

Corporate Medical Policy

Botulinum Toxin Injection

File Name: botulinum_toxin_injection
Origination: 8/1985
Last CAP Review: 1/2021
Next CAP Review: 1/2022
Last Review: 2/2021

Description of Procedure or Service

Description

Botulinum is a family of toxins produced by the anaerobic organism *Clostridia botulinum*. Multiple formulations of botulinum toxin have been approved by the U.S. Food and Drug Administration (FDA). Labeled indications of these agents differ; however, all are FDA-approved for treating cervical dystonia in adults. Botulinum toxin products are also used for a range of off-label indications.

Background

There are seven distinct serotypes designated as type A, B, C-1, D, E, F, and G. In the U.S., four preparations of botulinum are commercially available, three using type A serotype and one using type B. The drug names of the botulinum toxin products were changed in 2009; trade names and product formulations did not change. The three formulations of botulinum toxin type A are currently called onabotulinumtoxinA (Botox®), abobotulinumtoxinA (Dysport®), and incobotulinumtoxinA (Xeomin®). Botox has been available for the longest time in the United States and has been the most widely used. Xeomin, the newest product marketed in the U.S., consists of the pure neurotoxin without complexing proteins and is the only product that is stable at room temperature for up to four years. RimabotulinumtoxinB contains botulinum toxin type B; the current name of this drug is Myobloc.

The following is a list of the FDA-Approved indications for **Botox**:

- Treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication
- Treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition in adults who have an inadequate response to or are intolerant of an anticholinergic medication
- Treatment of neurogenic detrusor overactivity (NDO) in pediatric patients 5 years of age and older who have an inadequate response to or are intolerant of anticholinergic medication
- Prophylaxis of headaches in adults with chronic migraine (≥ 15 d/mo with headache lasting 4 hours a day or longer)
- Treatment of spasticity in patients ≥ 2 years of age
- 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 adults
- Treatment of blepharospasm associated with dystonia in patients ≥ 12 years of age

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- Treatment of strabismus in patients ≥ 12 years of age

Safety and effectiveness have not been established for:

- Prophylaxis of episodic migraine (14 headache days or fewer per month)
- Treatment of hyperhidrosis in body areas other than axillary

The following is a list of the FDA-Approved indications for **Dysport**:

- Treatment of cervical dystonia in adults
- Treatment of spasticity in patients ≥ 2 years of age

The following is a list of the FDA-Approved indications for **Xeomin**:

- Treatment of cervical dystonia in adults
- Treatment of upper-limb spasticity in adults
- Treatment of upper-limb spasticity in pediatric patients 2 to 17 years of age, excluding spasticity caused by cerebral palsy
- Treatment of blepharospasm in adults
- Treatment of chronic sialorrhea in patients ≥ 2 years of age

The following is the FDA-Approved indication for **Myobloc**:

- Treatment of cervical dystonia in adults to reduce the severity of abnormal head position and neck pain
- Treatment of chronic sialorrhea in adults

Three products, Botox (marketed as Botox Cosmetic), Dysport, and Xeomin are approved for temporarily improving the appearance of glabellar (frown) lines in adults.

The botulinum toxin products have also been used for a wide variety of off-label indications.

In rare cases, patients do not respond to botulinum toxin (primary resistance), and a small percentage of adults develop secondary resistance after long-term treatment. Reasons for resistance include injection of incorrect muscles, unrealistic expectations of a complete cure, and interference from associated disorders that mask perception of response. In 3% to 10% of adults, true secondary resistance arises due to the development of antibodies that specifically neutralize the activity of botulinum toxin. That neutralizing antibodies directly cause resistance has been shown in a case study in which a patient with severe dystonia, secondary resistance, and detectable neutralizing antibodies was treated with repeated plasma exchange and depletion of serum antibodies; subsequent treatment with the same botulinum toxin type was successful. Non-neutralizing antibodies may also develop in patients but have no effect on outcomes. The predisposing factors are not completely understood but include the use of higher doses, shorter intervals between repeat treatments, and younger age. In two studies of pediatric patients treated for spasticity, neutralizing antibodies were detected in 28% to 32% of patients. Recommendations for avoiding eventual resistance are using the lowest dose possible to obtain a clinical response and scheduling intervals of 10 to 12 weeks between injections, if possible.

Patients who develop secondary resistance to botulinum toxin type A may stop treatment for several months and then undergo retreatment with likely success; however, the duration of response is often short, because neutralizing antibodies may redevelop quickly. Alternatively, the patient may be administered botulinum toxin type B, with which neutralizing antibodies to toxin type A will not

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interfere. However, the duration of effect is shorter, and adverse effects have occurred at higher frequencies than for botulinum toxin type A.

Confirmation of neutralizing antibodies to botulinum toxin type A in research studies (mice) has most often been accomplished using two techniques: (1) an injection of patient serum or (2) an in vitro toxin-neutralizing assay based on a mouse diaphragm nerve-muscle preparation. While sensitive, neither assay is appropriate for a clinical laboratory setting. Other assay formats have been explored, such as immunoprecipitation, Western blot, and enzyme-linked immunosorbent assay. However, unless only the protein sequences that specifically react with neutralizing antibodies are employed, these formats detect both neutralizing and non-neutralizing antibodies, and would therefore result in significant numbers of false-positive results. An option for some patients might be to inject toxin into the frontal muscle above 1 eyebrow; a toxin-responsive patient would have asymmetry of the forehead on attempted frowning, whereas a nonresponsive patient would not.

Regulatory Status

Botox® (Allergan, Irvine, CA) was approved by the FDA in 1991, Myobloc® (Solstice Neurosciences) in 2000, Dysport® (Medicis Pharmaceutical Corporation, now Ipsen Biopharm) in 2009, and Xeomin® (Merz Pharmaceuticals) in 2010.

Related Medical Policies

Eptinezumab-jjmr (Vyepi™)
Hyperhidrosis, Treatment of

Related Pharmacy Policies:

CGRP Therapy for Migraine

***Please note that the US Food & Drug Administration (FDA) now requires a boxed warning and a Risk Evaluation and Mitigation Strategy (REMS) for all Botulinum Toxin products. Refer to the FDA Website for additional information located at <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/ucm174949.htm>.

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

BCBSNC will provide coverage for Botulinum Toxin Injection when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Botulinum Toxin Injection is covered

The use of botulinum toxin may be considered medically necessary for the following:

1. Cervical dystonia (spasmodic torticollis; applicable whether congenital, due to child birth injury, or traumatic injury). For this use, cervical dystonia must be associated with sustained

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- head tilt or abnormal posturing with limited range of motion in the neck AND a history of recurrent involuntary contraction of one or more of the muscles of the neck, e.g., sternocleidomastoid, splenius, trapezius, or posterior cervical muscles*. (See additional details in Policy Guidelines section), and
- a. If the request is for Botox or Myobloc, the patient has tried and had an inadequate response to OR has a clinical contraindication or intolerance to Xeomin and Dysport; OR
 2. Strabismus*; OR
 3. Blepharospasm or facial nerve (VII) disorders (including hemifacial spasm)*, and
 - a. If the request is for Botox and the patient is 18 years of age or older, the patient has tried and had an inadequate response to OR has a clinical contraindication or intolerance to Xeomin; OR
 4. Spasticity*, and
 - a. If the request is for Botox, the patient has tried and had an inadequate response to OR has a clinical contraindication or intolerance to Xeomin and Dysport; OR
 5. Prevention (treatment) of chronic migraine headache in the following situations*:
(See Policy Guidelines), and
 - a. The patient has tried and had an inadequate response to OR has a clinical contraindication or intolerance to a calcitonin gene-related peptide (CGRP) antagonist, such as fremanezumab, galcanezumab, erenumab, or eptinezumab; and
 - b. Initial 6-month trial: Adult patients who meet International Classification of Headache Disorders (ICHD) diagnostic criteria for chronic migraine headache and have symptoms that persist despite adequate trials of at least 2 agents from different classes of medications used in the treatment of chronic migraine headaches (e.g., antidepressants, antihypertensives, antiepileptics). (Patients who have contraindications to preventive medications are not required to undergo a trial of these agents); or
 - c. Continuation of treatment beyond 6 months:
 - Migraine headache frequency reduced by at least 7 days per month compared to pre-treatment level, or
 - Migraine headache duration reduced at least 100 hours per month compared to pre-treatment level; and
 - d. For both initial and continuation treatment, botulinum toxin will not be used concomitantly with a CGRP antagonist for chronic migraine headache; OR
 6. Dystonia/spasticity resulting in functional impairment (interference with joint function, mobility, communication, nutritional intake) with or without pain. Examples include but are not limited to patients with any of the following:
 - a. Focal dystonias:
 - Focal upper limb dystonia (e.g., organic writer's cramp)
 - Oromandibular dystonia (orofacial dyskinesia, Meige syndrome)
 - Laryngeal dystonia (adductor spasmodic dysphonia)
 - Idiopathic (primary or genetic) torsion dystonia
 - Symptomatic (acquired) torsion dystonia
 - b. Spastic conditions:
 - Cerebral palsy
 - Spasticity related to stroke
 - Acquired spinal cord or brain injury
 - Hereditary spastic paraparesis
 - Spastic hemiplegia
 - Neuromyelitis optica
 - Multiple sclerosis or Schilder's disease; **AND**
 - c. If the request is for Botox, the patient has tried and had an inadequate response to OR has a clinical contraindication or intolerance to Xeomin and Dysport; OR
 7. Esophageal achalasia in patients who have not responded to dilation therapy or who are considered poor surgical candidates; OR

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8. Sialorrhea (drooling) associated with a neurological disorder (e.g., amyotrophic lateral sclerosis, atypical parkinsonian disorders, cerebral palsy, Parkinson disease, stroke, traumatic brain injury);
OR
9. Chronic anal fissure; OR
10. Urinary incontinence due to detrusor overreactivity* associated with neurogenic causes (e.g., spinal cord injury, multiple sclerosis), that is inadequately controlled with anticholinergics;
OR
11. Neurogenic detrusor overactivity (NDO)* in pediatric patients 5 years of age or older who have an inadequate response to or are intolerant of an anticholinergic medication; OR
12. Overactive bladder* (OAB) with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication; OR
13. Hirschsprung disease in patients who develop obstructive symptoms after a pull-through operation.

For continuation of therapy for any diagnosis, the following criteria must be met:

1. Documentation of positive clinical response to botulinum toxin therapy, and
2. Statement of expected frequency and duration of proposed botulinum toxin treatment, and
3. Botulinum toxin administration is no more frequent than every 12 weeks, regardless of diagnosis.

**FDA-approved indication for at least one of the agents.*

*****Use of botulinum toxin for off-label indications should only be done when the treating physician has determined that the benefits of the treatment clearly outweigh the risks of the therapy.**

When Botulinum Toxin Injection is not covered

With the exception of cosmetic indications, the use of botulinum toxin is considered investigational for all other indications not specifically mentioned above, including, but not limited to:

- headaches, except as noted above for prevention (treatment) of chronic migraine headache
- chronic low back pain
- joint pain
- mechanical neck disorders
- neuropathic pain after neck dissection
- myofascial pain syndrome
- temporomandibular joint disorders
- trigeminal neuralgia
- pain after hemorrhoidectomy or lumpectomy
- tremors such as benign essential tremor (upper extremity)
- tinnitus
- sialorrhea (drooling) except that associated with neurological disorders
- chronic motor tic disorder, and tics associated with Tourette syndrome (motor tics)
- lateral epicondylitis
- benign prostatic hyperplasia
- interstitial cystitis
- detrusor sphincteric dyssynergia (after spinal cord injury)
- piriformis
- prevention of pain associated with breast reconstruction after mastectomy
- gastroparesis
- facial wound healing
- internal anal sphincter (IAS) achalasia
- depression

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The use of botulinum toxin is **not** medically necessary as a treatment of wrinkles or other cosmetic indications.

The use of assays to detect antibodies to botulinum toxin is considered **investigational**.

Policy Guidelines

This drug may require prior review. In cases for which botulinum toxin has been approved in the past, medical records may be required yearly to document ongoing effectiveness. For the indication of prevention of chronic migraine headaches, medical records may be required to document effectiveness after the initial 6-month trial and yearly thereafter.

International Classification of Headache Disorders (ICHD-3) diagnostic criteria for chronic migraine headache include the following:

Headaches occurring on at least 15 days per month for more than 3 months, which, on at least 8 days per month has features of migraine headaches.

Features of migraine headache:

- Lasts 4 to 72 hours (when untreated or unsuccessfully treated);
- Has at least 2 of the following 4 characteristics:
 - Unilateral location
 - Pulsating quality
 - Moderate or severe pain intensity
 - Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
- During headache, associated with at least one of the following:
 - Nausea and/or vomiting
 - Photophobia and phonophobia

(In ICHD-2, absence of medication overuse was one of the diagnostic criteria for chronic migraine. In the ICHD-3, this criterion was removed from the chronic migraine diagnosis and “medication overuse headache” is now a separate diagnostic category.)

Continuing treatment with botulinum toxin beyond 6 months for chronic migraine includes the following:

The policy includes the requirement that migraine headache frequency be reduced by at least 7 days per month compared with pretreatment level, or that migraine headache duration be reduced by at least 100 hours per month compared with pretreatment level in order to continue treatment beyond 6 months. The 7 days per month represents a 50% reduction in migraine days for patients who have the lowest possible number of migraine days (15) that would allow them to meet the ICHD-3 diagnostic criteria fewest chronic migraine. A 50% reduction in frequency is a common outcome measure for assessing the efficacy of headache treatments and was one of the end points of the PREEMPT study.

For complete classification of primary migraine and non-migraine headaches, please see the International Headache Classification (ICHD-3) at <http://www.ihs-classification.org/downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf> .

Cervical dystonia is a movement disorder (nervous system disease) characterized by sustained muscle contractions. This results in involuntary, abnormal, squeezing and twisting muscle contractions in the head and neck region. These muscle contractions result in sustained abnormal positions or posturing. Sideways or lateral rotation of the head and twisting of the neck are the most common findings in cervical dystonia. Muscle hypertrophy occurs in most patients. When using

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botulinum toxin to treat cervical dystonia, the postural disturbance and pain must be of a severity to interfere with activities of daily living; and the symptoms must have been unresponsive to a trial of standard conservative therapy. In addition, before using botulinum toxin, alternative causes of symptoms such as cervicogenic headaches must have been considered and excluded. Clinical improvement generally begins within the first two weeks after injection with maximum clinical benefit at approximately six weeks post-injection. Most patients have returned to pre-treatment status by 3 months post-treatment.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 46505, 52287, 64611, 64612, 64615, 64616, 64617, 64642, 64643, 64644, 64645, 64646, 64647, 64653, 67345, 95873, 95874, J0585, J0586, J0587, J0588, S2340, S2341

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

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Policy Implementation/Update Information

- | | |
|--------|--|
| 8/85 | Original Policy National Association - Investigational for blepharospasm |
| 6/94 | Evaluated: Local Policy issued covering Blepharospasm, Strabismus, Hemifacial spasm, Facial spasm, Spasmodic dysphonia, and Spasmodic torticollis. Investigational for chronic paralytic strabismus, treatment of dynamic deformity secondary to cerebral palsy. |
| 4/96 | Revised: Added additional covered indications and investigational indications, TEC Bulletin 2/96 |
| 4/97 | Reaffirmed |
| 5/99 | Reaffirmed |
| 7/99 | Reformatted, Description of Procedure or Service changed, Medical Term Definitions added. |
| 4/2000 | Statement added to section, "When Botulinum-A Toxin Injection is not covered", which says, "1) For conditions other than those listed above." System coding changes. |
| 7/00 | Added Gustatory sweating (Frey's Syndrome) as a covered indication. Specialty Matched Consultant Advisory Panel. |
| 9/00 | Medical Policy Advisory Group review. Approved. No change in criteria. |

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- 10/00 Revised. Criteria changes. Botulinum now eligible for coverage for achalasia, chronic anal fissure, and investigational for headache or migraine, myofascial pain syndrome, or tremors such as benign essential tremor, chronic motor tic disorder and tics associated with Tourette syndrome. Medical Policy Advisory Group - Approved.
- 04/01 Changes in formatting.
- 10/01 Policy name changed from Botulinum A Toxin Injection. Revised description to include type B Botulinum (Myobloc) and FDA labeled indications to include cervical dystonia. System application guidelines revised.
- 3/02 System coding changes. Added code J0587 to policy and removed code J3490.
- 5/02 Revised under when it is covered, number 3. a. to include, "and/or". Codes 64612-64614, and 67345 added to Billing and Coding section.
- 8/03 Description section revised for clarity. Added spasmodic dysphonia under "When Covered" section. Added chronic low back pain under "When Not Covered" section. Reformatted "When Covered" and "When Not Covered" sections for ease of reading. Removed codes 64040 and 67399 from Billing and Coding section. Added Codes S2340 and S2341 to Billing and Coding section. Added references.
- 8/26/04 Specialty Matched Consultant Advisory Panel review. No changes to criteria. Benefits Application and Billing/Coding sections updated for consistency. Reference sources added.
- 2/17/05 Added the following statement to "When Covered" and "Policy Guidelines" sections: Refer to separate policy number MED1215, titled "Hyperhidrosis, Treatment of" regarding Botulinum toxin injection guidelines for patients with primary Hyperhidrosis. Key word added.
- 1/19/06 Added 2006 CPT codes 46505, 64653, 95873, 95874 to Billing/Coding section.
- 9/18/06 Under "When Covered" section, added "Botulinum toxin may be considered medically necessary as a treatment of incontinence due to detrusor overreactivity caused by spinal cord injury that is inadequately controlled with anticholinergic therapy." Under "When not Covered" section, 3.c. now reads "headache including migraine, chronic tension, chronic daily, and cervicodystonic headaches". Added 3.i. sialorrhea (drooling); 3.j. lateral epicondylitis; 3.k. benign prostatic hyperplasia; 3.l. detrusor overreactivity not due to spinal cord injury; 3.m. detrusor sphincteric dyssynergia. Medical term definitions added. Reference sources added.
- 6/4/07 Specialty Matched Consultant Advisory Panel review (re: urological indications) 5/2007. No changes to criteria. Reference sources added.
- 8/27/07 Under "When Covered" section: 1.c.- added "such as hemifacial spasm"; 1.d.- added "(see "Policy Guidelines" section for use of Botulinum Toxin for this indication)"; 2.i.- added "or to demyelinating conditions such as multiple sclerosis."; deleted 2.k. Spasmodic torticollis; 3.b.- revised to "lower esophageal achalasia where the patient has not responded to dilation therapy or where the patient is considered a poor surgical candidate." Under "When not Covered" section: 3.a.- end of sentence revised to "and cervicogenic or "cervicodystonic"; added 3.l. priformis syndrome. Under "Policy Guidelines" section: Added A.1-5: Use of Botulinum Toxin for Cervical Dystonia (Spasmodic Torticollis): ALL of the following criteria must be met: 1) Postural disturbance and pain must be of moderate or greater

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severity as documented by interference with specific activities of daily living and unresponsive to a trial of appropriate standard conservative therapy that may include non-narcotic analgesics, muscle relaxants and physical modalities; AND 2) There are clonic and/or tonic involuntary contractions of multiple neck muscles (that is, sternocleidomastoid, splenius, trapezius and/or posterior cervical muscles); AND 3) There is sustained head torsion and/or tilt with limited range of motion in the neck; AND 4) The duration of the condition must be greater than six months; AND 5) Alternative causes of the patient's symptoms have been considered and ruled out including chronic neuroleptic treatment, cervicogenic headaches, myofascial pain syndrome, contractures or other neuromuscular conditions. Added B. Contraindications for use of Botulinum toxin: 1) Absolute: a. Inflammation or infection at the site of injection. b. Allergy to the drug. 2) Relative: a. Inability of patient to cooperate b. Coagulopathy c. Disease of neuromuscular transmission: i. Myasthenia Gravis ii. Eaton Lambert Syndrome iii. Amyotrophic lateral sclerosis iv. Peripheral neuropathy v. Motor neuron disease d. Concurrent use of medications that affect neuromuscular transmission such as aminoglycoside antibiotics. Medical Term Definitions added. Notification given 8/27/07. Effective date 11/5/07.

- 4/7/08 Added FDA warning information to the "Description" section; "Please note that the US Food & Drug Administration (FDA) has issued a warning regarding the use of botulinum toxin. It has been reported that there have been serious systemic adverse reactions including respiratory distress and death from botulinum toxins types A and B. The adverse events have occurred in both FDA approved and unapproved uses. Most of the adverse events have occurred in children treated for cerebral palsy associated limb spasticity. Safety, efficacy and dosage have not be established of the use of Botulinum toxins for limb spasticity of cerebral palsy or any condition in children under the age of 12. Also added the following to the "When Covered" section; "The treating physician should carefully review the above FDA issued warning. Use of botulinum toxin for off-label indications should only be done when the treating physician has determined that the benefits of the treatment clearly outweigh the risks of the therapy." References added.
- 7/14/08 Specialty Matched Consultant Advisory review 5/29/08. Added comment; "(See "Policy Guidelines" section for use of Botulinum Toxin for this indication)" to 3.a. under the "When Covered" section. Changed the wording in #5 under the "When Covered" section to read "either idiopathic or due to neurogenic causes" and added "multiple sclerosis" as an example. Added additional examples of non-covered indications under the "When Covered" section. These are "c. joint pain, d. mechanical neck disorders, e. neuropathic pain after neck dissection, g. pain after hemorrhoidectomy or lumpectomy, and n. interstitial cystitis." No change to policy intent. Added "Myoclonus and Tics" to "Definition" section. References added.
- 1/12/09 Revised "Description" section to add; "Type A (Botox®) is more potent and longer acting than type B (Myobloc®). Units and dosing are not equivalent and cannot be interchanged." The word "warning" was removed from the statement; "(FDA) has issued an early communication regarding an on-going safety review" and added "The FDA plans to communicate to the public its findings, resulting recommendations, and any regulatory actions after the review of the data are completed." Updated the "When Covered" section with the following changes; "2. dystonia/spasticity resulting in functional impairment (interference with joint function, mobility, communication, nutritional intake)" and statement "The treating physician should carefully review the above FDA issued warning." Added additional wording for clarifications to various indications and an additional indication; "2.k.Spinal cord or traumatic brain injury;". Added additional wording for clarification to various indications in the "When Not Covered" section and "4.The use of assays to detect antibodies to botulinum toxin is considered investigational." Added "In cases for which botox has been approved in the past, medical records are required yearly to

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document ongoing effectiveness of botox" to the "Policy Guidelines section. References added.

- 10/26/09 Revised "Description" section. Added information related to the FDA approval of Dysport for cervical dystonia, new established names of Botox and Myobloc, and the FDA requirement of a boxed warning and a Risk Evaluation and Mitigation Strategy (REMS) for all Botulinum Toxin products. Changed "paraplegia" to paraparesis" in 2.e. under the "When Covered" section. Added 3.d. "Sialorrhea (drooling) associated with Parkinson disease" to the "When covered" section. Changed the wording under the "Policy Guidelines" section in A.2. from "involuntary contractions of multiple neck muscles" to "involuntary contractions of one or more neck muscles". Reviewed with the Senior Medical Director 9/16/09. References added. (btw)
- 1/5/10 Added new HCPCS code, J0586, to "Billing/Coding" section. (btw)
- 6/22/10 Policy Number(s) removed. (amw)
- 12/21/10 Specialty Matched Consultant Advisory Panel review 11/29/2010. Revised "Description" section to add information regarding Xeomin (incobotulinumtoxinA). Reformatted the "When Covered" section to include upper limb spasticity. Added 2011 HCPCS code, C9278 to "Billing/Coding" section. Updated "Policy Guidelines" section. References added. (btw)
- 2/1/11 Updated "Description" section to include information regarding FDA approval of onabotulinumtoxinA (Botox) for the prevention of chronic headache. Added #5 to the "When Covered" section to indicate; "5. Prevention (treatment) of chronic migraine headache in the following situations*": (see Policy Guidelines) a. Initial 6-month trial: Adult patients who meet established diagnostic criteria for chronic migraine headache and have symptoms that persist despite trials of at least 2 agents used to prevent migraines or reduce migraine frequency representing different classes of medications. (Patients who have contraindications to preventive medications are not required to undergo a trial of these agents). b. Continuing treatment beyond 6 months: Migraine headache frequency reduced by at least 7 days per month, or Migraine headache duration reduced at least 100 hours per month." Added the International Headache Classification definition of migraine to "Policy Guidelines" section. References added. Reviewed by Medical Director 1/25/2011. (btw)
- 3/29/11 Added new HCPCS code, Q2040" to "Billing/Coding" section. Removed deleted code, C9278. (btw)
- 12/20/11 Specialty Matched Consultant Advisory Panel review 11/30/2011. Added the following indications to the "When Not Covered" section for clarification: prevention of pain associated with breast reconstruction after mastectomy, Hirschsprung's disease, and gastroparesis. Changed wording in number 6 to "Examples include but are not limited to patients with any of the following:". No change to policy intent. Added 2012 HCPCS code, J0588, to "Billing/Coding" section and deleted Q2040 and C9278. References added. (btw)
- 11/13/12 Specialty Matched Consultant Advisory Panel review 10/17/2012. No change to policy intent. The definition of "chronic migraine" was updated in the Policy Guidelines to include "with greater than or equal to 8 meeting criteria for migraines; provided there is no medication overuse." Reference added. (btw)
- 12/28/12 Effective 1/1/2013, new CPT codes, 52287 and 64615, added to Billing/Coding section. (btw)

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- 2/26/13 Added “urgency, and frequency” and the “*” indicating FDA approval to number 10 under the When Covered section. Medical Director review 2/2/2013. (btw)
- 5/28/13 Removed “urgency and frequency” from #10 under the When Covered section. Added #11. “Overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication”. Reference added. Senior Medical Director review 5/18/2013. (btw)
- 12/31/13 Specialty Matched Consultant Advisory Panel review 10/16/2013. Description section updated. Changed the wording in #6 under the When Covered section from “and/or” to “with or without” for clarification. Added Facial wound healing and internal anal sphincter (IAS) achalasia to the When Not Covered section. Added new 2014 CPT codes, 64616, 64617, 64642, 64643, 64644, 64645, 64646, and 64647 to Billing/Coding section. Removed deleted codes, 64613 and 64614. Reference added. (btw)
- 2/24/15 Reference added. Specialty Matched Consultant Advisory Panel review 10/28/2014. Added trigeminal neuralgia to investigational list. (sk)
- 11/24/15 Reference added. Temporomandibular joint disorders and depression added to list of investigational indications. Specialty Matched Consultant Advisory Panel review 10/29/2015. (sk)
- 1/26/16 Reference added. FDA approval given for Xeomin® to treat upper limb spasticity in adult patients. (sk)
- 1/27/17 Reference added. Policy Guidelines updated with ICHD-3 criteria. Specialty Matched Consultant Advisory Panel review 10/26/2016. Criteria for continuation of therapy added to Policy Guidelines. (sk)
- 11/10/17 Specialty Matched Consultant Advisory Panel review 10/25/2017. (sk)
- 1/12/18 Reference added. Table added to summarize the FDA approved uses for the four botulinum toxin products, replacing information previously presented in narrative form. Information regarding primary and secondary resistance added to Description section. (sk)
- 11/9/18 Updated Description section to include “treatment of chronic sialorrhea in adults” as an FDA approved use for Xeomin. References added. Specialty Matched Consultant Advisory Panel review 10/24/2018. (krc)
- 10/1/19 Added the following to “When Covered” section for chronic migraine headache: “requests for Botox may be approved for members who have had an inadequate response to or are intolerant to a CGRP antagonist, such as fremanezumab, galcanezumab, or erenumab”, and for cervical dystonia and upper limb spasticity: “requests for Botox may be approved for members who have had an inadequate response to or are intolerant to Xeomin and Dysport”. Under “When Covered,” added the following for chronic migraine headache: “Botox will not be used concomitantly with a CGRP antagonist for chronic migraine headache”. Updated “Description” section to remove “with onabotulinumtoxinA prior treatment” for Xeomin blepharospasm indication, and added indication for Myobloc for treatment of chronic sialorrhea in adults. Added reference to related pharmacy policy: “CGRP Therapy for Migraine”. References added. Medical Director review 9/2019. Notification given 10/1/2019 for effective date 1/1/2020. (krc)

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- 10/15/19 Revised wording in “When Covered” section for cervical dystonia to state: “Requests for Botox and Myobloc may be approved for members who have had an inadequate response to or are intolerant to Xeomin and Dysport.” **Policy remains on notice for effective date 1/14/2020.** (krc)
- 1/14/20 Updated “Description” section to include “treatment of upper-limb spasticity in pediatric patients ≥ 2 years of age, excluding spasticity caused by cerebral palsy” as an FDA approved use for Dysport. References added. Specialty Matched Consultant Advisory Panel review 10/16/2019. (krc)
- 2/11/20 Under “When Covered” section, added “and” and “or” between chronic migraine Policy Statements for clarity. Added “for both initial and continuation treatment” in “When Covered” section for chronic migraine indication for clarity. No change to policy intent. Medical Director review 2/2020. (krc)
- 5/12/20 Added reference to related medical policy: “Eptinezumab-jjmr (Vyepti™)”. Added “eptinezumab” to list of CGRP antagonists in “When Covered” section. Updated language in Policy Guidelines for ICHD-3 chronic migraine diagnostic criteria to more closely align with ICHD-3 guidelines, for clarity with no change to policy intent. (krc)
- 10/13/20 Added “AND/OR” throughout “When Covered” section for clarity of policy intent. The following edits made to preferred product criteria within “When Covered” section for clarity and consistency: “the patient has tried and had an inadequate response to OR has a clinical contraindication or intolerance to.” Updated indications in “Description” section for Botox and Xeomin. References added. Medical Director review 10/2020. (krc)
- 10/27/20 Added the following to “When Covered” section for blepharospasm, “if the request is for Botox and the patient is 18 years of age or older, the patient has tried and had an inadequate response to OR has a clinical contraindication or intolerance to Xeomin.” Updated criteria for requirement of trial of CGRP product for chronic migraine for clarity with no change to policy intent. Added the following criteria requirement for Dystonia/Spasticity: “If the request is for Botox, the patient has tried and had an inadequate response to OR has a clinical contraindication or intolerance to Xeomin and Dysport.” Updated “When Covered” section from “upper limb spasticity” to “spasticity” for consistency with FDA label. Updated indications in “Description” section for Dysport. Reference added. Medical Director review 10/2020. Specialty Matched Consultant Advisory Panel review 10/21/2020. **Notification given 10/27/2020 for effective date 1/1/2021.** (krc)
- 12/31/20 Added the following indication to “When Covered” section: “Hirschsprung disease in patients who develop obstructive symptoms after a pull-through operation.” Removed “Hirschsprung disease” from “When Not Covered” section. Reference added. Medical Director review 11/2020. (krc)
- 1/26/21 Updated indication for Xeomin for chronic sialorrhea to patients ≥ 2 years of age to be consistent with FDA labeling. Added the following to “When Covered” for sialorrhea: “associated with a neurological disorder (e.g., amyotrophic lateral sclerosis, atypical parkinsonian disorders, cerebral palsy, Parkinson disease, stroke, traumatic brain injury).” Reference added. Blue Cross NC Pharmacy and Therapeutics Committee 1/5/2021. (krc)
- 2/23/21 Updated indication for Botox for neurogenic detrusor overactivity in pediatric patients 5 years of age and older to be consistent with FDA labeling. Added the following indication to “When Covered” section: neurogenic detrusor overactivity (NDO) in pediatric patients 5 years of age or older who have an inadequate response to or are intolerant of an anticholinergic medication.” Reference added. (krc)

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