Medical Policy Bulletin
Title:
Botulinum Toxin Agents
Policy#:
MA08.017m

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

BOTULINUM TOXIN A
OnabotulinumtoxinA (Botox), abobotulinumtoxinA (Dysport), incobotulinumtoxinA (Xeomin), daxibotulinumtoxinA-lanm (Daxxify)

OnabotulinumtoxinA (Botox), abobotulinumtoxinA (Dysport), incobotulinumtoxinA (Xeomin), and daxibotulinumtoxinA-lanm (Daxxify) are considered medically necessary and, therefore, covered in adult individuals for the following indications:

- Achalasia and cardiospasm when at least one of the following criteria is met:
    - The individual whose condition has failed to respond to conventional therapy (e.g., sitting upright after eating, use of achalasia wedge for positioning, use of protein pump inhibitors or calcium channel blockers) or has a contraindication to such therapy.
    - The individual is at high risk of complications from pneumatic dilation or surgical myotomy.
    - The individual whose condition has failed to respond to prior myotomy or dilation.
    - The individual has prior dilation-induced esophageal perforation.
    - The individual has an epiphrenic diverticulum or hiatal hernia.
    - The individual is a poor surgical candidate.
- Blepharospasm in individuals 12 years of age and older
- Cervical dystonia (spasmodic torticollis)
- Chronic anal fissure with anal spasm (proctalgia fugax) with documentation that the individual has been unresponsive to one of the following:

    - Conservative treatments (e.g., sitz baths, topical anesthetics and steroids, topical glyceryl trinitrate [nitroglycerin])
    - Lateral sphincterotomy
- Prevention of chronic migraine headache or probable migraine headache occurring at least 15 days per month for at least 3 months when the duration of untreated headache on average is at least 4 hours per day. Initial treatment for botulinum toxin A is medically necessary when all of the following criteria are met:
    - A neurologist, headache specialist (headache specialist is a physician certified by the United Council for Neurologic Subspecialties [UCNS]), or pain specialist has established a diagnosis of either of the following:
        - Chronic migraine headache **OR**
        - Chronic probable migraine headache when the individual has experienced either of any two of the following pain criteria:
            - Moderate-to-severe headache pain intensity
            - Unilateral headache pain
                1. Pain aggravated by movement or pain that prohibits movement
                2. Throbbing headache pain

OR

            - One of the above pain criteria and one of the following associated symptoms:
                1. Nausea
                2. Sensitivity to light (photophobia) and sound (phonophobia)

- Prevention of chronic migraine headache or probable migraine headache with continued treatment will be medically necessary every 12 weeks when all of the following criteria are met:
    - The provider reports a clinically significant decrease in the frequency of headache days from the reported baseline of frequency prior to the initiation of the first series of botulinum toxin injections.
    - The re-treatment is based on continued, sustained improvement.
- Essential hand tremor in individuals, whose condition has failed to respond to treatment with an oral agent(s) (e.g., propranolol [Inderal], primidone [Mysoline])
- Focal dystonia or spastic dystonia: to relieve pain; to assist in posturing and walking; to increase range of motion; to assist in the outcome of physical therapy; and/or to reduce spasm, thus allowing adequate perineal hygiene after failure of conventional treatment methods (e.g., trihexyphenidyl [Artane], tetrabenazine [Xenazine]) or if a contraindication to such treatments exist
- Hemifacial spasm
- Interstitial cystitis, as a fourth-line treatment option, after documented failure, intolerability, or contraindication to medical therapy (e.g., behavior/diet modification, pharmacologic therapy, pelvic floor physical therapy, intravesical instillations, hydrodistention)
- Isolated oromandibular dystonia
- Plantar-palmar hyperhidrosis refractory to conventional treatment options, including both topical and systemic pharmacotherapy (e.g., topical: astringents, iontophoresis; systemic: anticholinergic drugs; psychotherapy), unless clinically contraindicated AND one of the following:
    - The condition is significantly interfering with the ability to perform activities of daily living
    - The condition is causing persistent or chronic cutaneous complications, such as skin maceration, dermatitis, secondary fungal and microbial infections
- Severe primary axillary hyperhidrosis that is inadequately managed by topical agents in individuals, who manifest focal, visible, severe sweating beyond physiological needs for at least 6 months without apparent cause when at least two of the following criteria are met:
    - Age of onset is younger than 25 years of age
    - Focal sweating is bilateral and relatively symmetric
    - Focal sweating does not occur during sleep
    - Family history is positive for severe primary focal hyperhidrosis
    - Hyperhidrosis significantly impairs the individual's ability to participate in daily activities
- Sialorrhea (excessive drooling) due to disabling conditions such as motor neuron disease or Parkinson's disease in individuals whose condition has failed to respond to a reasonable trial of traditional therapies (i.e., anticholinergics, speech therapy, surgical therapy) or who have a contraindication to such therapy
- Spasmodic dysphonia/laryngeal dystonia (e.g., abductor dysphonia, adductor dysphonia)
- Spasticity of upper and lower limbs in adult individuals, related to any of the following conditions:

    - Cerebral palsy, including use for the treatment of equinus foot deformity
    - Demyelinating diseases of the central nervous system
    - Brain injury
    - Hemiplegia or paraplegia
    - Multiple sclerosis
    - Spinal cord injury
    - Stroke
- Bothersome simple motor tics (e.g., eye blinking, nose movement, head jerks) in individuals 10 years of age and older and when the benefits of treatment outweigh the risks
- Severely disabling or aggressive vocal tics in individuals 10 years of age and older when the benefits of treatment outweigh the risks
- Tourette's disorder with chronic motor or vocal tics in individuals 10 years of age and older
- Urinary incontinence due to neurogenic bladder after documented failure, intolerability, or contraindication to medical therapy (e.g., pelvic floor exercises, diet/fluid management, anticholinergics, intermittent catheterization)
- Urinary incontinence due to overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency
    - The individual has a documented failure, intolerability, or contraindication to to one of the following:
        - Anticholinergic medication (e.g., darifenacin [Enablex], trospium [Trosec]).
        - Beta-3 adrenergic agonist (e.g., Myrbetriq or one generic alternative [solifenacin, oxybutynin tabs/tab ER/syrup, tolterodine, etc])

OnabotulinumtoxinA (Botox), abobotulinumtoxinA (Dysport), incobotulinumtoxinA (Xeomin) and daxibotulinumtoxinA-lanm (Daxxify) are considered medically necessary and, therefore, covered in pediatric individuals for the following indications:

- Spasticity of upper limbs, in pediatric individuals who are two years or older, related to cerebral palsy or stroke when all of the following criteria are met:
    - Bodyweight 10 kg or over
    - Modified Ashworth Scale (MAS*) score of 2 or more in affected elbow or wrist flexors
- Spasticity of lower limbs related to cerebral palsy in pediatric individuals who are two years or older, when all of the following criteria are met:
    - Bodyweight 10 kg or over
    - Cerebral palsy with dynamic muscle contracture of the ankle
- Strabismus in visually mature individuals (12 years of age or older) who have vision in both eyes, are unable to maintain fusion of image, and have at least one of the following:
    - Diplopia
    - Abnormal head turn
    - Asthenopia
    - Impairment of peripheral vision due to esotropia
- Chronic sialorrhea in individuals 2 years of age or older when any of the following criteria are met:
    - The individual is diagnosed with a neurological disorder (e.g., cerebral palsy or traumatic brain injury) and/or intellectual disability associated with chronic troublesome sialorrhea for at least 3 months.
    - The individual has an intellectual disability (ID) without neurological disorders, and the diagnosis of ID was established by a specialist, e.g. pediatrician, or by a center for developmental medicine.
    - The individual has severe drooling (modified Teacher´s Drooling Scale [mTDS] ≥6; clothing occasionally becomes damp)
- Neurogenic detrusor overactivity (NDO) in pediatric individuals 5 years of age and older when all of the following criteria are met:
    - The individual had an inadequate response to or was intolerant of at least one anticholinergic agent (e.g., Oxybutynin [Ditropan XL, Oxytrol], Tolterodine [Detrol]).
    - The individual regularly using clean intermittent catheterization to empty the bladder
    - The individual does not have any of the following:
        - Surgery of the spinal cord within 6 months
        - Diagnosis of cerebral palsy

- Use of an indwelling catheter for urinary incontinence
- Myasthenia gravis, Eaton-Lambert syndrome, or amyotrophic lateral sclerosis

BOTULINUM TOXIN B

RimabotulinumtoxinB (Myobloc)

RimabotulinumtoxinB (Myobloc) is considered medically necessary and, therefore, covered in adult individuals for the following indications:

- Cervical dystonia (spasmodic torticollis)
- Sialorrhea (excessive drooling) due to disabling conditions such as motor neuron disease or Parkinson's disease in an individual whose condition has failed to respond to a reasonable trial of traditional therapies (i.e., anticholinergics, speech therapy, surgical therapy) or who have a contraindication to such therapy

OTHER TREATMENT PARAMETERS

PEDIATRIC INDIVIDUALS

Treatment of pediatric individuals with spasticity of upper or lower limbs who are 2 years and older on abotulinumtoxinA (Botox) and abobotulinumtoxinA (Dysport), and of pediatric individuals with neurogenic detrusor overactivity (NDO) who are 5 years and older on abotulinumtoxinA (Botox), is considered medically necessary and, therefore, covered.

For pediatric individuals with chronic sialorrhea who are 2 years old and older, incobotulinumtoxinA (Xeomin) is considered medically necessary and, therefore, covered.

The safety and effectiveness of rimabotulinumtoxinB (Myobloc) have not been established in individuals less than 18 years of age.

Safety and effectiveness of daxibotulinumtoxinA-lanm (Daxxify) in individuals less than 18 years of age have not been established.

NOT MEDICALLY NECESSARY

Muscle spasm not associated with one of the conditions identified in this policy is considered not medically necessary and, therefore, not covered. Diagnosis codes representing not medically necessary diagnoses are not covered.

Continuation of treatment of larger muscle groups is considered not medically necessary if no response has been elicited with a maximum dose per site. Treatment may be resumed if deemed clinically appropriate. If two consecutive treatments of the appropriate dosage and type of botulinum toxin fail to produce a satisfactory clinical response, a continuation of treatment is considered not medically necessary and, therefore, not covered.

EXPERIMENTAL/INVESTIGATIONAL

All other uses of onabotulinumtoxinA (Botox), rimabotulinumtoxinB (Myobloc), abobotulinumtoxinA (Dysport), prabotulinumtoxinA-xvfs (Jeuveau), incobotulinumtoxinA (Xeomin), and letibotulinumtoxinA (Letybo), including those listed below, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics:

- Bruxism
- Constipation
- Episodic migraine headache (i.e., ≤14 headache days)
- Myofascial pain
- Orofacial dyskinesia
- Temporomandibular joint syndrome
- Tension-type headache
- Voiding dysfunction due to benign prostatic hyperplasia

COSMETIC SERVICES

The use of onabotulinumtoxinA (Botox and Botox Cosmetic), rimabotulinumtoxinB (Myobloc), abobotulinumtoxinA (Dysport), prabotulinumtoxinA-xvfs (Jeuveau), incobotulinumtoxinA (Xeomin®), daxibotulinumtoxinA-lanm (Daxxify), and letibotulinumtoxinA (Letybo) for the treatment of skin wrinkles (e.g., glabellar creases, smoker's lines, lipstick lines, crow's feet, laugh lines, wrinkled neck, aging neck) is considered cosmetic and is, therefore, a benefit contract exclusion.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Guidelines

There is no Medicare coverage determination addressing this drug; therefore, the Company policy is applicable.

OnabotulinumtoxinA (Botox), rimabotulinumtoxinB (Myobloc), incobotulinumtoxinA (Xeomin), abobotulinumtoxinA (Dysport) and daxibotulinumtoxinA-lanm (Daxxify) are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when onabotulinumtoxinA (Botox), rimabotulinumtoxinB (Myobloc), incobotulinumtoxinA (Xeomin), abobotulinumtoxinA (Dysport) and daxibotulinumtoxinA-lanm (Daxxify) are covered under a member's medical benefit. It does not address instances when onabotulinumtoxinA (Botox), rimabotulinumtoxinB (Myobloc), incobotulinumtoxinA (Xeomin), abobotulinumtoxinA (Dysport), and daxibotulinumtoxinA-lanm (Daxxify) are covered under a member’s pharmacy benefit.

DRUG FREQUENCY

The generally accepted frequency for the treatment of spasticity or excessive muscular contractions is one botulinum toxin injection every 3 months.

Because the potency of each botulinum toxin agent is specific to its own method of preparation, units of biologic activity for each distinct preparation of botulinum toxin cannot be compared with or converted to units of other botulinum toxins.

THE YALE GLOBAL TIC SEVERITY SCALE (YGTSS)

The Yale Global Tic Severity Scale (YGTSS) is a psychological measure designed to assess the severity and frequency of symptoms of disorders such as tic disorder, Tourette syndrome, and obsessive-compulsive disorder (OCD) in children and adolescents.

The questionnaire consists of one section identifying symptoms of motor and phonic tics, severity, and age of onset. Another section is about OCD symptoms, severity, and age of onset. The last section is about environmental effects on symptoms.

BLACK BOX WARNINGS

Refer to the specific manufacturer's prescribing information for any applicable Black Box Warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, onabotulinumtoxinA (Botox), rimabotulinumtoxinB (Myobloc), incobotulinumtoxinA (Xeomin), abobotulinumtoxinA (Dysport), and

daxibotulinumtoxinA-lanm (Daxxify) are covered under the medical benefits of the Company's products when the medical necessity criteria and dosing and frequency requirements listed in this medical policy are met.

Services that are experimental/investigational or cosmetic are excluded for the Company's Medicare Advantage plans because they are not covered by Medicare. Therefore, they are not eligible for reimbursement.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

OnabotulinumtoxinA (Botox) was initially approved by the FDA on December 9, 1991, for the treatment of blepharospasm and strabismus associated with dystonia. Supplemental approvals have since been issued by the FDA.

On April 15, 2002, Botox A, marketed as Botox Cosmetic (now also known as onabotulinumtoxinA) was approved. It is intended to improve the appearance of moderate-to-severe glabellar lines (e.g., frown lines, wrinkles). Supplemental approvals have since been issued by the FDA.

RimabotulinumtoxinB (Myobloc) was approved by the FDA on December 8, 2000, for the treatment of adults with cervical dystonia (CD) to reduce the severity of abnormal head position and associated neck pain. Supplemental approvals have since been issued by the FDA.

AbobotulinumtoxinA (Dysport) was approved by the FDA on April 29, 2009, for the treatment of CD in adults and the cosmetic use for the temporary improvement of glabellar lines associated with the procerus and corrugator muscle activity in adult patients younger than 65 years old. Supplemental approvals for abobotulinumtoxinA (Dysport) have since been issued by the FDA.

IncobotulinumtoxinA (Xeomin) was approved by the FDA on July 30, 2010, for treatment of adults with CD (for both botulinum toxin–naive and previously treated individuals) and for treatment of adults with blepharospasm who were previously treated with onabotulinumtoxinA (Botox). Supplemental approvals for incobotulinumtoxinA (Xeomin) have since been issued by the FDA.

PrabotulinumtoxinA-xvfs (Jeuveau) was approved by the FDA on February 1, 2019, for use in adults to temporarily improve the appearance of moderate-to-severe glabellar lines (wrinkles between the eyebrows) in adults.

DaxibotulinumtoxinA-lanm (Daxxify) was approved by the FDA on August 11, 2023, for the treatment of CD in adult individuals. Daxxify was previously approved on September 7, 2022, for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult individuals.

Description

Botulinum toxins have traditionally been associated with foodborne diseases, but medically there has been much interest in the ability of the toxins to block neuromuscular conduction. Botulinum toxin is a neurotoxin derived from the organism *Clostridium botulinum (C. botulinum)*. The seven distinct neurotoxins (A, B, C, D, E, F, G) produced from *C. botulinum* differ in their binding and pharmacologic activity, but they all exhibit a similar molecular structure and share primarily the same mechanism of action: the inhibition of acetylcholine release at the neuromuscular junction.

The blocking of neuromuscular conduction is believed to be a three-step process: (1) extracellular binding of the toxin with the presynaptic site of the neuromuscular junction; (2) internalization and release of the toxin into the cytosol of the nerve terminals; and (3) ultimate inhibition of acetylcholine release from the nerve terminals. The resulting decrease of contractility, strength, and tension of certain muscle groups may improve clinical outcomes in individuals who have diseases associated with inappropriate or exaggerated muscle contractions.

Currently, five US Food and Drug Administration (FDA)-approved botulinum toxin products are available in the United States:

- OnabotulinumtoxinA (Allergan) (Botox and Botox Cosmetic)
- PrabotulinumtoxinA-xvfs (Jeuveau)
- RimabotulinumtoxinB (Solstice Neurosciences, Inc.) (Myobloc)
- AbobotulinumtoxinA (Ipsen Biopharmaceuticals) (Dysport)
- IncobotulinumtoxinA (Merz Pharmaceuticals, Raleigh, NC) (Xeomin)

- LetibotulinumtoxinA-wlbg (Croma Pharma; Hugel) (Letybo)
- DaxibotulinumtoxinA-lanm (Revance Therapeutics, Inc. Newark, CA) (Daxxify)

These products are distinct and are not interchangeable with other botulinum toxin agents; thus, the units of each product cannot be compared or converted into units of another botulinum toxin product.

The FDA-approved uses of these products are as follows:

- Axillary hyperhidrosis, primary (severe underarm sweating):
  - OnabotulinumtoxinA (Botox)
- Blepharospasm (abnormal tics and twitches of the eyelids):
  - OnabotulinumtoxinA (Botox) in those ages 12 years and older
  - IncobotulinumtoxinA (Xeomin) in adults previously treated with onabotulinumtoxinA (Botox)
- Cervical dystonia (a condition that affects the muscles in the neck that control the position of the head):
  - OnabotulinumtoxinA (Botox)
  - AbobotulinumtoxinA (Dysport)
  - RimabotulinumtoxinB (Myobloc)
  - IncobotulinumtoxinA (Xeomin) (botulinum toxin–naive and previously treated individuals)
  - DaxibotulinumtoxinA-lanm (Daxxify)
- Forehead lines associated with frontalis muscle activity (to temporarily improve the appearance):
  - OnabotulinumtoxinA (Botox Cosmetic)
- Glabellar lines (to temporarily improve the appearance of frown lines between the eyebrows):
  - OnabotulinumtoxinA (Botox Cosmetic)
  - AbobotulinumtoxinA (Dysport)
  - PrabotulinumtoxinA-xvfs (Jeuveau)
  - IncobotulinumtoxinA (Xeomin)
  - DaxibotulinumtoxinA-lanm (Daxxify)
- Lateral canthal lines (crow's feet) associated with orbicularis oculi activity (to temporarily improve the appearance):
  - OnabotulinumtoxinA (Botox Cosmetic)
- Migraine, chronic:
  - OnabotulinumtoxinA (Botox)
- Overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency:
  - OnabotulinumtoxinA (Botox)
- Sialorrhea, chronic in individuals 2 years of age and older:
  - IncobotulinumtoxinA (Xeomin)
- Sialorrhea, chronic in adults:
  - RimabotulinumtoxinB (Myobloc)
- Spasticity of upper limb:
  - IncobotulinumtoxinA (Xeomin)
- Spasticity of lower limb:
  - OnabotulinumtoxinA (Botox) in adults
  - AbobotulinumtoxinA (Dysport) in children 2 years of age and older and adults
- Spasticity of upper limb in adults:
  - IncobotulinumtoxinA (Xeomin)
- Spasticity of upper and lower limbs in children 2 years of age and older and adults:
  - OnabotulinumtoxinA (Botox)
  - AbobotulinumtoxinA (Dysport)
- Strabismus (crossed eyes):
  - OnabotulinumtoxinA (Botox) in those ages 12 years and older
- Urinary incontinence due to neurogenic bladder:
  - OnabotulinumtoxinA (Botox)

The FDA has issued an import alert stating that "only botulinum toxin manufactured under US license and bearing the US license number on its labeling may be imported into the United States unless the unlicensed version has an Investigational New Drug (IND) application accepted by the Center for Drug Evaluation and Research."

OnabotulinumtoxinA (Botox and Botox Cosmetic) block neuromuscular transmission by cleaving synaptosomal-associated protein (SNAP)-25, a protein responsible for the release of acetylcholine from nerve endings. This, in turn,

produces a decrease in chemical muscle denervation, resulting in reduced muscular contractions. Similarly, rimabotulinumtoxinB (Myobloc) and abobotulinumtoxinA (Dysport) use a mechanism of like action to inhibit the release of acetylcholine.

RimabotulinumtoxinB (Myobloc) is a purified neurotoxin that acts at the neuromuscular junction to produce flaccid paralysis. The neurotoxin is produced by fermentation of the bacterium *Clostridium botulinum* type B (Bean strain) and exists in noncovalent association with hemagglutinin and nonhemagglutinin proteins as a neurotoxin complex.

DaxibotulinumtoxinA-lanm is an acetylcholine release inhibitor and neuromuscular blocking agent. DaxibotulinumtoxinA-lanm is a 150-kDa botulinum toxin without accessory proteins purified from the bacterium *C. botulinum* type A.

On August 11, 2023, the FDA approved Revance Therapeutics' Daxxify (daxibotulinumtoxinA-lanm) for the treatment of cervical dystonia (CD) in adult individuals. Daxxify was previously approved on September 7, 2022, for the temporary improvement in the appearance of moderate-to-severe glabellar lines associated with corrugator and/or procerus muscle activity in adult individuals. Approval for Daxxify's label expansion for CD was based on data from the Phase 3 ASPEN clinical program (ASPEN-1 and ASPEN open-label study [OLS]), which included 382 individuals with moderate-to-severe CD. In ASPEN-1, individuals received a single low dose of Daxxify (125 units), a high dose of Daxxify (250 units), or a placebo. ASPEN-1 met its primary endpoint, a mean change from baseline on the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) at Weeks 4 and 6. The low-dose group showed a reduction from baseline of 12.7 points and the high-dose group showed a reduction of 10.9 points compared to a 4.3-point reduction for the placebo group. The median duration of effect was 24.0 weeks for the low-dose group and 20.3 weeks for the high-dose group. In ASPEN-OLS, symptoms continued to improve with successive Daxxify treatments at doses of up to 300 units, while adverse events (AEs) remained low. The recommended dose of Daxxify for CD is 125 to 250 units given via intramuscular injection as a divided dose among affected muscles.

On February 10, 2021, the FDA approved onabotulinumtoxinA (Botox) for the treatment of pediatric individuals for detrusor overactivity associated with a neurologic condition. The safety and efficacy of onabotulinumtoxinA (Botox) were evaluated in a multicenter, randomized, double-blind, parallel-group clinical study conducted in individuals from 5 to 17 years of age with urinary incontinence due to detrusor overactivity associated with a neurologic condition and using clean intermittent catheterization. A total of 113 individuals (including 99 with spinal dysraphism such as spina bifida, 13 with spinal cord injury, and one with transverse myelitis) who had an inadequate response to or were intolerant of at least one anticholinergic medication were enrolled. These individuals were randomly assigned to 50 Units, 100 Units, or 200 Units, not to exceed 6 Units/kg (U/kg) body weight. The study results demonstrated within group improvements in the primary efficacy variable of change from baseline in daytime urinary incontinence episodes (normalized to 12 hours) at the primary efficacy time point (week 6) for all three onabotulinumtoxinA (Botox) treatment groups. Botox 200 Units showed an additional reduction in maximum bladder pressure when compared to 50 Units. The most common adverse reactions in the studies were bacteriuria (20%), urinary tract infection (7%), leukocyturia (7%), and hematuria (3%).

On December 18, 2020, the FDA approved incobotulinumtoxinA (Xeomin) for the treatment of pediatric individuals (from 2–17 years of age) with chronic sialorrhea. The efficacy and safety of incobotulinumtoxinA (Xeomin) were evaluated in a prospective, randomized, double-blind, placebo-controlled, parallel-group, multicenter trial that enrolled and treated a total of 216 pediatric individuals from 6 to 17 years of age with chronic sialorrhea associated with cerebral palsy (CP), other genetic or congenital disorders, or traumatic brain injury. An additional 35 individuals, from 2 to 5 years of age, were treated with open-label incobotulinumtoxinA (Xeomin) in the study. The co-primary endpoints among individuals age 6 to 17 years were defined as the change in unstimulated salivary flow rate (uSFR) from baseline to week 4 and the Global Impression of Change Scale (GICS) score from baseline to week 4, representing the functional improvement in drooling, as assessed by the caregiver. Xeomin demonstrated significantly reduced uSFR and improved GICS versus placebo at week 4 among individuals age 6 to 17 years, and sustained efficacy over 64 weeks. Improvement in chronic sialorrhea increased with each injection cycle in comparison to the baseline. GICS scores were comparable among individuals ages 2 to 5 years, who received Xeomin treatment and not placebo throughout the study. No individuals demonstrated clinical resistance or secondary treatment failure due to neutralizing antibodies (Nab), supporting the importance of incobotulinumtoxinA's (Xeomin) unique purification process through XTRACT Technology. The most common adverse reactions affecting 1% or greater of individuals were bronchitis, headache, and nausea/vomiting. The most common adverse reaction affecting individuals age 2 to 5 years was nasopharyngitis.

On October 24, 2019, the FDA approved onabotulinumtoxinA (Botox) for the treatment of pediatric individuals (from

2–17 years of age) with lower limb spasticity. The efficacy and safety of onabotulinumtoxinA (Botox) for the treatment of lower limb spasticity in pediatric individuals was evaluated in a randomized, multicenter, double-blind, placebo-controlled study that included 381 pediatric individuals (125 received 4 U/kg [maximum 150 Units], 127 received 8 U/kg [maximum 300 Units], and 129 received placebo) with lower limb spasticity (Modified Ashworth Scale [MAS] ankle score of at least 2). Individuals were followed for 12 weeks after injection. The primary efficacy endpoint was average change of spasticity in S score (ankle) at weeks 4 and 6. Secondary efficacy endpoints included clinical global impression ([CGI; scales that measure symptom severity, treatment response, and the efficacy of treatments]), Modified Tardieu Scale ([MTS, which identifies the point in the muscle's range where spasticity is occurring), goal attainment scale** (GAS), and measures of gait. Safety and tolerability of treatments were also assessed. Botox decreased spasticity average S score at weeks 4 and 6 by 1.1 in the 8-U/kg group and by 1.0 in the 4-U/kg group; both doses were significantly superior to placebo (-0.8, $P<0.05$). The onabotulinumtoxinA (Botox) dose of 8 U/kg significantly improved CGI by 1.6 versus placebo (1.4; $P=0.023$); the onabotulinumtoxinA (Botox) dose of 4 U/kg, 1.5 ($P=0.229$ vs placebo). Both onabotulinumtoxinA (Botox) groups significantly improved active and passive GAS versus placebo; onabotulinumtoxinA (Botox) dose of 8 U/kg significantly improved measures of gait versus placebo. Rates of patients reporting one or more AEs were similar across treatment groups: onabotulinumtoxinA (Botox), 43.3 percent (n=110); placebo, 49.2 percent (n=63). Serious AEs were reported by 1.2 percent (n=3) and 3.1 percent (n=4), respectively. No new safety concerns were identified.

On September 25, 2019, the FDA expanded the use of abobotulinumtoxinA (Dysport) to include the treatment of upper limb spasticity in pediatric individuals 2 years of age and older. The efficacy and safety of abobotulinumtoxinA (Dysport) for the treatment of upper limb spasticity in children with CP was evaluated in a phase III, multicenter, double-blind, prospective, randomized, low-dose controlled, multiple treatment study. A total of 208 botulinum toxin naïve or non-naïve (66 percent had prior treatment with a botulinum toxin) individuals weighing at least 10 kg, with a baseline MAS* of grade 2 or greater at the primary targeted muscle groups (PTMG), were enrolled in the modified intention-to-treat population (mITT). Individuals received abobotulinumtoxinA (Dysport) at the following doses: (16 U/kg up to maximum of 640 U [n=70]), Dysport (8 U/kg up to maximum of 320 U [n=69]), or Dysport® (2 U/kg [n=69]) injected into the upper limb. The elbow flexors and wrist flexors, respectively, were the PTMG in 57 percent and in 43 percent of individuals.

The primary efficacy endpoint was the mean change from baseline in MAS* in the PTMG at week 6. The secondary efficacy endpoint was the mean Physician Global Assessment (PGA)*** score assessed at week 6. AbobotulinumtoxinA (Dysport) demonstrated statistically significant improvements from baseline at week 6 with doses of 8 U/kg and 16 U/kg, as measured by the MAS* in the elbow or wrist flexors.

The most common adverse reactions (>10%) in pediatric individuals with upper limb spasticity for abobotulinumtoxinA (Dysport) were upper respiratory tract infection and pharyngitis.

On June 21, 2019, the FDA approved onabotulinumtoxinA (Botox) for the treatment of pediatric individuals from 2 to 17 years of age with upper limb spasticity. The approval for upper limb spasticity was based on a randomized, multicenter, double-blind, placebo-controlled study (NCT01249417) that included 234 pediatric individuals who received the following doses: 78 individuals received Botox 3 U/kg, 77 received Botox 6 U/kg [maximum 200 Units], and 79 received placebo) with upper limb spasticity (MAS* elbow or wrist score of at least 2) because of CP or stroke. Individuals were followed up for 12 weeks after injection. Primary endpoints were the average of the change from baseline in MAS* principal muscle group score (elbow or wrist) at week 4 and week 6, and the average of the Clinical Global Impression of Overall Change by Physician (CGI) at week 4 and week 6. The CGI evaluated the response to treatment in terms of how the individual was doing in their life using a nine-point scale (−4=very marked worsening; +4=very marked improvement). Compared to placebo, significant improvements in MAS* change from baseline were observed at all time points for onabotulinumtoxinA (Botox)-treated individuals. The CGI scores numerically favored onabotulinumtoxinA (Botox) over placebo, but the difference was not statistically significant.

In July 2016, the FDA approved abobotulinumtoxinA (Dysport) for lower limb spasticity in pediatric individuals. The safety and efficacy of abobotulinumtoxinA (Dysport) for the treatment of lower limb spasticity due to CP causing dynamic equinus foot deformity in pediatric individuals from 2 to 17 years of age was evaluated in a double-blind, placebo-controlled, multicenter study. A total of 235 (158 Dysport® and 77 placebo) toxin-naive or non-naive individuals with a MAS* of grade 2 or greater at the ankle plantar flexors were enrolled to receive abobotulinumtoxinA (Dysport) at the following doses: 10 U/kg/leg (n=79), Dysport 15 U/kg/leg (n=79), or placebo (n=77) injected into the gastrocnemius and soleus muscles. Forty-one percent of individuals (n=66) were treated bilaterally and received a total lower limb abobotulinumtoxinA (Dysport) dose of either 20 U/kg (n=37) or 30 U/kg (n=29). The primary efficacy endpoint was the mean change from baseline in MAS* in ankle plantar flexor at week 4; a co-primary endpoint was the mean PGA*** score at week 4.

Study results showed an improvement in the abobotulinumtoxinA (Dysport) group versus placebo on muscle tone at both doses at week 4 postinjection (Primary endpoint – Assessment scale: MAS)*. The PGA treatment differences versus placebo were also significant. The most frequent treatment-emergent AEs were common childhood infections (upper respiratory tract infections).

On October 15, 2010, the FDA approved onabotulinumtoxinA (Botox) for prophylaxis of headaches in adults with chronic migraine headache (at least 15 days per month with headache lasting at least 4 hours per day). The approval for chronic migraine was based on results of the Phase III Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) program, which consisted of two double-blind, placebo-controlled clinical trials that included 1384 adults from 122 centers in North America and Europe. In both of these studies, individuals receiving onabotulinumtoxinA (Botox) had a significantly greater decrease in the frequency of headache days from baseline compared with placebo at 24 weeks: 7.8 and 9.2 fewer days for the treated groups versus 6.4 and 6.9 days for the placebo groups, respectively. Treated individuals also had a total cumulative reduction in headache hours by 107 and 134 hours, respectively, compared with 70 and 95 hours for the placebo groups.

On April 29, 2009, abobotulinumtoxinA (Dysport) was approved by the FDA for the treatment of cervical dystonia. AbobotulinumtoxinA (Dysport) was evaluated in two randomized, double-blind, placebo-controlled, single-dose, parallel group studies in treatment-naïve cervical dystonia individuals. A total of 252 individuals were enrolled. The primary assessment of efficacy was based on the total TWSTRS change from baseline at week 4 for both studies. The scale evaluates the severity of dystonia, individual perceived disability from dystonia, and pain. The adjusted mean change from baseline in the TWSTRS total score was statistically significantly greater for the abobotulinumtoxinA (Dysport) group than the placebo group at weeks 4 in both studies.

On December 8, 2000, the FDA approved rimabotulinumtoxinB (Myobloc) for the treatment of cervical dystonia. The approval for cervical dystonia was based on two phase III, randomized, multicenter, double-blind, placebo-controlled studies. Both studies enrolled only adult individuals who had a history of receiving botulinum toxin type A. Study #301 enrolled individuals who were perceived as having an acceptable response to type A toxin, while Study #302 enrolled only individuals who had secondarily lost responsiveness to type A toxin. Study #301 enrolled 109 individuals, and 77 individuals were enrolled into Study #302. Individual evaluations continued for 16 weeks postinjection. The primary efficacy outcome variable for both studies was the TWSTRS total score (scale range of possible scores, 0–87) at week 4. The secondary endpoints were the Patient Global and Physician Global Assessments of change at Week 4. TWSTRS Total Score at Week 4 and Patient Global Assessment among subgroups by gender or age showed consistent treatment-associated effects across these subgroups.

*****MAS score measures resistance during passive soft-tissue stretching and is used as a simple measure of spasticity. (Scoring: 0=No increase in muscle tone to 4=Affected part(s) rigid in flexion or extension).

**The GAS is a functional five-point scale used to measure progress towards individual therapy goals.

***The PGA is a five- or six-point scoring system used to assess disease severity.

COSMETIC SERVICES

Cosmetic services are those provided to improve an individual's physical appearance, from which no significant improvement in physiologic function can be expected. Emotional and/or psychological improvement alone does not constitute improvement in physiologic function.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issues by leading professional organizations and government entities.

References

Ababneh OH, Cetinkaya A, Kulwin DR. Long-term efficacy and safety of botulinum toxin A injections to treat blepharospasm and hemifacial spasm. *Clin Exp Ophthalmol*. 2014;42:254-261.

Abram SE. Does botulinum toxin have a role in the management of myofascial

pain? *Anesthesiology.* 2005;103(2):223-224.

Acquadro MA, Borodic GE. Botulinum toxin efficacy for the treatment of pain. *J Clin Anesth.* 2005;17(5):328-330.

Adler CH, Bansberg SF, Krein-Jones K, Hentz JG. Safety and efficacy of botulinum toxin type B (Myobloc) in adductor spasmodic dysphonia. *Mov Disord.* 2004;19(9):1075-1079.

Allergan, Inc., Irvine, California. OnabotulinumtoxinA (Botox®) Product Information. [Allergan Web site]. Updated 11/2023. Available at: http://www.botox.com/ and https://www.botoxspasticity.com/about-spasticity/causes. Accessed February 6, 2025.

Allergan, Inc., Irvine, California. OnabotulinumtoxinA (Botox®Cosmetic) Product Information. [Allergan Web site]. Updated 10/2024. Available at: https://www.botoxcosmetic.com/. Accessed February 6, 2025.

American Gastroenterological Association. Technical review on the diagnosis and treatment of gastroparesis. *Gastroenterology* 2004;127:1592-1622. Available at: https://www.gastrojournal.org/article/S0016-5085(04)01634-8/pdf. Accessed February 6, 2025.

American Hospital Formulary Service (AHFS). Drug Info 2016. AbobotulinumtoxinA, PraotulinumtoxinA, OnabotulinumtoxinA, RimabotulinumtoxinB. [Lexicomp Online Web site]. 02/17/25. Available at: http://online.lexi.com/lco/action/search?q=botulinum&t=name [via subscription only]. Accessed February 26, 2025.

American Hospital Formulary Service (AHFS). Drug Info 2016. Daxxify (daxibotulinumtoxinA-lanm). [Lexicomp Online Web site]. 02/17/25. Available at: http://online.lexi.com/lco/action/search?q=botulinum&t=name [via subscription only]. Accessed February 17, 2025.

American Hospital Formulary Service (AHFS). Drug Info 2016. Jeuveau™ (prabotulinumtoxinA-xvfs). [Lexicomp Online Web site]. 02/17/25. Available at: http://online.lexi.com/lco/action/search?q=botulinum&t=name [via subscription only]. Accessed February 17, 2025.

Ansari NN, Naghdi S, Arab TK, Jalaie S. The interrater and intrarater reliability of the Modified Ashworth Scale in the assessment of muscle spasticity: limb and muscle group effect. *NeuroRehabilitation*. 2008;23(3):231-237.

Andersen PM, Abrahams S, Borasio GD, et al. EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)—revised report of an EFNS task force. *Eur J Neurol*. 2012;19(3):360-375.

Argoff CE. The use of botulinum toxins for chronic pain and headaches. *Curr Treat Options Neurol.* 2003;5(6):483-492.

Ashkenazi A, Silberstein SD. Botulinum toxin and other new approaches to migraine therapy. *Annu Rev Med.* 2004;55:505-518.

Batisti JPM, Kleinfelder ADF, Galli NB, et al. Treatment of hemifacial spasm with botulinum toxin type a: effective long lasting and well tolerated. *Arq Neuropsiquiatr*. 2017;75:87-91.

Baumann LS, Halem ML. Botulinum toxin-B and the management of hyperhidrosis. *Clin Dermatol.* 2004;22(1):60-65.

Bentivoglio AR, Fasano A, Ialongo T, et al. Outcome predictors, efficacy and safety of Botox and Dysport in the long-term treatment of hemifacial spasm. *Eur J Neurol*. 2009;16:392-398.

Binder WJ, Brin MF, Blitzer A, et al. Botulinum toxin type A (BOTOX) for treatment of migraine headaches: an open-label study. *Otolaryngol Head Neck Surg.* 2000;123(6):669-676.

Blitzer A, Sulica L. Botulinum toxin: Basic science and clinical uses in otolaryngology. *Laryngoscope.* 2001;111(2):218-226.

Blumenfeld AM, Binder W, Silberstein SD, Blitzer A. Procedures for administering botulinum toxin type A for migraine and tension-type headache. *Headache.* 2003;43(8):884-891.

Blumenfeld AM, Dodick DW, Silberstein SD. Botulinum neurotoxin for the treatment of migraine and other primary headache disorders. *Dermatol Clin.* 2004;22(2):167-175.

Bobkiewicz A, Francuzik W, Krokowicz L, et al. Botulinum Toxin Injection for Treatment of Chronic Anal Fissure: Is There Any Dose-Dependent Efficiency? A Meta-Analysis. *World J Surg.* 2016;40(12): 3064-3072. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5104788/.

Brashear A, McAfee AL, Kuhn ER, Ambrosius WT. Treatment with botulinum toxin type B for upper-limb spasticity. *Arch Phys Med Rehabil.* 2003;84(1):103-107.

Brin MF. Botulinum toxin therapy: Basic science and overview of other therapeutic applications. In: Blitzer A, Binder WJ, Boyd JB, Carruthers A (eds). *Management of Facial Lines and Wrinkles.* Philadelphia, PA: Lippincott, Williams and Wilkins; 2000.

Camilleri M. Treatment of gastroparesis. [UpToDate]. 02/21/19. Available at: https://www.uptodate.com/contents/treatment-of-gastroparesis?topicRef=2638&source=related_link#H18. Accessed February 6, 2025.

Camilleri M, Parkman H, Henry P. Clinical Guideline: Management of gastroparesis. *Am J Gastroenterol*. 2013;108(1):18-37.

Chen S. Clinical Uses of Botulinum Neurotoxins: Current Indications, Limitations and Future Developments. *Toxins*. 2012;4(10):913-939. https://doi.org/10.3390/toxins4100913.

Choe WJ, Kim J. Increasing the area and varying the dosage of botulinum toxin a injections for effective treatment of hemifacial spasm. *Acta Otolaryngol.* 2016;136:952-955.

Cision PR Newswire. Hugel America, Inc. announces U.S. FDA acceptance of biologics license application (BLA) for letibotulinumtoxinA for injection to treat glabellar (frown) lines. Press Release, June 15, 2021. Available at: https://www.prnewswire.com/news-releases/hugel-america-inc-announces-us-fda-acceptance-of-biologics-license-application-bla-for-letibotulinumtoxina-for-injection-to-treat-glabellar-frown-lines-301312900.html. Accessed February 6, 2025.

ClinicalTrials.gov. Single Treatment of DaxibotulinumtoxinA for Injection in Adults With Isolated Cervical Dystonia (ASPEN-1) (ASPEN-1). NCT03608397. First Posted: August 1,2018; Last Update Posted: December 5, 2022. Available at: Single Treatment of DaxibotulinumtoxinA for Injection in Adults With Isolated Cervical Dystonia (ASPEN-1) - Full Text View - ClinicalTrials.gov. Accessed February 6, 2025.

ClinicalTrials.gov. BOTOX® Treatment in Pediatric Upper Limb Spasticity. NCT01603602. First Posted: May 22,2012; Last Update Posted: August 14, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT01603602. Accessed February 6, 2025.

ClinicalTrials.gov. BOTOX® Treatment in Pediatric Lower Limb Spasticity. Identifier: NCT01603628. First Posted: May 22,2012; Last Update Posted: August 14, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT01603628?term=NCT01603628&draw=2&rank=1. Accessed February 6, 2025.

ClinicalTrials.gov. Efficacy and Safety of Dysport in the Treatment of Upper Limb Spasticity in Children (PUL). ClinicalTrials.gov Identifier: NCT02106351. First Posted: April 8, 2014; Last Update Posted: September 28, 2022. Available at: https://clinicaltrials.gov/ct2/show/NCT02106351. Accessed February 6, 2025.

ClinicalTrials.gov. Dysport® Pediatric Lower Limb Spasticity Study. ClinicalTrials.gov Identifier: NCT01249417. First Posted: November 29, 2010; Last Update Posted: September 28, 2022. Available at: https://clinicaltrials.gov/ct2/show/NCT01249417. Accessed February 6, 2025.

ClinicalTrials.gov. XEOMIN® Clinical Study to Investigate the Efficacy and Safety of NT 201 Compared to Placebo in the Treatment of Chronic Troublesome Drooling Associated With Neurological Disorders and/or Intellectual Disability (SIPEXI). NCT02270736. First Posted: October 21,2014; Last Update Posted: August 10, 2021. Available at:https://clinicaltrials.gov/ct2/show/NCT02270736. Accessed February 6, 2025.

CMS.gov. Centers for Medicare and Medicaid Services. Billing and Coding: Botulinum Toxins. Article ID# A58423.

Original Effective Date 3/21/2021; Revision Effective Date 4/01/2024. Available at: https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=58423&ver=14&contractorName=6&updatePeriod=976&sortBy=updated&bc=13. Accessed February 6, 2025.

Costa J, Espirito-Santo C, Borges A, et al. Botulimum toxin type A therapy for hemifacial spasm. *Cochrane Database Syst Rev*. 2005;(1):CD004899.

Costa J, Espírito-Santo CC, Borges AA, et al. Botulinum Toxin type A (BtA) muscular injections are beneficial in treating hemifacial spasm. *Cochrane Database Syst Rev.* 2005; CD004899.

Dashtipour K, Chen JJ, Frei K, et al. Systematic Literature Review of AbobotulinumtoxinA in Clinical Trials for Blepharospasm and Hemifacial Spasm. *Tremor Other Hyperkinet Mov (NY).* 2015;5:338.

(Daxxify) daxibotulinumtoxinA-lanm [prescribing information]. Newark, CA: 08/2023.Revance Therapeutics, Inc. Available at: Long-lasting Frown Line Treatment - DAXXIFY®. Accessed February 6, 2025.

De Andres J, Cerda-Olmedo G, Valia JC, et al. Use of botulinum toxin in the treatment of chronic myofascial pain. *Clin J Pain.* 2003;19(4):269-275.

Defazio G, Abbruzzese G, Girlanda P, et al. Botulinum toxin A treatment for primary hemifacial spasm: a 10-year multicenter study. *Arch Neurol.* 2002;59(3):418-420.

Delgado MR, Tilton A, Russman R, et al. AbobotulinumtoxinA for equinus foot deformity in cerebral palsy: a randomized controlled trial. *Pediatrics*. 2016;137(2):1-9.

Diamond S. A fresh look at migraine therapy. New treatments promise improved management. *Postgrad Med.* 2001;109(1):49-60.

Diener HC, Dodick DW, Aurora SK, et al. PREEMPT 2 Chronic Migraine Study Group. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. *Cephalalgia.* 2010;30(7):804-814.

Difazio M, Jabbari B. A focused review of the use of botulinum toxins for low back pain. *Clin J Pain.* 2002;18(6 Suppl):S155-S162.

Dodick DW, Turkel CC, DeGryse RE, et al; PREEMPT Chronic Migraine Study Group. OnabotulinumtoxinA for treatment of chronic migraine: Pooled results from the double-blind, randomized, placebo-controlled phases of the PREEMPT clinical program. *Headache.* 2010;50(6):921-936.

Dodick DW, Turkel CC, DeGryse RE, et al. OnabotulinumtoxinA for treatment of chronic migraine: Pooled results form the double-blind, randomized, placebo-controlled phases of the PREEEMPT clinical program. *Headache.* 2010;50:221-236.

Dressler D, Adib Saberi F, Benecke R. Botulinum toxin type B for treatment of axillar hyperhidrosis. *J Neurol.* 2002;249(12):1729-1732.

Dursun N, Bonikowski M, Dabrowski E, et al. Efficacy of repeat abobotulinumtoxinA (Dysport®) injections in improving gait in children with spastic cerebral palsy. *Dev Neurorehabil.* 2019;1751-8431.

(Dysport®) abobotulinumtoxinA [prescribing information]. Basking Ridge, NJ: Ipsen Biopharmaceuticals. 09/2023. Available at: https://www.dysport.com/. Accessed February 6, 2025.

Egevad G, Petkova VY, Vilholm OJ. Sialorrhea in patients with Parkinson's disease: safety and administration of botulinum neurotoxin. *J Parkinsons Dis.* 2014;4(3):321-326.

Elkind AH, O'Carroll P, Blumenfeld A, et al. A series of three sequential, randomized, controlled studies of repeated treatments with botulinum toxin type A for migraine prophylaxis. *J Pain.* 2006;7(10):688-696.

Ellies M, Gottstein U, Rohrbach-Volland S, et al. Reduction of salivary flow with botulinum toxin: extended report on 33 patients with drooling, salivary fistulas, and sialadenitis. *Laryngoscope.* 2004;114(10):1856-1860. http://ucdvoice.org/wp-content/uploads/2013/11/Reduction-of-salivary-flow-with-botulinum-toxin.pdf.

Elsevier's Clinical Pharmacology Compendium. abobotulinumtoxinA. 09/28/24. [Clinical Key Web site]. Available at: https://www.clinicalkey.com/#!/ [via subscription only]. Accessed February 6, 2025.

Elsevier's Clinical Pharmacology Compendium. PrabotulinumtoxinA-xvfs. 09/29/23. [Clinical Key Web site]. Available at: https://www.clinicalkey.com/#!/ [via subscription only]. Accessed February 6, 2025.

Elsevier's Clinical Pharmacology Compendium. IncobotulinumtoxinA. 09/28/20/24. [Clinical Key Web site]. Available at: https://www.clinicalkey.com/#!/ [via subscription only]. Accessed February 6, 2025.

Elsevier's Clinical Pharmacology Compendium. OnabotulinumtoxinA. 02/03/25. [Clinical Key Web site]. Available at: https://www.clinicalkey.com/#!/ [via subscription only]. Accessed February 6, 2025.

Elsevier's Clinical Pharmacology Compendium. RimabotulinumtoxinB. 09/28/24. [Clinical Key Web site]. Available at: https://www.clinicalkey.com/#!/ [via subscription only]. Accessed February 6, 2025.

Elsevier's Clinical Pharmacology Compendium. DaxibotulinumtoxinA-lanm. 09/28/24. [Clinical Key Web site]. Available at: https://www.clinicalkey.com/#!/ [via subscription only]. Accessed February 6, 2025.

Evers S. Investigating prophylactic botulinum toxin type A for chronic headache disorders. *Expert Opin Investig Drugs.* 2006;15(10):1161-1166.

Ferrante FM, Bearn L, Rothrock R, King L. Evidence against trigger point injection technique for the treatment of cervicothoracic myofascial pain with botulinum toxin type A. *Anesthesiology.* 2005;103(2):377-383.

Ferrari AP Jr, Siqueira ES, Brant CQ. Treatment of achalasia in Chagas' disease with botulinum toxin. *N Engl J Med.* 1995;332(12):824-825.

Fried GW, Fried KM. Spinal cord injury and use of botulinum toxin in reducing spasticity. *Phys Med Rehabil Clin N Am.* 2003;14(4):901-910.

Weiner G. Reassessing botulinum toxin for childhood strabismus. Available at: https://www.aao.org/eyenet/article/reassessing-botulinum-toxin-childhood-strabismus. Accessed February 6, 2025.

Goadsby PJ, Lipton RB, Ferrari MD. Migraine: current understanding and treatment. *N Engl J Med.* 2002;346(4):257-270.

Gómez-Caravaca MT, Cáceres-Redondo MT, Huertas-Fernández I, et al. The use of botulinum toxin in the treatment of sialorrhea in parkinsonian disorders. *Neurol Sci.* 2015;36(2):275-279.

Gormley E, Lightner D, Burgio K, et al. Diagnosis and treatment of overactive bladder (nonneurogenic) in adults: AUA/SUFU guideline. 2015. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25623739.

Gormley E, Lightner D, Burgio K, et al. Diagnosis and treatment of overactive bladder (nonneurogenic) in adults: AUA/SUFU guideline. 2019. Available at: https://www.auanet.org/guidelines/overactive-bladder-(oab)-guideline.

Gwynn MW, English JB, Baker TS. Double-blind, placebo-controlled study of Myobloc (botulinum toxin type B) for the treatment of chronic headache. *Headache.* 2003;43(5):577-578.

Hanno PM, Burks DA, Clemens JQ, et al. Diagnosis and treatment of interstitial cystitis/bladder pain syndrome. [AUA Web site] 2014. Available at: https://www.auanet.org/guidelines/interstitial-cystitis-(ic/bps)-guideline.

Hassell, JW, Charles, D. Treatment of blepharospasm and oromandibular dystonia with botulinum toxins. *Toxins*. 2020;12(4):269.

Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia.* 1988;8(Suppl 7):1-96.

Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders: 2nd edition. *Cephalalgia.* 2004;24(Suppl 1):9-60.

Ho CC, Khan SA, WhealyMA. Trigeminal neuralgia. [UpToDate]. 01/26/2020. Available at: https://www.uptodate.com/contents/trigeminal-neuralgia?search=trigeminal neuralgia&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Accessed March 25, 2024.

International Headache Society. Headache Classification Subcommittee. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia.* 2004;24(1):9-160.

Jackson CE, Gronseth G, Rosenfeld J, et al. Randomized double-blind study of botulinum toxin type B for sialorrhea in ALS patients. *Muscle Nerve.* 2009;39(2):137-143.

Jeuveau™ (prabotulinumtoxinA-xvfs) [prescribing information]. Evolus, Inc: Daewoong Pharmaceutical Co., Ltd. Updated 04/2023. Available at: http://www.xeomin.com/physicians/. Accessed February 6, 2025.

Jongerius PH, van den Hoogen FJ, van Limbeek J, et al. Effect of botulinum toxin in the treatment of drooling: a controlled clinical trial. *Pediatrics.* 2004;114(3):620-627.

Joo JS, Agachan F, Wolff B, Nogueras JJ, Wexner SD. Initial North American experience with botulinum toxin type A for treatment of anismus. *Dis Colon Rectum.* 1996;39(10):1107-1111.

Karp BI, Alter K. Botulinum toxin treatment of blepharospasm, orofacial/oromandibular dystonia and hemifacial spasm. *Semin Neurol*. 2016;36(1):84-91.

Klein AW. Complications and adverse reactions with the use of botulinum toxin. *Semin Cutan Med Surg.* 2001;20(2):109-120.

Kobak KA, Katzelnick DJ, Sands G, et al. Prevalence and burden of illness of migraine in managed care patients. *J Manag Care Pharm.* 2005;11(2):124-136.

Lagalla G, Millevolte M, Capecci M, et al. Botulinum toxin type A for drooling in Parkinson's disease: a double-blind, randomized, placebo-controlled study. *Mov Disord.* 2006;21(5):704-707.

Lang AM. A preliminary comparison of the efficacy and tolerability of botulinum toxin serotypes A and B in the treatment of myofascial pain syndrome: a retrospective, open-label chart review. *Clin Ther.* 2003;25(8):2268-2278.

Lexi-Drugs Compendium. AbobotulinumtoxinA. 01/28/25. [Lexicomp Online Web site]. Available at: http://online.lexi.com/lco/action/search?q=botulinum&t=name [via subscription only]. Accessed February 6, 2025.

Lexi-Drugs Compendium. IncobotulinumtoxinA. 01/14/25. [Lexicomp Online Web site]. Available at: http://online.lexi.com/lco/action/search?q=botulinum&t=name [via subscription only]. Accessed February 6, 2025.

Lexi-Drugs Compendium. OnabotulinumtoxinA. 02/11/25. [Lexicomp Online Web site]. Available at: http://online.lexi.com/lco/action/search?q=botulinum&t=name [via subscription only]. Accessed February 6, 2025.

Lexi-Drugs Compendium. PrabotulinumtoxinA-xvfs. 10/15/24. [Lexicomp Online Web site]. Available at: http://online.lexi.com/lco/action/search?q=botulinum&t=name [via subscription only]. Accessed February 6, 2025.

Lexi-Drugs Compendium. RimabotulinumtoxinB. 01/17/25. [Lexicomp Online Web site]. Available at: http://online.lexi.com/lco/action/search?q=botulinum&t=name [via subscription only]. Accessed February 6, 2025.

Lexi-Drugs Compendium. DaxibotulinumtoxinA-lanm. 08/22/24. [Lexicomp Online Web site]. Available at: http://online.lexi.com/lco/action/search?q=botulinum&t=name [via subscription only]. Accessed February 6, 2025.

Li VJ, Huang Y, Ding Q, et al. Evaluation of concentrations of botulinum toxin A for the treatment of hemifacial spasm: a randomized double-blind trial. *Genet Mol Res*. 2015;14:1136-1144.

Lipp A, Trottenberg T, Schink T, et al. A randomized trial of botulinum toxin A for treatment of drooling. *Neurology.* 2003;61(9):1279-1281.

Lipton RB. Methodologic issues in acute migraine clinical trials. *Neurology.* 2000;55(9 Suppl 2):S3-S7.

MacGregor EA, Brandes J, Eikermann A. Migraine prevalence and treatment patterns: The Global Migraine and Zolmitriptan Evaluation survey. *Headache.* 2003;43(1):19-26.

Morra ME, Elgebaly A, Elmaraezy A, et al. Therapeutic efficacy and safety of Botulinum Toxin A therapy in trigeminal neuralgia: a systematic review and meta-analysis of randomized controlled trials. *J Headache Pain*. 2016;17:63.

Myobloc® [prescribing information]. South San Francisco, CA: Solstice Neurosciences, Inc; 03/2021. Available at: https://www.myobloc.com/. Accessed February 6, 2025.

National Institute of Neurological Disorders and Stroke. Hemifacial spasm information page. Undated. Available at: https://www.ninds.nih.gov/Disorders/All-Disorders/Hemifacial-Spasm-Information-Page#disorders-r1. Accessed February 6, 2025.

Naumann MK, Hamm H, Lowe NJ. Botox Hyperhidrosis Clinical Study Group. Effect of botulinum toxin type A on quality of life measures in patients with excessive axillary sweating. A randomized controlled trial. *Br J Dermatol.* 2002;147(6):1218-1226.

Naumann M, So YS, Argoff CE, et al. Assessment: Botulinum neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review). Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. May 5, 2008. Available at: https://doi.org/10.1212/01.wnl.0000311390.87642.d8.

Naumann M, So Y, Argoff CE, et al. Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: Botulinum neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2008;70(19):1707-1714.

Novitas Solutions, Inc. *Local Coverage Determination (LCD).* LCD L38809: Botulinum Toxins. [Novitas Solutions, Inc. Web site]. Original: 03/21/2021. Revision: 02/10/2022. Available at: https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=58423&ver=14&contractorName=6&updatePeriod=976&sortBy=updated&bc=13. Accessed February 6, 2025.

Ondo WG, Hunter C, Moore W. A double-blind placebo-controlled trial of botulinum toxin B for sialorrhea in Parkinson's disease. *Neurology.* 2004;62(1):37-40.

Ondo WG, Simmons JH, Shahid MH, et al. Onabotulinum toxin-A injections for sleep bruxism. A double-blind, placebo-controlled study. *Neurology*. 2018;90 (7).

Osako M, Keltner JL. Botulinum A toxin (Oculinum®) in ophthalmology. *Surv Ophthalmol.* 1991;36(1):28-46.

Pasricha PJ, Miskovsky EP, Kalloo AN. Intrasphincteric injection of botulinum toxin for suspected sphincter of Oddi dysfunction. *Gut.* 1994;35(9):1319-1321.

Porta M, Gamba M, Bertacchi G, Vaj P. Treatment of sialorrhea with ultrasound guided botulinum toxin type A injection in patients with neurological disorders. *J Neurol Neurosurg Psychiatry.* 2001;70:538-540.

Prajapati DN, Hogan WJ. Sphincter of Oddi dysfunction and other functional biliary disorders: evaluation and treatment. *Gastroenterol Clin North Am.* 2003;32(2):601-618.

Pringsheim T, Okun MS, Müller-Vahl K, et al. Practice guideline recommendations summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders. *Neurology*. 2019;92:896-906.

Racette BA, Good L, Sagitto S, Perlmutter JS. Botulinum toxin B reduces sialorrhea in parkinsonism. *Mov Disord.* 2003;18(9):1059-1061.

Raj PP. Botulinum toxin therapy in pain management. *Anesthesiol Clin North America.* 2003;21(4):715-731.

Reddihough D, Erasmus CE, Johnson H, et al.; Cerebral Palsy Institute. Botulinum toxin assessment, intervention and aftercare for paediatric and adult drooling: international consensus statement. *Eur J Neurol.* 2010;17(Suppl 2):109-121.

Rollnik JD, Tanneberger O, Schubert M, et al. Treatment of tension-type headache with botulinum toxin type A: a

double-blind, placebo-controlled study. *Headache.* 2000;40(4):300-305.

Romero FR, Haddad GR, Miot HA, et al., Palmar hyperhidrosis: clinical, pathophysiological, diagnostic and therapeutic aspects. *An Brs Dermatol.* 2016;91(6):716-725.

Rowe FJ, Noonan CP. Botulinum toxin for the treatment of strabismus. *Cochrane Database Syst Rev.* 2012 Feb 15;(2):CD006499.

Rusciani L, Severino E, Rusciani A. Type A botulinum toxin: a new treatment for axillary and palmar hyperhidrosis. *J Drugs Dermatol.* 2002;1:147-151.

Sataloff RT, Heman-Ackah YD, Simpson LL, et al. Botulinum toxin type B for treatment of spasmodic dysphonia: a case report. *J Voice.* 2002;16(3):422-424.

Scheffer AR, Erasmus C, van Hulst K, et al. Efficacy and duration of botulinum toxin treatment for drooling in 131 children. *Arch Otolaryngol Head Neck Surg.* 2010; Sep;136(9):873-877.

Schmitt WJ, Slowey E, Fravi N, et al. Effect of botulinum toxin A injections in the treatment of chronic tension-type headache: a double-blind, placebo-controlled trial. *Headache.* 2001;41(7):658-664.

Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2000;55(6):754-762.

Silberstein S, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology.* 2012;78(17):1337-45. Erratum: Feb 2013;80(9): 871.

Silberstein SD, Stark SR, Lucas SM, et al. BoNTA-039 Study Group. Botulinum toxin type A for the prophylactic treatment of chronic daily headache: a randomized, double-blind, placebo-controlled trial. *Mayo Clin Proc.* 2005;80(9):1126-1137.

Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology*. 2012 Apr 24;78(17):1337-1345.

Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache. Report of the Guideline Development Subcommittee of the American Academy of Neurology. [ANN Web site] 05/10/2016. Available at: https://n.neurology.org/content/86/19/1818.long.

Simpson DM, Blitzer A, Brashear A, et al. Assessment: Botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology.* 2008;70(19):1699-1706.

Simpson DM, Gracies JM, Yablon SA, Barbano R, Brashear A, BoNT/TZD Study Team. Botulinum neurotoxin versus tizanidine in upper limb spasticity: a placebo-controlled study. *J Neurol Neurosurg Psychiatry*. 2009;80(4):380-385.

Simpson DM, Hallett, M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology.* 2016;86:1818-1826.

Smith HS, Audette J, Royal MA. Botulinum toxin in pain management of soft tissue syndromes. *Clin J Pain.* 2002;18(6 Suppl):S147-S154.

Sokol T. Anal fissure. [MedicineNet Web Site]. Last reviewed 01/22/19. Available at: http://www.medicinenet.com/anal_fissure/article.htm. Accessed February 6, 2025.

Soares A, Andriolo R, Atallah A, et al. Botulinum toxin for myofascial pain syndromes in adults. *Cochrane Database Syst Rev*. 2012;4:CD007533.

Squires N, Humberstone M, Wills A, Arthur A. The use of botulinum toxin injections to manage drooling in

amyotrophic lateral sclerosis/motor neurone disease: a systematic review. *Dysphagia*. 2014;29(4):500-508.

Taqi D, Gunyea I, Bhakta B, et al. Botulinum toxin type B (Myobloc) in the treatment of refractory myofascial pain. *Pain Med.* 2002;3(2):174.

Tfelt-Hansen P, Block G, Dahlof C, et al. Guidelines for controlled trials of drugs in migraine: second edition. *Cephalalgia.* 2000;20(9):765-786.

Tilton A, Russman R, Aydin R, et al. AbobotulinumtoxinA (Dysport®) improves function according to goal attainment in children with dynamic equinus due to cerebral palsy. *J Child Neurol*. 2017; 32(5):482-487.

Truven Health Analytics. Micromedex® DrugDex® Compendium. AbobotulinumtoxinA (Dysport). 02/27/25. Greenwood Village, CO. [Micromedex® Solutions Web site]. Available at: http://www.micromedexsolutions.com/micromedex2/librarian [via subscription only]. Accessed February 27, 2025.

Truven Health Analytics. Micromedex® DrugDex® Compendium. Jeuveau™ (prabotulinumtoxinA-xvfs). 03/20/24. Greenwood Village, CO. [Micromedex® Solutions Web site]. Available at: http://www.micromedexsolutions.com/micromedex2/librarian [via subscription only]. Accessed February 6, 2025.

Truven Health Analytics. Micromedex® DrugDex® Compendium. IncobotulinumtoxinA (Xeomin®). 01/15/25. Greenwood Village, CO. [Micromedex® Solutions Web site]. Available at: http://www.micromedexsolutions.com/micromedex2/librarian [via subscription only]. Accessed February 6, 2025.

Truven Health Analytics. Micromedex® DrugDex® Compendium. OnabotulinumtoxinA (Botox). 02/27/25. Greenwood Village, CO. [Micromedex® Solutions Web site]. Available at: http://www.micromedexsolutions.com/micromedex2/librarian [via subscription only]. Accessed February 6, 2025.

Truven Health Analytics. Micromedex® DrugDex® Compendium. RimabotulinumtoxinB (Myobloc). 02/27/25. Greenwood Village, CO. [Micromedex® Solutions Web site]. Available at: http://www.micromedexsolutions.com/micromedex2/librarian [via subscription only]. Accessed February 27, 2025.

Truven Health Analytics. Micromedex® DrugDex® Compendium. DaxibotulinumtoxinA-lanm (Daxxify). 02/27/25. Greenwood Village, CO. [Micromedex® Solutions Web site]. Available at: http://www.micromedexsolutions.com/micromedex2/librarian [via subscription only]. Accessed February 27, 2025.

Ukleja A, Tandon K, Shah K, Alvarez A. Endoscopic botox injections in therapy of refractory gastroparesis. *World J Gastrointest Endosc*. 2015 Jul 10;7(8):790-8.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. Jeuveau™ (prabotulinumtoxinA-xvfs) drug label and approval information. [FDA Web site]. 07/2019. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed February 6, 2025.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. Botulinum toxin type A (Botox) drug label and approval information. [FDA Web site]. 10/2024. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed February 6, 2025.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. Botulinum toxin type B (Myobloc) drug label and approval information. [FDA Web site]. 03/2021. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed February 6, 2025.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. Botulinum toxin type A (Botox Cosmetic) drug label and approval information. [FDA Web site]. 10/2024. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed February 6, 2025.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. AbobotulinumtoxinA (Dysport) drug label and approval information. [FDA Web site]. labeling updated 09/2023. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed March 25, 2024.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. IncobotulinumtoxinA (Xeomin) drug label and approval information. [FDA Web site]. labeling updated 07/2024. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed February 6, 2025.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. DaxibotulinumtoxinA-lanm (Daxxify) drug label and approval information. [FDA Web site]. labeling updated 08/2023. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed February 6, 2025.

Vadoud-Seyedi J, Heenen M, Simonart T. Report of idiopathic palmar hyper-hidrosis with botulinum toxin. Review of 23 cases and review of the literature. *Dermatology.* 2001;203:318-321.

Walshe M, Smith M, Pennington L. Interventions for drooling in children with cerebral palsy. *Cochrane Database Syst Rev*. 2012 Nov 14;11:CD008624. doi: 10.1002/14651858.CD008624.pub3.

Welch KM. Botulinum toxin type A for the treatment of headache: con. *Headache.* 2004;44(8):831-833.

(Xeomin®) incobotulinumtoxinA [prescribing information]. Raleigh, NC: Merz Pharmaceuticals, LLC. 07/2024. Available at: http://www.xeomin.com/physicians/. Accessed February 6, 2025.

Young CA, Ellis C, Johnson J, Sathasivam S, Pih N. Treatment for sialorrhea (excessive saliva) in people with motor neuron disease/amyotrophic lateral sclerosis. *Cochrane Database Syst Rev.* 2011;5:CD006981.

Zalvan C, Bentsianov B, Gonzalez-Yanes O, Blitzer A. Noncosmetic uses of botulinum toxin. *Dermatol Clin.* 2004;22(2):187-195.

Zesiewicz TA, Elble RJ, Louis ED, et al. Evidence-based guideline update: Treatment of essential tremor. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2011;77(19):1752-1755.

Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)

Botulinum Toxin Agents ICD-10 Dx Coc

HCPCS Level II Code Number(s)
MEDICALLY NECESSARY

THE FOLLOWING CODE REPRESENTS BOTOX (ONABOTULINUMTOXINA)
J0585 Injection, onabotulinumtoxinA, 1 unit

THE FOLLOWING CODE REPRESENTS DYSPORT (ABOBOTULINUMTOXINA)
J0586 Injection, abobotulinumtoxinA, 5 units

THE FOLLOWING CODE REPRESENTS MYOBLOC (RIMABOTULINUMTOXINB)
J0587 Injection, rimabotulinumtoxinB, 100 units

THE FOLLOWING CODE REPRESENTS XEOMIN (INCOBOTULINUMTOXINA)
J0588 Injection, incobotulinumtoxinA, 1 unit

THE FOLLOWING CODE REPRESENTS DAXXIFY (DAXIBOTULINUMTOXINA-LANM)
J0589 Injection, daxibotulinumtoxina-lanm, 1 unit

BENEFIT CONTRACT EXCLUSION
THE FOLLOWING CODES REPRESENT PRABOTULINUMTOXINA (JEUVEAU) AND LETIBOTULINUMTOXINA (LETYBO)
C9399 Unclassified drugs or biologicals
J3590 Unclassified biologics

Policy History

Revisions From MA08.017m

12/15/2025	This policy has been identified for the ICD-10 CM code update, effective 12/15/2025. The following ICD-10 CM code has been termed from this policy: G35 Multiple sclerosis The following ICD-10 CM codes have been added to this policy: G35.A Relapsing-remitting multiple sclerosis G35.B0 Primary progressive multiple sclerosis, unspecified G35.B1 Active primary progressive multiple sclerosis G35.B2 Non-active primary progressive multiple sclerosis G35.C0 Secondary progressive multiple sclerosis, unspecified G35.C1 Active secondary progressive multiple sclerosis G35.C2 Non-active secondary progressive multiple sclerosis G35.CD Multiple sclerosis, unspecified

Revisions From MA08.017l:

06/13/2025	This version of the policy will become effective 06/13/2025. This policy has been updated to communicate removal of step therapy for prevention of chronic migraine headache or probable migraine headache, and additional options for the treatment of overactive bladder for onabotulinumtoxinA.

Revisions From MA08.017jk:

09/16/2024	This version of the policy will become effective 09/16/2024. The policy has been updated to communicate expanded indications for daxibotulinumtoxinA-lanm (Daxxify) The ICD-10 CM codes with unspecified laterality have been removed from this policy:

	G51.39, G81.10, G83.10, G83.20, G83.30, H49.00, H49.20, H49.30, H49.40, H49.889, H51.20, H53.039, I69.039, I69.049, I69.069, I69.139, I69.149, I69.159,I69.169, I69.239, I69.249, I69.269, I69.339, I69.349, I69.369, I69.839, I69.849, I69.939, I69.949

Revisions From MA08.017j:

05/07/2024	The policy has been reviewed and reissued to communicate the Company's continuing position on Botulinum Toxin Agents.
10/01/2023	This policy has been identified for the ICD-10 CM code update, effective 10/01/2023. The following ICD-10 CM code has been termed from this policy: G37.8 Clonic hemifacial spasm The following ICD-10 CM codes have been added to this policy: G37.81 Myelin oligodendrocyte glycoprotein antibody disease G37.89 Other specified demyelinating diseases of central nervous system G43.E09 Chronic migraine with aura, not intractable, without status migrainosus G43.E11 Chronic migraine with aura, intractable, with status migrainosus G43.E19 Chronic migraine with aura, intractable, without status migrainosus

Revisions From MA08.017i:

09/05/2023	This policy has been reissued in accordance with the Company's annual review process.
04/10/2023	This version of the policy will become effective 04/10/2023. The policy has been updated to communicate the removal of Initial treatment for botulinum toxin A is medically necessary for two cycles (i.e., 24 weeks). Clarification of headache specialist (a headache specialist is physician certified by the United Council for Neurologic Subspecialties [UCNS])

Revisions From MA08.017h:

10/01/2022	This policy has been identified for the ICD-10 CM code update, effective 10/01/2022. The following ICD-10 CM codes have been added to this policy: S06.0XAA Concussion with loss of consciousness status unknown, initial encounter S06.0XAD Concussion with loss of consciousness status unknown, subsequent encounter S06.0XAS Concussion with loss of consciousness status unknown, sequela S06.1XAA Traumatic cerebral edema with loss of consciousness status unknown, initial encounter S06.1XAD Traumatic cerebral edema with loss of consciousness status unknown, subsequent encounter S06.1XAS Traumatic cerebral edema with loss of consciousness status unknown, sequela S06.2XAA Diffuse traumatic brain injury with loss of consciousness status unknown, initial encounter S06.2XAD Diffuse traumatic brain injury with loss of consciousness status unknown, subsequent encounter S06.2XAS Diffuse traumatic brain injury with loss of consciousness status unknown, sequela S06.30AA Unspecified focal traumatic brain injury with loss of consciousness status unknown, initial encounter S06.30AD Unspecified focal traumatic brain injury with loss of consciousness status unknown, subsequent encounter S06.30AS Unspecified focal traumatic brain injury with loss of consciousness status unknown, sequela S06.81AA Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, initial encounter S06.81AD Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, subsequent encounter S06.81AS Injury of right internal carotid artery, intracranial portion, not elsewhere classified with

	loss of consciousness status unknown, sequela S06.82AA Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, initial encounter S06.82AD Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, subsequent encounter S06.82AS Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, sequela S06.89AA Other specified intracranial injury with loss of consciousness status unknown, initial encounter S06.89AD Other specified intracranial injury with loss of consciousness status unknown, subsequent encounter S06.89AS Other specified intracranial injury with loss of consciousness status unknown, sequela S06.8A0A Primary blast injury of brain, not elsewhere classified without loss of consciousness, initial encounter S06.8A0D Primary blast injury of brain, not elsewhere classified without loss of consciousness, subsequent encounter S06.8A0S Primary blast injury of brain, not elsewhere classified without loss of consciousness, sequela S06.8A1A Primary blast injury of brain, not elsewhere classified with loss of consciousness of 30 minutes or less, initial encounter S06.8A1D Primary blast injury of brain, not elsewhere classified with loss of consciousness of 30 minutes or less, subsequent encounter S06.8A1S Primary blast injury of brain, not elsewhere classified with loss of consciousness of 30 minutes or less, sequela S06.8A2A Primary blast injury of brain, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, initial encounter S06.8A2D Primary blast injury of brain, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, subsequent encounter S06.8A2S Primary blast injury of brain, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, sequela S06.8A3A Primary blast injury of brain, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, initial encounter S06.8A3D Primary blast injury of brain, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, subsequent encounter S06.8A3S Primary blast injury of brain, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, sequela S06.8A4A Primary blast injury of brain, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, initial encounter S06.8A4D Primary blast injury of brain, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, subsequent encounter S06.8A4S Primary blast injury of brain, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, sequela S06.8A5A Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, initial encounter S06.8A5D Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, subsequent encounter S06.8A5S Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, sequela S06.8A6A Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, initial encounter S06.8A6D Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, subsequent encounter S06.8A6S Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, sequela S06.8A7A Primary blast injury of brain, not elsewhere classified with loss of consciousness of any duration with death due to brain injury prior to regaining consciousness, initial encounter S06.8A8A Primary blast injury of brain, not elsewhere classified with loss of consciousness of any duration with death due to other cause prior to regaining consciousness, initial encounter S06.8A9A Primary blast injury of brain, not elsewhere classified with loss of consciousness of unspecified duration, initial encounter

	S06.8A9D Primary blast injury of brain, not elsewhere classified with loss of consciousness of unspecified duration, subsequent encounter S06.8A9S Primary blast injury of brain, not elsewhere classified with loss of consciousness of unspecified duration, sequela S06.8AAA Primary blast injury of brain, not elsewhere classified with loss of consciousness status unknown, initial encounter S06.8AAD Primary blast injury of brain, not elsewhere classified with loss of consciousness status unknown, subsequent encounter S06.8AAS Primary blast injury of brain, not elsewhere classified with loss of consciousness status unknown, sequela S06.9XAA Unspecified intracranial injury with loss of consciousness status unknown, initial encounter S06.9XAD Unspecified intracranial injury with loss of consciousness status unknown, subsequent encounter S06.9XAS Unspecified intracranial injury with loss of consciousness status unknown, sequela

Revisions From MA08.017g:

05/09/2022	This version of the policy will become effective 05/09/2022. The policy has been updated to communicate expanded indications for Bothersome simple motor tics (e.g., eye blinking, nose movement, head jerks) in adolescents (age 10-19 years old) and adults when the benefits of treatment outweigh the risks. Severely disabling or aggressive vocal tics in adolescents (age 10-19 years old) and adults when the benefits of treatment outweigh the risks . Tourette's disorder with chronic motor or vocal tics in adolescents (age 10 -19 years old) and adult individuals . **THE FOLLOWING ICD-10 CODES HAVE BEEN ADDED TO THE POLICY** F95.2 Tourette's disorder

Revisions From MA08.017f:

05/03/2021	This version of the policy will become effective 05/03/2021. The policy has been updated to communicate expanded indications for adult individuals with Isolated oromandibular dystonia, bothersome simple motor tics in adolescents and adults, severely disabling or aggressive vocal tics in older adolescents and adults and pediatric individuals two years of age or older with chronic sialorrhea, neurogenic detrusor overactivity (NDO) in pediatric individuals five years of age and olderfor onabotulinumtoxinA, (Botox®, Dysport® and Xeomin®). THE FOLLOWING CODE WAS ADDED TO THE POLICY **F95.1 Chronic motor or vocal tic disorder**

Revisions From MA08.017e:

06/08/2020	This version of the policy will become effective 06/08/2020. The policy has been updated to communicate expanded indications for spasticity of upper and lower limbs in pediatric individuals two years and older for onabotulinumtoxinA, (Botox® and Dysport®).

Revisions From MA08.017d:

12/16/2019	The policy has been updated to communicate expanded indications and corresponding diagnosis codes for onabotulinumtoxinA, (Botox® and Botox Cosmetic® [Allergan]), prabotulinumtoxinA-xvfs (Jeuveau™ [Evolus]), rimabotulinumtoxinB (Myobloc® [Solstice Neurosciences, Inc]), abobotulinumtoxinA (Dysport® [Ipsen Biopharmaceuticals]), and incobotulinumtoxinA (Xeomin® [Merz Pharmaceuticals, Raleigh, NC]).

	The following codes were ADDED for onabotulinumtoxinA G25.0 Essential tremor N30.10 Interstitial cystitis (chronic) without hematuria N30.11 Interstitial cystitis (chronic) with hematuria Dual diagnosis for spasticity of limbs has been added, M62.838 another muscle spasm (added), I69.398 Other sequelae of cerebral infarction (policy language stroke) – added. The following codes were REMOVED for onabotulinumtoxinA G43.821 Menstrual migraine, not intractable, with status migrainosus G43.829 Menstrual migraine, not intractable, without status migrainosus G43.831 Menstrual migraine, intractable, with status migrainosus G43.839 Menstrual migraine, intractable, without status migrainosus G43.A0 Cyclical vomiting, not intractable G43.C0 Periodic headache syndromes in child or adult, not intractable G43.C1 Periodic headache syndromes in child or adult, intractable G24.01 Drug induced subacute dyskinesia G24.4 Idiopathic orofacial dystonia

Revisions From MA08.017c:

01/28/2019	The policy has been updated to communicate expanded indications and corresponding diagnosis codes for Botox® (onabotulinumtoxinA), Myobloc® (rimabotulinumtoxinB), Dysport® (abobotulinumtoxinA), and Xeomin® (incobotulinumtoxinA). **The following codes were removed for Botox since more appropriate codes are available:** K60.0 Acute anal fissure K60.2 Anal fissure, unspecified L74.52 Secondary focal hyperhidrosis R25.0 Abnormal head movements R25.8 Other abnormal involuntary movements R25.9 Unspecified abnormal involuntary movements **The following codes were added for all 4 agents (Botox, Myobloc, Dysport, Xeomin) due to cosmetic use (benefit contract exclusion):** L57.2 Cutis rhomboidalis nuchae L57.4 Cutis laxa senilis L57.8 Other skin changes due to chronic exposure to nonionizing radiation L98.8 Other specified disorders of the skin and subcutaneous tissue The dosage and frequency requirements for Botox® (onabotulinumtoxinA) has been removed from the policy.

Revisions From MA08.017b:

10/01/2018	This policy has been identified for the ICD-10 CM code update, effective 10/01/2018. The following ICD-10 CM code has been **termed** from this policy: G51.3 Clonic hemifacial spasm The following ICD-10 CM codes have been **added** to this policy: G51.31 Clonic hemifacial spasm, right G51.32 Clonic hemifacial spasm, left G51.33 Clonic hemifacial spasm, bilateral G51.39 Clonic hemifacial spasm, unspecified

Revisions From MA08.017a:

03/11/2015	Medical Policy MA08.017a will become effective 03/11/2015. There are no changes to the medical necessity criteria from the previous iteration of this policy.

Revisions From MA08.017:

01/01/2015	This is a new policy.

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