EFFECTIVE DATE: 09|17|2007
POLICY LAST UPDATED: 10|07|2015

OVERVIEW

Botulinum toxin is produced by the anaerobic clostridium botulinum. Four 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.

MEDICAL CRITERIA

Hyperhidrosis
BlueCHiP for Medicare
Severe Primary Axillary Hyperhidrosis
Treatment is considered medically necessary with any of the following criteria:

- Treatment of severe primary axillary hyperhidrosis that is inadequately managed with topical therapy.
- Focal, visible, severe sweating of at least six (6) months duration without apparent cause with at least 2 of the following characteristics:
  - Bilateral and relatively symmetric significant impairment in daily activities
  - Age of onset less than 25 years
  - Positive family history
  - Cessation of focal sweating during sleep

Primary Focal Hyperhidrosis
Commercial Products
Treatment of primary focal hyperhidrosis is considered medically necessary with any of the following complications:

- Acrocyanosis of the hands
- History of recurrent skin maceration with bacterial or fungal infections
- History of recurrent secondary infections
- History of persistent eczematous dermatitis in spite of medical treatments with topical dermatological or systemic anticholinergic agents
- Inadequately managed with topical agents for the following:
  - Axillary focal region
  - Palmar focal region (botulinum toxin A)
  - Axillary focal region:

Migraines
BlueCHiP for Medicare
Headache/migraine coverage is medically necessary for those patients who meet the criteria for chronic daily headaches or chronic migraine headache.

1. Chronic daily headaches including tension-type headache — Headache disorders occurring greater than 15 days a month, in many cases daily with a duration of 4 or more hours for a period of at least 3 months who

have significant disability due to the headaches and have been refractory to standard and usual conventional therapy.

2. Chronic migraine (CM) — CM is characterized by headache on > 15 days per month, of which at least 8 headache days per month meet criteria for migraine without aura or respond to migraine-specific treatment.

Continuing therapy is medically necessary when both of the criteria below are met:

- Demonstrate a significant decrease in the number and frequency of headaches; and
- Improvement in function upon receiving botulinum toxin.

Commercial Products

Prevention (treatment) of chronic migraine headache is medically necessary when all of the criteria below is met:

1. Initial 6-month trial: Adult patients who:
    a. Meet International Headache Classification (ICHD-2) diagnostic criteria for chronic migraine headache (e.g., migraine headaches lasting at least 4 hours on at least 15 days per month; migraine headaches for at least 3 months in the absence of medication overuse); and
2. 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 and antiepileptics. Patients who have contraindications to preventive medications are not required to undergo a trial of these agents.

Continuing treatment beyond 6 months is medically necessary when one of the criteria below is met:

1. Migraine headache frequency reduced by at least 7 days per month compared to pretreatment level, or
2. Migraine headache duration reduced at least 100 hours per month, compared to pretreatment level.

PRIOR AUTHORIZATION

Prior authorization is required for BlueCHiP for Medicare and recommended for Commercial products for the Botulinium Toxin A, for the treatment of migraines or hyperhidrosis.

POLICY STATEMENT

BlueCHiP for Medicare and Commercial Products

The use of botulinum toxin may be considered medically necessary for the treatment of migraines and hyperhidrosis when the criteria is met:

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

- Cervical dystonia (spasmodic torticollis; applicable whether congenital, due to child birth injury, or traumatic injury)
- Strabismus*
- Blepharospasm or facial nerve (VII) disorders (including hemifacial spasm)*
- Upper limb spasticity*
- Dystonia/spasticity resulting in functional impairment (interference with joint function, mobility, communication, nutritional intake) and/or pain
- Organic writer's cramp

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

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 disease
- Esophageal achalasia in patients who have not responded to dilation therapy or who are considered poor surgical candidates
- Sialorrhea (drooling) associated with Parkinson disease
- Chronic anal fissure
- Urinary incontinence due to detrusor overactivity associated with neurogenic causes (e.g., spinal cord injury, multiple sclerosis) in patients unresponsive to or intolerant of anticholinergics*
- Overactive bladder in adults unresponsive to or intolerant of anticholinergics*

Other conditions:

- Chronic anal fissures

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

Use of botulinum toxin for all other indications are not medically necessary as there is insufficient peer-reviewed scientific literature that demonstrates that the procedure service is effective.

The use of assays to detect antibodies to botulinum toxin is considered not medically necessary as there is insufficient peer-reviewed scientific literature that demonstrates that the procedure service is effective.

COVERAGE

Benefits may vary between groups/contracts. Please refer to the appropriate Member Certificate, Subscriber Agreement, and Benefits Booklet for applicable physician office injection coverage/benefits.

Botulinum toxin is covered under the member's medical benefit for those contracts with no specialty pharmacy benefit and is subject to any applicable copay/coinsurance and/or deductible.

BACKGROUND

There are 7 distinct botulinum serotypes designated as type A, B, C-1, D, E, F, and G. In the United States, 4 preparations of botulinum are commercially available, 3 using type A serotype and 1 using type B. The drug names of the botulinum toxin products were changed in 2009; trade names and product formulations did not change. The 3 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 formulation. Xeomin, the newest product marketed in the United States, consists of the pure neurotoxin without complexing proteins and is the only product that is stable at room temperature for up to 4 years. Myobloc® contains botulinum toxin type B; the current name of this drug is rimabotulinumtoxinB.

All 4 products are approved by the FDA for the treatment of cervical dystonia in adults; this is the only FDA-approved indication for Myobloc. Dystonia is a general term describing a state of abnormal or disordered tonicity of muscle. As an example, esophageal achalasia is a dystonia of the lower esophageal sphincter, while cervical dystonia is also known as torticollis. Spasticity is a subset of dystonia, describing a velocity-dependent

increase in tonic-stretch reflexes with exaggerated tendon jerks. Spasticity typically is associated with injuries to the central nervous system. Spasticity is a common feature of cerebral palsy. Botox is also approved for treating upper limb spasticity in adults.

Among the botulinum toxin products, onabotulinumtoxinA (Botox) is FDA approved for the largest number of indications. Other than the indications mentioned above, this includes axillary hyperhidrosis in adults and in individuals at least 12 years of age, blepharospasm, and strabismus. On October 15, 2010, the FDA approved Botox injection for prevention of chronic migraine. Chronic migraine is defined as episodes that otherwise meet criteria for migraine (e.g., at least 4 hours in duration) that occur on at least 15 days per month for more than 3 months, in the absence of medication overuse. OnabotulinumtoxinA is also approved for treatment of urinary incontinence due to neurogenic conditions causing detrusor overactivity in patients unresponsive to or intolerant to anticholinergic medication. Most recently, in 2013, onabotulinumtoxinA received FDA approval for treatment of overactive bladder in adults who are unresponsive to or intolerant of anticholinergic medication.

The newest product, Xeomin, is approved for treating blepharospasm.

Two products, Botox (marketed as Botox Cosmetic) and Dysport, are approved for temporarily improving the appearance of glabellar (frown) lines in adults younger than 65 years of age.

The botulinum toxin products have also been used for a wide variety of off-label indications, ranging from achalasia, spasticity after strokes, cerebral palsy, and anal fissures.

Primary focal hyperhidrosis: BlueCHiP for Medicare
OnabotulinumtoxinA has been approved by the FDA for treatment of severe primary axillary hyperhidrosis (primary focal hyperhidrosis) that is inadequately managed with topical therapy. Compendia list onabotulinumtoxinA and rimabotulinumtoxinB as acceptable off-label agents for this condition. The definition of primary focal hyperhidrosis is severe sweating, beyond physiological needs; focal, visible, severe sweating of at least six (6) months duration without apparent cause with at least two (2) of the following characteristics: bilateral and relatively symmetric, significant impairment in daily activities, age of onset less than 25 years, positive family history, and cessation of focal sweating during sleep.

- The definition of primary focal hyperhidrosis is severe sweating, beyond physiological needs:
- Focal, visible, severe sweating of at least six (6) months duration without apparent cause with at least (2) of the following characteristics:
    - bilateral and relatively symmetric
    - significant impairment in daily activities
    - age of onset less than 25 years
    - positive family history
    - cessation of focal sweating during sleep

Migraines: BlueCHiP for Medicare
The etiology of the chronic daily headache may be chronic tension-type headache or chronic migraine. CM is characterized by headache on > 15 days per month, of which at least 8 headache days per month meet criteria for migraine without aura or respond to migraine-specific treatment. For continuing botulinum toxin therapy the patients must demonstrate a significant decrease in the number and frequency of headaches and an improvement in function upon receiving botulinum toxin.

Primary focal hyperhidrosis: Commercial Products
Hyperhidrosis may be defined as excessive sweating, beyond a level required to maintain normal body temperature in response to heat exposure or exercise. It can be classified as either primary or secondary. Primary focal hyperhidrosis is idiopathic in nature, typically involving the hands (palmar), feet (plantar), or

axillae (underarms). Secondary hyperhidrosis can result from a variety of drugs, such as tricyclic antidepressants, selective serotonin reuptake inhibitors, or underlying diseases/conditions, such as febrile diseases, diabetes mellitus, or menopause.

A multispecialty working group defines primary focal hyperhidrosis as a condition that is characterized by visible, excessive sweating of at least six (6)months in duration without apparent cause and with at least two (2) of the following features: bilateral and relatively symmetric sweating, impairment of daily activities, frequency of at least once per week, age at onset younger than 25 years, positive family history, and cessation of focal sweating during sleep.

Hyperhidrosis Disease Severity Scale

Using the hyperhidrosis disease severity scale, patients rate the severity of symptoms on a scale of 1-4:

1. My underarm sweating is never noticeable and never interferes with my daily activities.
2. My underarm sweating is tolerable but sometimes interferes with my daily activities.
3. My underarm sweating is barely tolerable and frequently interferes with my daily activities.
4. My underarm sweating is intolerable and always interferes with my daily activities.

Secondary hyperhidrosis is usually generalized or craniofacial sweating. Secondary gustatory hyperhidrosis is excessive sweating on ingesting highly spiced foods. This trigeminovascular reflex typically occurs symmetrically on the scalp or face and predominately over the forehead, lips, and nose. Secondary facial gustatory sweating, in contrast, is usually asymmetric and occurs independently of the nature of the ingested food. This phenomenon frequently occurs after injury or surgery in the region of the parotid gland. Frey syndrome is an uncommon type of secondary gustatory hyperhidrosis that arises from injury to or surgery near the parotid gland resulting in damage to the secretory parasympathetic fibers of the facial nerve. After injury, these fibers regenerate, and miscommunication occurs between them and the severed postganglionic sympathetic fibers that supply the cutaneous sweat glands and blood vessels. The aberrant connection results in gustatory sweating and facial flushing with mastication. Aberrant secondary gustatory sweating follows up to 73% of surgical sympathectomies and is particularly common after bilateral procedures.

The consequences of hyperhidrosis are primarily psychosocial in nature. Symptoms such as fever, night sweats, or weight loss require further investigation to rule out secondary causes. Sweat production can be assessed with the Minor starch iodine test, which is a simple qualitative measure to identify specific sites of involvement.

A variety of therapies have been investigated for primary hyperhidrosis, including topical therapy with aluminum chloride, oral anticholinergic medications, iontophoresis, intradermal injections of botulinum toxin, endoscopic transthoracic sympathectomy, and surgical excision of axillary sweat glands. Treatment of secondary hyperhidrosis focuses on treatment of the underlying cause, such as discontinuing certain drugs or hormone replacement therapy as a treatment of menopausal symptoms.

Botulinum toxin is a potent neurotoxin that blocks cholinergic nerve terminals; symptoms of botulism include cessation of sweating. Therefore, intracutaneous injections have been investigated as a treatment of gustatory hyperhidrosis and focal primary hyperhidrosis, most frequently involving the axillae or palms. The drawback of this approach is the need for repeated injections, which have led some to consider surgical approaches.

The outcome of different surgical and medical treatment modalities is best assessed by using a combination of tools. Quantitative tools include gravimetry, evaporimetry, and the Minor starch iodine test. Qualitative assessment tools include general health surveys and hyperhidrosis-specific surveys. Of these, the Hyperhidrosis Disease Severity Scale has been found to have a good correlation to other assessment tools and to be practical in the clinical setting.

There is less evidence in support of botulinum toxin type A for treating plantar hyperhidrosis. No RCTs or large uncontrolled studies were identified in literature searches.

Evidence evaluating botulinum toxin A for gustatory hyperhidrosis as a result of Frey syndrome includes uncontrolled or nonrandomized studies, all showing favorable treatment outcomes. Patient inclusion criteria varied across studies and case reports; ages varied (16-87 years); patients had undergone varied types of parotid surgery (i.e., bilateral, partial); and not all studies documented gustatory sweating with Minor starch test as part of the patient screening.

Multiple RCTs support the efficacy and safety of botulinum toxin A for treating severe axillary and palmar hyperhidrosis. There is a lack of RCTs on use of botulinum toxin A for plantar hyperhidrosis and gustatory hyperhidrosis.

There are few RCTs evaluating botulinum toxin type B for treating hyperhidrosis. One small placebo-controlled RCT did not clearly demonstrate the efficacy of botulinum toxin type B in patients with palmar hyperhidrosis. Two RCTs supported the efficacy of this treatment for patients with axillary hyperhidrosis. An additional RCT in patients with axillary hyperhidrosis compared botulinum toxin type B with suction curettage and found that botulinum toxin type B resulted in outcomes that did not differ significantly from suction-curettage.

Chronic Migraine: Commercial Products

On October 15, 2010, the FDA approved Botox injection for prevention of chronic migraine. Chronic migraine is defined as episodes that otherwise meet criteria for migraine (e.g., at least 4 hours in duration) that occur on at least 15 days per month for more than 3 months, in the absence of medication overuse. Headache Classification (ICD-2) (ihs-classification.org/en/), diagnostic criteria for migraine without aura are:

1. At least 5 attacks fulfilling criteria B-D
2. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
3. Headache has at least two of the following characteristics:
    a. unilateral location
    b. pulsating quality
    c. moderate or severe pain intensity
    d. aggravation by or causing avoidance of routine activity (e.g., walking or climbing stairs)
4. During at least one of the following:
    a. nausea and/or vomiting
    b. photophobia and phonophobia
5. Not attributed to another disorder

CODING

BlueCHiP for Medicare and Commercial Products

Botulinum Toxin: The HCPC codes below require pre-authorization for hyperhidrosis and migraines:

J0585 Injection, Onabolulinumtoxina, 1 unit (A)
J0586 Injection, Abobotulinumtoxina, 5 units (A)
J0588 Injection, Incobotulinumtoxin A, 1 unit
J0587 Injection, rimabotulinumtoxin B100 units (B):

BlueCHiP for Medicare

The following HCPCS codes (J0585, J0586, J0587 and J0588), are covered without authorization when submitted with one of the ICD-10 codes in the attachment below:
(for indications other than Migraine or Hyperhidrosis)

2015 NGS ICD10 other indications.xlsx

CMS other indications 030716.pc

Commercial Products

The following HCPCS codes, (J0585, J0586, J0587 and J0588), are covered without authorization when submitted with one of the ICD-10 codes in the attachment below:
(for indications other than Migraine or Hyperhidrosis)

2015 Commercial ICD10 other indications.xlsx

2015_ commercial_ICD10_ot

ICD9 Codes

ICD9 Migraine hyperhidrosis range 2015.xlsx

ICD9 Migraine hyperhidrosis range 2

ICD9 2015 other indications.xlsx

ICD9 2015 other indications.pdf

RELATED POLICIES

Not applicable

PUBLISHED

Provider Update, December 2015
Provider Update, September 2014
Provider Update, June 2013
Provider Update, October 2012
Provider Update, May 2011
Provider Update, January 2011
Provider Update, February 2010
Provider Update, July 2009
Policy Update, November 2006
Policy Update, October 2001
Policy Update, May 2001
Policy Update, November 2000

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