduce the severity of abnormal head position and neck pain
		• Treatment of severe axillary hyperhidrosis that is inadequately managed by topical agents in adult patients
		• Treatment of blepharospasm associated with dystonia in **patients 12 years** of age and older
		• Treatment of strabismus in **patients 12 years of age and older**
		• Temporary improvement in the appearance of:
		  ○ moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity
		  ○ moderate to severe lateral canthal lines associated with orbicularis oculi activity
		  ○ moderate to severe forehead lines associated with frontalis muscle activity
		  ○ moderate to severe platysma bands associated with platysma muscle activity

AbobotulinumtoxinA	DYSPORT[14]	• Cervical dystonia in adults • Temporary improvement in the appearance of moderate to severe glabellar lines associated with the procerus and corrugator muscle activity in **adults < 65 years** of age • Treatment of spasticity in **patients 2 years** of age and older

IncobotulinumtoxinA	XEOMIN[9]	• Chronic sialorrhea in **patients 2 years** of age and older
		• Upper limb spasticity in adults
		• Upper limb spasticity in pediatric **patients 2 to 17** years of age, excluding spasticity caused by cerebral palsy
		• Cervical dystonia in adults
		• Blepharospasm in adults
		• Appearance of upper facial lines in adults:
		  ○ moderate to severe glabellar lines with corrugator and/or procerus muscle activity
		  ○ moderate to severe horizontal forehead lines associated with frontalis muscle activity
		  ○ moderate to severe lateral canthal lines associated with orbicularis oculi muscle activity

Prabotunlinum toxin A	JEUVEAU[15]	• Temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients
RimabotulinumtoxinB	MYOBLOC[16]	• Cervical dystonia to reduce severity of abnormal head position and neck pain associated with cervical dystonia in adults • Chronic sialorrhea in adults
DaxibotulinumtoxinA	DAXXIFY[7]	• Temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients. • Treatment of cervical dystonia in adult patients.

Table 2. Indications for Botulinum Therapy with Associated Outcomes and Coverage under the Oregon Health Plan

Indication	Outcome Assessment	Prioritized List of Health Services Coverage*
Cervical Dystonia[17,18]	Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)	Line 358 DYSTONIA (UNCONTROLLABLE); LARYNGEAL SPASM Chemodenervation with botulinum toxin injection (CPT 64612, 64616) is

• Movement disorder characterized by disabling, painful muscle contractions of the neck • BoNT-A is recommended as a first-line treatment	• Range 0-85, higher is worse • 12 point change is considered the MCID[23] Tsui Scale • 6 item scale accessing involuntary neck movement • Scores range from 1-25 • MCID not determined	included on this line only for treatment of blepharospasm (ICD-10-CM G24.5), spasmodic torticollis (ICD-10-CM G24.3), and other fragments of torsion dystonia (ICD10-CM G24.9).
Spasticity[19] • Abnormal increase in muscle tone or stiffness • Standard therapy is occupational and/or physiotherapy with antispasticity pharmacotherapy	Ashworth Scale • Scale ranges from 0-4 (4 is more rigid) • MCID is a change of 1 point or more Global Impression of Change Scale (GICS) • Scale ranges from -3 to +3 (higher is better)	Line 290 NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS Chemodenervation with botulinum toxin injection (CPT 64642-64647) is included on this line for treatment of upper and lower limb spasticity (ICD-10-CM codes G24.02, G24.1, G35, G36.0, I69.03- I69.06 and categories G71, and G80-G83)
Overactive bladder[20] (Neurogenic detrusor overactivity / Urinary incontinence) • Associated with urgency, frequency and with or without incontinence • First-line therapy recommendations include antimuscarinic therapy	Overactive bladder symptom score (OABSS) • Scores range from 0-15, with higher scores indicating more symptoms • A decrease of 3 points is the MCID	Line 324 FUNCTIONAL AND MECHANICAL DISORDERS OF THE GENITOURINARY SYSTEM INCLUDING BLADDER OUTLET OBSTRUCTION Chemodenervation of the bladder (CPT 52287) is included on this line only for treatment of idiopathic detrusor over-activity or neurogenic detrusor over-activity (ICD-10-CM N32.81) in patients who have not responded to or been unable to tolerate at least two urinary incontinence antimuscarinic or beta-3 adrenergic therapies (e.g. fesoterodine, oxybutynin, solifenacin, darifenacin, tolterodine, trospium, mirabegron, vibegron). Treatment is limited to 90 days, with additional treatment only if the patient shows documented positive response. Positive response to therapy is defined as a reduction on of urinary frequency of 8 episodes per day or urinary incontinence of 2 episodes per day compared to baseline frequency.
Sialorrhea[21] • Excessive drooling often due to a neurologic disorder	There are no validated outcome measures with MCIDs	Not covered – falls below line 469. Line 493 SIALOLITHIASIS, MUCOCELE, DISTURBANCE OF SALIVARY SECRETION, OTHER AND UNSPECIFIED DISEASES OF SALIVARY GLANDS Chemodenervation with botulinum toxin injection (CPT 64611) is included on this line for the treatment of excessive salivation. (ICD-10 -CM K11.5-K11.9,R68.2)

Blepharospasm[22] • Focal dystonia characterized by involuntary eyelid closure • Botulinum toxin is considered first-line therapy	Jankovic Rating Scale (JRS) severity subscore • Values of 0-4 with lower values being better • MCID not determined Patient Evaluation of Global Response (PEGR) • Values of -4 to +4 with higher scores suggesting benefit • MCID not determined	Line 358 DYSTONIA (UNCONTROLLABLE); LARYNGEAL SPASM Chemodenervation with botulinum toxin injection (CPT 64612, 64616) is included on this line only for treatment of blepharospasm (ICD-10-CM G24.5), spasmodic torticollis (ICD-10-CM G24.3), and other fragments of torsion dystonia (ICD10-CM G24.9).
Strabismus • Misalignment of the eye • Managed with corrective lenses, eye exercises, surgery or botulinum injection	Correction of eye alignment	Line 348 STRABISMUS DUE TO NEUROLOGIC DISORDER Chemodenervation with botulinum toxin injection (CPT 67345) is included on this line for the treatment of strabismus due to other neurological disorders (ICD-10-CM H50.89).
Migraine Headaches[23] • Moderate to severe headache attacks • First-line treatment options include: beta-blockers, anticonvulsants and tricyclic antidepressants • Botulinum is indicated for chronic migraine headaches	Migraine frequency Migraine Disability Assessment Score (MIDAS) • Scores of 0-5 are indicative of little or no disability, 6-10 mild disability, 11-20 moderate disability, and 21 or greater as severe disability. • MCID is 4.5 points	Line 407 MIGRAINE HEADACHES Chemodenervation for treatment of chronic migraine (CPT 64615) is included on this line for prophylactic treatment of adults who meet all of the following criteria: A) have chronic migraine defined as headaches on at least 15 days per month of which at least 8 days are with migraine B) has not responded to or have contraindications to at least three prior pharmacological prophylaxis therapies (e.g. beta-blocker, anticonvulsant or tricyclic antidepressant) C) their condition has been appropriately managed for medication overuse D) treatment is administered in consultation with a neurologist or headache specialist. Treatment is limited to two injections given 3 months apart. Additional treatment requires documented positive response to therapy. Positive response to therapy is defined as a reduction of at least 7 headache days per month compared to baseline headache frequency.
Reduction in moderate to severe glabellar lines	Improved appearance	Not a covered indication.
Esophageal stricture • Trouble swallowing • Narrowing of the esophagus	Not FDA approved for this indication	Covered by OHP: Line 375 ESOPHAGEAL STRICTURE; ACHALASIA Chemodenervation with botulinum toxin injection (CPT 43201) is included on this line for treatment of achalasia (ICD-10 K22.0).
Abbreviations: BoNT-A = botulinum toxin A; FDA = Food and Drug Administration; MCID = minimal clinically important difference; NA = not applicable; OHP = Oregon Health Plan. Key: * As determined by the Health Evidence Review Commission (HERC) Guideline Notes for January 1, 2025 Prioritized List of Health Services.		

Additional botulinum toxin indications not covered by the HERC Prioritized List:

- Guideline Note 37, surgical interventions for conditions of the back and spine other than scoliosis
- Guideline Note 145, treatments for benign prostate enlargement with lower urinary tract symptoms
- Line 510 disorders of sweat glands, chemodenervation with botulinum toxin injection (CPT 64650, 64653) is included on this line for the treatment of axillary hyperhidrosis and palmar hyperhidrosis (ICD-10-CM L74.52, R61).
- Line 519 chronic anal fissure, chemodenervation with botulinum toxin injection (CPT 46505) is included on this line for the treatment of anal fissures.

Methods:
A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 3**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, the Scottish Intercollegiate Guidelines Network (SIGN), and Canada's Drug Agency (CDA-AMA) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:
After review, 63 systematic reviews were excluded due to poor quality (e.g, indirect network-meta analyses or failure to meet AMSTAR criteria), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).

Botulinum toxin injection vs topical nitrates for chronic anal fissure: an updated systematic review and meta-analysis of randomized controlled trials
A systematic review evaluated BoNT injections compared to TN for chronic anal fissures.[3] Six RCTs (n=194 BoNT, n=199 TN) with similar numbers of men and women were included. The mean participant age ranged from 34.4 to 44.1 years.[3] There was significant heterogeneity between studies with treatment drugs and dose for both TN interventions (i.e., 0.2% nitroglycerin ointment twice daily for 6 weeks, 0.2% nitroglycerin ointment three times daily for 8 weeks, 1% isosorbide dinitrate ointment 6 times daily with duration not specified, etc.) and BoNT (i.e., BOTOX 20 units, 30 units, 40 units, or 60 units total, often divided into to two injections; DYSPORT 90 units, etc.).[3] Follow-up ranged from 6.2 to 60 months.[3] All studies had low risk of bias for randomization and other sources of bias. Two studies had high risk of bias in multiple categories and the others had low or unclear ratings in all categories. [3] Endpoints of fissure healing and recurrence varied between trials and do not have formalized, uniform definitions.[3] One study used the Wexner Fecal Incontinence Questionnaire to assess transient anal incontinence while 4 studies reported the outcome without a formal questionnaire.[3]

Rate of incomplete fissure healing in was lower in the BoNT group (28.6%) versus the TN group (42.1%), though this was not statistically significant (OR=0.47; 95% CI 0.13 to 1.67, p=0.24; 5 studies; n=313) and heterogeneity among trials was statistically significant (p=0.0005; I^2=80%).[3] The same 5 studies report twice as much transient anal incontinence in the BoNT group (BoNT 10.4% vs. TN 4.4%, OR 2.53; 95% CI 0.98 to 6.57, p=0.06, I^2=0%), though the difference was not statistically significant.[3] Fissure recurrence was reported in all included studies and was not statistically significantly different (BoNT 18.5% vs. TN 25.1%, OR 0.7; 95% CI 0.39 to 1.25, p=0.22, I^2=4%).[3] Total side effects (BoNT 6.4% vs. TN 33.1%, OR 0.12; 95% CI 0.02 to 0.63, p=0.01, I^2=72%) and headache (BoNT 4.8% vs. TN

27.9%, OR 0.10; 95% CI 0.02 to 0.60, p=0.01, I^2=69%) were more common in patients receiving TN, though heterogeneity was also statistically significant for both outcomes.[3]

Botulinum toxin for the treatment of strabismus

A Cochrane systematic review was published in 2023 assessing the use of BoNT in the treatment of strabismus in people of all ages.[6] This was an update from a previous 2017 review. Literature was searched through July 6, 2022 for RCTs comparing BoNT to alternative therapies including strabismus surgery, alternative medications (e.g., bupivacaine), and conservative treatments (e.g., orthoptic exercises, prisms, or lens therapy).[6] Four RCTs (n=242) in adults with esotropia or exotropia, children with acquired esotropia, and children with infantile esotropia were included.[6] Enrollment ranged from 30 to 110 patients and were conducted in Spain, Canada, and South Africa.[6] Most patients were children (88.2%).[6] Duration of follow-up ranged from 6 to 36 months and most studies had high or unclear risk of bias for randomization, allocation concealment, blinding of investigators and participants as well as unclear risk of bias for reporting and other bias categories.[6] Improvement or corrected strabismus was defined as less than or equal to 10 prism diopters at 6 months or less than or equal to 8 prism diopters at 1 year.[6] Patients who receive surgery may be more likely to improve or correct strabismus compared with those who treated with BoNT (risk ratio (RR) 0.72, 95% CI 0.53 to 0.99; I^2 = 50%; 4 studies, 242 participants; low-certainty evidence).[6]

Two studies compared BoNT with surgery in children who required retreatment for acquired or infantile esotropia and found BoNT may have little to no difference in achieving sensory fusion (RR 0.88, 95% CI 0.63 to 1.23; I^2 = 0%; 2 studies, 102 participants; low-certainty evidence) and stereopsis (RR 0.86, 95% CI 0.59 to 1.25; I^2 = 0%; 2 studies, 102 participants; low-certainty evidence) when compared to surgery.[6]

Three studies reported non-serious adverse events.[6] Partial transient ptosis (range 16.7% to 37.0%) and transient vertical deviation (range 5.6% to 18.5%) were observed among participants treated with botulinum toxin in three studies.[6] In one study, 44.7% participants in the surgery group experienced discomfort.[6] No studies reported serious adverse events or post-treatment quality of life.[6]

New Guidelines:

High Quality Guidelines:

Veterans Affairs Practice Guideline for Management of Headache

The VA released updated guidelines on the management of headache in 2023.[1] Published literature was included through August 16, 2022.[1] The recommendations relating to use of botulinum toxins were not changed from the previous guideline iteration.[1] A new section for comparative effectiveness and combination therapy was added and included no strong recommendations.[1] Those recommendations are included in **Table 3**.[1]

Table 3. Preventive migraine pharmacotherapy with botulinum toxins[1]

Recommendation	Strength	Category
We suggest onabotulinumtoxinA injection for the prevention of chronic migraine.	Weak for	Reviewed, not changed
We suggest against abobotulinumtoxinA or onabotulinumtoxinA injection for the prevention of episodic migraine.	Weak against	Reviewed, not changed
We suggest against botulinum/neurotoxin injection for the prevention of chronic tension-type headache	Weak against	Reviewed, not changed
There is insufficient evidence to recommend for or against any specific medication over another for the prevention of migraine headache, tension headache, or cluster headache.	Neither for nor against	Reviewed, new-added

The American Society of Colon and Rectal Surgeons (ASCRS) Clinical Practice Guidelines for the Management of Anal Fissures

The ASCRS published updated guidelines in 2023 for use by all practitioners, health care workers, and patients interested in information related to the management of anal fissures.[2] Published data was included through March 20, 2022 and prospective RCTs and meta-analyses were given preference, though lower quality sources such as peer-reviewed observational and retrospective studies were included in the absence of higher-level evidence.[2] Recommendations were assessed via the GRADE system.[2] Selected recommendations are included in **Table 4**.[2] Recommendations solely focused on surgical technique rather than place in therapy were not included in the summary below.

Table 4. Treatment Recommendations for Acute and Chronic Anal Fissures[2]

Recommendations	**Strength of Recommendation**	**Quality of Evidence**
Acute Fissures		
Non-operative treatment of acute anal fissures is safe and should typically be first-line treatment.	Strong	Moderate
Chronic Fissures		
Anal fissures may be treated with topical nitrates, although headache symptoms may limit their efficacy.	Strong	Moderate
Compared with topical nitrates, the use of calcium channel blockers for chronic anal fissures has similar efficacy, with a superior side-effect profile, and can be used as first-line treatment.	Strong	Moderate
Botulinum toxin has similar results compared with topical therapies as first-line therapy for chronic anal fissures and modest improvement in healing rates as second-line therapy following failed treatment with topical therapies.	Strong	Moderate
Lateral internal sphincterotomy may be offered in selected pharmacologically naive patients with chronic anal fissure.	Strong	High
Lateral internal sphincterotomy is the treatment of choice for chronic anal fissures in selected patients without baseline fecal incontinence.	Strong	High
Short-term outcomes of repeat lateral internal sphincterotomy or botulinum injection for recurrent anal fissure have shown good healing rates with a low risk of fecal incontinence, but the data are limited and require further study.	Weak	Low
The addition of an anocutaneous flap to botulinum toxin injection or to lateral internal sphincterotomy may decrease postoperative pain and allow for primary wound healing.	Weak	Low

In the treatment of acute anal fissures, a small study of 103 patients found sitz baths plus fiber supplementation to be more likely to achieve pain relief than patients receiving either topical anesthetics or topical hydrocortisone (91% vs. 60% vs. 68%; $p<0.05$).[2] A small double-blind trial of fiber compared to placebo in patients with healed acute anal fissures found a lower recurrence rate with fiber (16% vs. 60%; $p<0.01$).[2] For acute fissures that fail to heal and become chronic, there were no specific recommendations for timing of initiation of treatments for chronic anal fissures versus waiting for spontaneous healing with supportive care.

When using topical vasodilators in the treatment of chronic anal fissures, topical nitroglycerin is associated with a roughly 50% healing rate.[2] A meta-analysis identified that topical nitroglycerin lowered the odds ratio of fissure persistence or recurrence when compared to placebo (OR 0.35; 95% CI 0.19 to 0.65; 18 studies; n=734).[2] Headache is a dose dependent side effect and has been seen in 30% of patients and may lead to drug discontinuation in 20% of treated patients.[2] Higher doses are not associated with improved healing.[2]

A study of 45 patients receiving topical glyceryl trinitrate compared to topical diltiazem found similar healing rates (54.9% vs. 66.7%; P=0.2).[2] In a systematic review (7 studies; n=238), topical diltiazem was associated with a lower risk of headache (relative risk 0.39; 95% CI 0.24 to 0.66).[2]

There is heterogeneity in dosing protocol and injection technique between studies of botulinum toxin.[2] Healing rates have not been found to be dose dependent and vary from 33% to 96% across various studies, while the complication of fecal incontinence remained stable at approximately 5%.[2] Multiple studies show similar healing rates when using botulinum toxins compared to topical vasodilators, and one randomized trial showed botulinum toxin had improved healing rates at 1 year when compared to topical nitroglycerin (67% vs. 33%; P=0.01).[2] Data of combination therapy are limited, but a small study of 30 patients suggests improved healing with topical nitroglycerin plus botulinum toxin over botulinum toxin alone (60% vs. 20%; P=0.025).[2]

Data suggest lateral internal sphincterotomy (LIS) to have superior healing rates over topical vasodilators or botulinum toxin.[2] This may be related to compliance with pharmacologic therapy long-term.[2] Additionally, those with symptoms from chronic anal fissure lasting more than one year are unlikely to respond to pharmacologic therapy.[2] One nonrandomized study (n=80) administered botulinum toxin for recurrent anal fissure after LIS, with a 74% healing rate at 2 months and 10% rate of temporary flatus incontinence.[2] Additional data are needed to direct therapy for treatment of recurrence after LIS.

Additional Guidelines for Clinical Context:
After review, 1 guideline was excluded due to obsolescence and poor quality.[24]

New Formulations or Indications:
DAXXIFY (daxibotulinumtoxinA-lanm) injection received a new indication in August 2023 for treatment of cervical dystonia in adult patients with up to 250 units via intramuscular injection.[7]

XEOMIN (incobotulinumtoxinA) injection received new indications in July 2024 for the appearance of upper facial lines in adults with moderate to severe horizontal forehead lines associated with frontalis muscle activity or moderate to severe lateral canthal lines associated with orbicularis oculi muscle activity.[9] This indication is not covered on the Oregon Health Plan.

BOTOX (onabotulinumtoxinA) injection received a new indication in August 2024 for temporary improvement in the appearance of moderate to severe platysma bands associated with platysma muscle activity.[8] This indication is not covered on the Oregon Health Plan.

New FDA Safety Alerts:
April 16, 2024: FDA safety alert that unsafe counterfeit version of BOTOX had been found in multiple states and administered to consumers for cosmetic purposes.[25] Adverse events, including hospitalizations, were linked to the counterfeit BOTOX. Symptoms included blurred or double vision, difficulty swallowing, dry mouth, constipation, incontinence, shortness of breath, weakness and difficulty lifting one's head following injection of these products. These symptoms are similar to those seen when botulinum toxin spreads to other parts of the body. These incidents have occurred when counterfeit BOTOX is injected by licensed and unlicensed individuals and/or in non-medical or unlicensed settings. The products appear to have been purchased from unlicensed sources. Medications purchased from unlicensed sources may be misbranded, adulterated, counterfeit, contaminated, improperly stored and transported, ineffective and/or unsafe.

Table 5. Description of new FDA Safety Alerts[9,14]

Generic Name	Brand Name	Month / Year of Change	Location of Change (Boxed Warning, Warnings, CI)	Addition or Change and Mitigation Principles (if applicable)
Incobotulinumtoxin A	XEOMIN	9/2023	Warning and Precaution	New subsection for pre-existing conditions at the injection site. Caution should be used when targeted muscle shows excessive weakness or atrophy.
Abobotulinumtoxin A	DYSPORT	9/2023	Warning and Precaution	Revision of risk when targeted muscle shows excessive weakness or atrophy. Information relocated from "facial anatomy in the treatment of glabellar lines" subsection to new subsection with application to all indications.

Randomized Controlled Trials:

A total of 75 citations were manually reviewed from the initial literature search. After further review, 73 citations were excluded because of wrong study design (eg, observational), comparator (eg, no control or placebo-controlled), or outcome studied (eg, non-clinical). The remaining 2 trials are summarized in the table below. Full abstracts are included in **Appendix 2**.

Table 6. Description of Randomized Comparative Clinical Trials.

Study	Comparison	Population	Primary Outcome	Results	Notes/Limitations
Herreros[4]	1. BoNT A 10 units at each inter-sphincteric groove (2 injections) plus diltiazem gel 8 mg topically three times daily x 12 wk (n=35) 2. BoNT A 10 units at each inter-sphincteric groove (2 injections) plus inert gel topically three times daily for x 12 wk (n=35) 1:1 randomization	*Inclusion* -Adults -CAF (≥ 8 wk) -significant pain >3 (10-point VAS) -fissure at posterior anal verge -able to fill out symptom diary *Exclusion* -anterior or lateral fissure -acute fissure -complication (stenosis, abscess, fistula, hemorrhoids)	Fissure healing at 12 wk	Per protocol 1. 13/25 (52%) 2. 11/30 (36.7%) OR 1.87; 95% CI 0.63-5.51 p=0.25 ITT 1. 37.1% 2. 31.4% OR 1.28; 95% CI 0.47-3.46 p=0.61 Excluded from ITT 1. LTFU=3 d/c due to side effect=4 d/c due to surgery=3	-Randomized -Double-blind -Small study population -Single study center (Spain) -59% male -Median age ~50 y -BoNT was reinjected if absence of clinical improvement at 4 weeks or fissure persistence at 8 weeks. -Secondary outcome of recurrence by 24 weeks was similar between groups -Compliance checked by personal interview and review of symptom diary. Patients

		-comorbidity (e.g., immunocompromise, chronic gastrointestinal condition) -specific medications		2. LTFU=2 d/c due to side effect=1 d/c due to surgery=2	withdrawn if <75% for diary and gel application. -All LTFU and discontinuations statistically imputed as failures
Hussain[5]	1. BoNT 0.2 mL at each inter-sphincteric plane (2 injections) (n=44) 2. BoNT 0.2 mL at each inter-sphincteric plane (2 injections) plus 0.2% topical glyceryl trinitrate cream 8 hourly with dose of 1g (n=44)	*Inclusion* -Adults -CAF >4 weeks or recurrent -symptoms of pain during defecation -mucosal tear on DRE *Exclusion* -perianal inflammatory disease (e.g., TB, Crohn) -colorectal or perianal mass/malignancy	Post-operative pain at 24 hours using 10-point VAS Healing at 4 wk	Postoperative pain 1. 4.67±1.16 2. 3.06±0.65 p=0.009 Wound healing 1. 69.7% 2. 90.9% p=0.03	-Randomized -Open label -Small study population -Single study center (Pakistan) -76% male -~1/2 of patients aged 18-30 years -Duration of topical nitrate not specified
Abbreviations: Botulinum toxin = BoNT; CAF = chronic anal fissure; CI = confidence interval; d/c = discontinue; DRE = digital rectal exam; ITT = intent to treat; LTFU = lost to follow-up; OR = odds ratio; RCT = randomized clinical trial; TB = tuberculosis; VAS = visual analog scale; wk = week; y = year.					

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Appendix 1: Current Preferred Drug List

Generic	Brand	Route	Form	PDL
onabotulinumtoxinA	BOTOX	INJECTION	VIAL	
onabotulinumtoxinA	BOTOX COSMETIC	INTRAMUSC	VIAL	
daxibotulinumtoxinA-lanm	DAXXIFY	INTRAMUSC	VIAL	
abobotulinumtoxinA	DYSPORT	INTRAMUSC	VIAL	
prabotulinumtoxinA-xvfs*	JEUVEAU	INTRAMUSC	VIAL	
rimabotulinumtoxinB	MYOBLOC	INTRAMUSC	VIAL	
incobotulinumtoxinA	XEOMIN	INTRAMUSC	VIAL	
incobotulinumtoxinA	XEOMIN	INTRAMUSC	VIAL	N

*Not a rebate eligible product

Appendix 2: Abstracts of Comparative Clinical Trials

Herreros B, Espi A, Monton Rodriguez C, et al. Botulinum Toxin Injection Plus Topical Diltiazem for Chronic Anal Fissure: A Randomized Double-Blind Clinical Trial and Long-term Outcome. *Dis Colon Rectum*. Dec 1 2021;64(12):1521-1530. doi:10.1097/DCR.0000000000001983

BACKGROUND: Chemical sphincterotomy avoids the risk of permanent incontinence in the treatment of chronic anal fissure, but it does not reach the efficacy of surgery and recurrence is high. Drug combination has been proposed to overcome these drawbacks.
OBJECTIVE: This study aimed to compare the clinical, morphological, and functional effects of combined therapy with botulinum toxin injection and topical diltiazem in chronic anal fissure and to assess the long-term outcome after healing.
DESIGN: This is a randomized, controlled, double-blind, 2-arm, parallel-group trial with a long-term follow-up.
SETTINGS: This study was conducted at a tertiary care center. PATIENTS: A total of 70 consecutive patients were referred to the gastroenterology department of a hospital in Valencia, Spain.
INTERVENTION: After botulinum toxin injection (20 IU), patients were randomly assigned to local diltiazem (diltiazem group) or placebo gel (placebo group) for 12 weeks.
MAIN OUTCOME MEASURES: The primary outcome was fissure healing (evaluated by video register by 3 independent physicians). Secondary outcomes included symptomatic relief (30-day diary), effect on anal sphincters (manometry), safety, and long-term recurrence (24 months and 10 years).
RESULTS: Healing was achieved per protocol in 13 of 25 (52%) patients of the diltiazem group and 11 of 30 (36.7%) patients of the placebo group ($p = 0.25$); on an intention-to-treat basis in 37.1% and 31.4% ($p = 0.61$). Both groups displayed significant reduction of anal pressures. Thirty percent reported minor and transitory incontinence, without differences between groups. Nine (69.2%) of the diltiazem group and 6 (54.5%) of the placebo group experienced a relapse at 24 months ($p = 0.67$). The overall recurrence rate at 10 years was 83.3% (20/24 patients).
LIMITATIONS: This study was limited by the loss of patients during the trial. The low healing rate led to a small cohort to assess recurrence. CONCLUSIONS: Combined botulinum toxin injection and topical diltiazem is not superior to botulinum toxin injection in the treatment of chronic anal fissure. Both options offer suboptimal healing rates. Long-term recurrence is high (>80% at 10 years) and might appear at any time after healing.

Hussain S, Ammar AS, Hameed AR, Aslam I, Afzal A. Comparison of outcome of botulinum toxin injection with and without glyceryl trinitrate in chronic anal fissure in terms of post operative pain and healing. Randomized Controlled Trial
Comparative Study. *JPMA J Pak Med Assoc*. Jul 2024;74(7):1245-1248. doi:https://dx.doi.org/10.47391/JPMA.9726

Objective: To compare the outcome of botulinum toxin injection with and without glyceryl trinitrate with respect to postoperative pain and healing in the treatment of anal fissures.
Method: The prospective, comparative study was conducted at the Department of General Surgery, Mayo Hospital, Lahore, Pakistan, from September 1, 2021, to August 31, 2022, and comprised adult chronic anal fissure patients of either gender. They were randomised using the lottery method into group A which received botulinum toxin injection, and group B which received botulinum toxin injection plus 1g of 0.2% topical glyceryl trinitrate cream. Post-operative pain was measured 24 hours after the procedure using the visual analogue scale. Healing was assessed by examining the wound for the appearance of granulation tissue 4 weeks post-procedure. Data was analysed using SPSS 26.
Results: Of the 88 patients, 44(50%) were in group A; 32(72.7%) males and 12(27.3%) females with mean age 33.91±14.8 years. There were 44(50%) patients in group B; 35(79.5%) males and 9(20.5%) females with mean age range 36.33±14.9 years. The mean postoperative pain at 24 hours in group A was 4.67±1.16 and it was 3.06±0.65 in group B ($p=0.009$). In group A, 23(69.7%) patients showed complete healing at 4 weeks compared to 30(90.9%) in group B ($p=0.030$).
Conclusion: Botulinum toxin injection with glyceryl trinitrate could be considered as first line of treatment for chronic anal fissure in patients who refuse surgery and with previous sphincter surgery

Appendix 3: Medline Search Strategy

Ovid MEDLINE(R) without Revisions 1996 to November Week 3 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations January 22, 2025

#	Query	Results from 22 Jan 2025
1	Botulinum Toxins, Type A/ or onabotulinumtoxin A.mp.	12,085
2	abobotulinumtoxin A.mp.	39
3	rimabotulinumtoxin B.mp.	7
4	incobotulinumtoxin A.mp.	58
5	prabotulinumtoxin A.mp.	19
6	abobotulinumtoxin.mp.	45
7	rimabotulinumtoxin.mp.	9
8	incobotulinumtoxin.mp.	69
9	prabotulinumtoxin.mp.	19
10	Botulinum Toxins/	8,495
11	onabotulinumtoxin.mp.	282
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	19,732
13	limit 12 to (english language and (clinical trial, all or clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or equivalence trial or guideline or multicenter study or practice guideline or randomized controlled trial or "systematic review"))	3,827
14	limit 13 to yr="2018"	141
15	anal fissures.mp.	725
16	anal fissure.mp.	1,477
17	15 or 16	1,866
18	13 and 17	85 (65 were later manually excluded as published prior to 2015)
19	Migraine Disorders/	31,344
20	limit 19 to yr="2023"	1,176
21	13 and 20	11
22	Hyperhidrosis/	3,528
23	13 and 22	132

Author: Fletcher

Date: April 2025

24	limit 13 to yr="2023"	114 (includes duplicate documents with disease specific searches above)

Appendix 4: Key Inclusion Criteria

Population	Patients with on-label or compendial indications for botulinum toxin or for chronic anal fissure
Intervention	Botulinum toxin A and botulinum toxin B
Comparator	Active pharmacologic control
Outcomes	Dependent upon indication being treated
Timing	Not applicable
Setting	Outpatient, excluding intraoperative use during concomitant surgical procedure

Botulinum Toxins

Goal(s):
- Approve use of botulinum toxins for conditions funded under the Oregon Health Plan (OHP) and supported by evidence of benefit.
- Require positive response to therapy for continued use to manage chronic migraine headaches or overactive bladder.
- Allow case-by-case review for members covered under the EPSDT program.

Length of Authorization:
- From 90 days to 12 months

Requires PA:
- Use of botulinum toxins (billed as a physician administered or pharmacy claim) without associated dystonia or neurological disease diagnosis in last 12 months.

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. Is this a request for renewal of a previously approved prior authorization for management of migraine headache or detrusor muscle over-activity ("overactive bladder") or hyperhidrosis?	**Yes:** Go to **Renewal Criteria**	**No:** Go to #2
2. What diagnosis is being treated?	Record ICD10 code	

Approval Criteria		
3. Is botulinum toxin treatment for any of the following? a. Upper or lower limb spasticity (G24.02, G24.1, G35, G36.0, I69.03- I69.06 and categories G71, and G80-G83) b. Strabismus due to a neurological disorder (H50.89) c. Blepharospasm (G24.5) d. Spasmodic torticollis (G24.3) e. Torsion dystonia (G24.9) f. Achalasia (K22.0)	**Yes:** Approve for up to 12 months	**No:** Go to #4
4. Is botulinum toxin treatment for chronic migraine, with ≥15 headache days per month, of which ≥8 days are with migraine?	**Yes:** Go to #5 Baseline headaches per month: _____	**No:** Go to #8
5. Is the botulinum toxin administered by, or in consultation with, a neurologist or headache specialist?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness.
6. Has the patient had an adequate trial (2-6 months) without response, or has contraindications, to at least 3 of the following OHP preferred drugs (in the same or different drug classes)? • Propranolol immediate-release, metoprolol, or atenolol • Topiramate, valproic acid, or divalproex sodium • Amitriptyline, nortriptyline, or venlafaxine • Candesartan or telmisartan	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness. Recommend trial of preferred alternatives at www.orpdl.org/drugs/

Approval Criteria		
7. Do chart notes indicate headaches are due to medication overuse?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Approve no more than 2 injections given ≥3 months apart within a 12 month time period. Additional treatment requires documented positive response to therapy from baseline (see Renewal Criteria).
8. Is botulinum toxin treatment for detrusor muscle over-activity ("overactive bladder")?	**Yes:** Go to #9	**No:** ~~Pass to RPh.~~ Go to #10
9. Has the patient had an inadequate response to, or is intolerant to at least two urinary incontinence antimuscarinic or beta-3 adrenergic therapies, such as those listed below? a. Fesoterodine (OHP preferred) b. Oxybutynin (OHP preferred) c. Solifenacin (OHP preferred) d. Darifenacin e. Flavoxate f. Mirabegron g. Tolterodine h. Trospium i. Vibegron	**Yes:** • Baseline urine frequency/day: _____. • Baseline urine incontinence episodes/day: _____. Approve for up to 90 days. Additional treatment requires documented positive response to therapy from baseline (see Renewal Criteria).	**No:** Pass to RPh. Deny; medical appropriateness.
10. Is botulinum toxin treatment for use in patient with chronic anal fissure documented to have lasted longer than 6 weeks?	**Yes:** Approve one-time dose for 6 months (may be injected into multiple sites on same day)	**No:** Go to #11

Approval Criteria		
11. Is botulinum toxin treatment of primary axillary hyperhidrosis? Note: secondary axillary hyperhidrosis related to comorbid conditions and non-axillary hyperhidrosis are not FDA-approved.	**Yes**: If not eligible for EPSDT review: Pass to RPh. Go to #16 If eligible for EPSDT review: Go to #12	**No:** Pass to RPh. Go to #16
12. Is the requested product prescribed by, or in consultation with, a neurologist or dermatologist?	**Yes:** Go to #13	**No**: Pass to RPh. Deny; medical appropriateness
13. Is there documentation that the diagnosis detrimentally impacts at least one of the following? a. disability or health impairment (e.g., complications, comorbidities, etc) b. age-appropriate growth or development c. independence in self-care or activities of daily living ~~a.~~d. ability to live and work in the setting of the patient's choice	**Yes:** Go to #14	**No:** Pass to RPh; Deny; medical necessity
14. Is there documentation of severe symptoms which interfere with daily activities more than once per week as indicated by one of the following: • Hyperhidrosis Disease Severity Scale (HDSS) ≥ 3 • Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax) ≥ 3 • Axillary Sweating Daily Diary – item 2 (sweating severity) ≥ 4 on a 0-10 point scale Note: these same assessments should be evaluated for continuation of treatment.	**Yes:** Go to #15	**No:** Pass to RPh. Deny; medical necessity.

Approval Criteria		
15. Is there documentation indicating lack of adequate treatment with non-pharmacologic management (e.g., trigger identification and avoidance, clothing modification, use of topical antiperspirants)?	**Yes**: Approve no more than 2 injections given ≥8 weeks apart within a 12--month time period.	**No:** Pass to RPh. Deny; medical appropriateness

~~11.~~16. ~~-~~Review treating condition, age, and ICD-10 code. ICD-10 codes included in the tables below are denied. If ICD-10 code is not included in the tables below, medical literature with evidence for use in funded conditions must be submitted by the prescriber. RPh may approve for up to 12 months for funded conditions with evidence of benefit.

If not eligible for EPSDT review: Deny for the following conditions; not funded by the OHP **If eligible for EPSDT review, evaluate FDA-approved indications and disease severity. If the drug is FDA approved for the condition AND prescriber submits documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc.), RPh may approve for up to 12 months.**
▪ Axillary hyperhidrosis (L74.510)~~and palmar hyperhidrosis (L74.52, R61)~~ ▪ Neurologic conditions with none or minimally effective treatment or treatment not necessary (G244; G2589; G2581; G2589; G259) ▪ Facial nerve disorders (G510-G519) ▪ Spastic dysphonia (J387) ~~▪ Anal fissure (K602)~~ ~~▪ Disorders of sweat glands (e.g., focal hyperhidrosis) (L301; L740-L759; R61)~~ ▪ Other disorders of cervical region (M436; M4802; M530; M531; M5382; M5402; M5412; M542; M6788) ▪ Acute and chronic disorders of the spine without neurologic impairment (M546; M545; M4327; M4328; M532X7; M532X8; M533; M438X9; M539; M5408; M545; M5430; M5414-M5417; M5489; M549) ▪ Disorders of soft tissue (M5410; M609; M790-M792; M797) ▪ Headaches (G44209; G44009; G44019; G44029; G44039; G44049; G44059; G44099; G44209; G44219; G44221; G44229; G44309; G44319; G44329; G4441; G4451-G4453; G4459; G4481-G4489; G441; R51) ▪ Gastroparesis (K3184) ▪ Lateral epicondylitis (tennis elbow) (M7710-M7712) ▪ Unspecified diseases of the salivary glands (sialorrhea) (K11.5-K11.9,R68.2)
Deny for medical appropriateness because evidence of benefit is insufficient

- Dysphagia (R130; R1310-R1319)
- Secondary and non-axillary focal hyperhidrosis (L74511-L7452)
- Other disorders of sweat glands (L301; L740-L744; L748-L749; R61)
- Other extrapyramidal disease and abnormal movement disorders (G10; G230-GG238; G2401; G244; G250-G26)
- Other disorders of binocular eye movements (e.g., esotropia, exotropia, mechanical strabismus, etc.) (H4900-H518)
- Tics (F950-F952; F959)
- Laryngeal spasm (J385)
- Spinal stenosis in cervical region or brachial neuritis or radiculitis NOS (M4802; M5412-M5413)
- Spasm of muscle in absence of neurological diagnoses (M6240-M62838)
- Contracture of tendon (sheath) in absence of neurological diagnoses (M6240; M62838)
- Amyotrophic sclerosis (G1221)
- Clinically significant spinal deformity or disorders of spine with neurological impairment (M4800; M4804; M4806; M4808; M5414-M5417)
- Essential tremor (G25.0)
- Hemifacial spasm (G513)
- Occupational dystonia (e.g., “Writer’s cramp”) (G248, G249)
- Hyperplasia of the prostate (N400-403; N4283)
- Conditions of the back and spine for the treatment of conditions on lines 346 and 527, including cervical, thoracic, lumbar and sacral conditions. See Guideline Note 37.

Renewal Criteria		
1. Is this a request for renewal of a previously approved prior authorization for management of migraine headache?	**Yes:** Go to #2	**No:** Go to #3
2. Is there documentation of a reduction of ≥7 migraine headache days per month compared to baseline migraine headache frequency?	**Yes:** Approve no more than 2 injections given ≥3 months apart. Baseline:____ migraine headaches/month Current:____ migraine headaches/month	**No:** Pass to RPh. Deny; medical appropriateness
3. Is this a request for renewal of a previously approved prior authorization for management of detrusor muscle over-activity ("overactive bladder")?	**Yes:** Go to #4	**No:** Go to ~~Approval Criteria~~#5
4. Is there a reduction of urinary frequency of ≥8 episodes per day or urinary incontinence of ≥2 episodes per day compared to baseline frequency?	**Yes:** Approve for up to 12 months • Baseline:____ urine frequency/day • Current:____ urine frequency/day -or- • Baseline:____ urine incontinence episodes/day • Current:____ urine incontinence episodes/day	**No:** Pass to RPh. Deny; medical appropriateness
5. Is the request for renewal of a previously approved prior authorization for axillary hyperhidrosis?	**Yes:** Go to #6	**No:** Go to **Approval Criteria**

Renewal Criteria		
6. Is there documentation of symptom improvement from baseline as assessed by the prescribing provider? Note: the following are described as clinically relevant responses to therapy: • Total score ≤ 2 on the Hyperhidrosis Disease Severity Scale (HDSS) or Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax) • ≥ 4 point improvement on the Axillary Sweating Daily Diary – item 2 (sweating severity)	**Yes:** approve for 12 months	**No:** Pass to RPh; Deny; medical appropriateness

P&T / DUR Review: *4/25 (SF/SS); 6/23 (KS),4/22 (AG); 5/19 (KS); 9/18; 5/18; 11/15; 9/14; 7/14*
Implementation: *TBD; 7/1/23; 5/1/22; 11/1/2018; 7/1/18; 10/13/16; 1/1/16*