Effective Date: 2/8/2018

Botox® (onabotulinumtoxinA)
Dysport® (abobotulinumtoxinA)
Xeomin® (incobotulinumtoxinA)

HCPCS: J0585, J0586, J0588
Benefit: Medical

I. Policy/Criteria

Note: Request must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided in patients with functional impairment originating from spasticity or dystonia (conditions of involuntary sustained muscle contraction) resulting from one of the following conditions:
   1. Blepharospasm
   2. Central demyelinating of corpus callosum
   3. Cerebral Palsy
   4. Cervical dystonia with documentation of involuntary contractions of the neck muscles resulting in twisting and repetitive movements, and/or abnormal postures
   5. Demyelinating diseases of CNS
   6. Facial nerve VII disorders
   7. Facial nerve disorders, other
      a. facial myokymia, Melkersson's syndrome, facial/hemifacial spasms
   8. Hereditary spastic paraplegia
   9. Laryngeal spasm; laryngeal adductor spastic dysphonia, or stridulus
   10. Leukodystrophy (CNS disease characterized by adrenal atrophy and diffuse cerebral demyelination)
   11. Multiple sclerosis
   12. Neuromyelitis optica
   13. Organic writer's cramp
   14. Orofacial dyskinesia (i.e., jaw closure dystonia), Meige syndrome
   15. Pelvic floor spasms
   16. Schilder's disease
   17. Spasmodic dysphonia
   18. Spastic hemiplegia
      a. spasticity related to stroke
      b. spasticity related to spinal cord injury
   19. Strabismus
   20. Torsion dystonia, idiopathic and symptomatic (also known as Oppenheim’s dystonia)
   21. Upper limb spasticity in adult patients to decrease the severity of increased muscle tone in elbow flexors, wrist flexors, finger flexors, and thumb flexors
   22. Lower limb spasticity in adults and pediatric patients 2 years of age and older to decrease the severity of increased muscle tone in ankle and toe flexors (gastrocnemius, soleus, tibialis posterior, flexor hallucis longus and flexor digitorum longus)
B. Botulinum toxin type A may be considered for approval in patients with functional impairment resulting from one of the following conditions when generally accepted treatments are not effective or not tolerated:

1. Anal fissures - patients will be assessed for trial and/or failure with other therapeutic alternatives, such as nitroglycerin ointment.
2. Achalasiasa/Cardiospasm - in patients who have not responded to dilation therapy or who are considered poor surgical candidates.
3. Primary axillary hyperhidrosis Botulinum toxin type A may be considered for approval when ALL of the criteria are met:
   a. Treatable primary medical conditions and contributing factors (including drugs) causing secondary hyperhidrosis are identified and addressed where possible.
   b. Documented adequate trial of available agents (e.g., Topical antiperspirants, anticholinergic drugs)
   c. Medical treatment of persistent hyperhidrosis is not considered for approval in the absence of significant medical complications associated with the condition.
4. Treatment of hyperhidrosis, including gustatory or palmer hyperhidrosis, may be considered for approval only when the hyperhidrosis is persistent and severe and has resulted in significant medical complications such as skin maceration with secondary infection.
5. Chronic migraine headache - Botulinum toxin type A may be considered for approval when all ALL FOUR (4) of the criteria in a, b, c, and d below are met:
   a. A neurologist has thoroughly evaluated the member and has established a diagnosis of chronic migraine headaches using the Revised International Headache Society (IHS) criteria for chronic migraine. and the patient was treated with adequate trials using abortive treatments AND
   b. There is a persistent history of recurring debilitating headaches (15 or more days per month with migraine headache lasting for 4 hours per day or longer) AND
   c. An evaluation has been performed to rule out rebound headaches caused by medication use. Medications that may be associated with rebound headache include, but are not limited to, narcotics, triptans exceeding more than 12 doses per month, caffeine, and NSAIDs. AND
   d. Adequate trials (at least 2 month trial) of prophylactic therapy from at least THREE different therapy classes listed in Appendix 3 were not effective, contraindicated, or not tolerated AND
   e. Other conditions or aggravating factors that are contributing to the development of chronic migraine headaches are being treated. Possible Examples: Dental or jaw problems, muscle tension, depression, fibromyalgia, sleep disorders and smoking.
6. Incontinence, either idiopathic or due to neurogenic causes (e.g., spinal cord injury, multiple sclerosis) when therapy with anticholinergic agents is not effective or not tolerated.
7. Overactive bladder with symptoms of urge incontinence, urgency, and frequency in adults who have an inadequate response to, or are intolerant of an anticholinergic medication.
8. Sialorrhea (drooling) in patients with Parkinson’s Disease
9. Pelvic floor spasms - patients will be assessed on a case by case basis after trial and failure with at least 2 other therapeutic alternatives, such as muscle relaxants and benzodiazepines

C. Patient must have trial and failure of preferred product
D. Quantity Limitations, Authorization Period and Renewal Criteria
   a) 6 months for initial therapy
   b) 1 year for continuation of therapy
   c) Authorization will be reviewed for objective clinical response to confirm the medication is effective
      i. For chronic migraine, the frequency or duration for chronic migraines will be reduced from the time of initial presentation with treatment by at least:
         • 7 days/month (frequency)
         • 100 hours/month (duration)
d) Quantity Limits will be approved when used in accordance with FDA approved dosing. Any requests greater than this may require supporting documentation.

E. Botulinum toxin type A is not covered for skin wrinkles or other cosmetic indications
F. Continuation of therapy requires documented positive clinical response
G. Botulinum toxin type A is considered investigational when used for all other conditions, including but not limited to:
   a. Allergic rhinitis
   b. Benign prostatic hyperplasia
   c. Chronic daily tension headache
   d. Chronic motor tic disorder
   e. Cluster headache
   f. Cranial facial hyperhidrosis
   g. Dermatochalasis
   h. Diabetic and idiopathic gastroparesis
   i. Interstitial cystitis
   j. Low back pain
   k. Medication overuse headache
   l. Myofascial pain
   m. Piriformis syndrome (entrapment of the sciatic nerve by the piriformis muscle)
   n. Obesity
   o. Plantar fasciitis pain
   p. Plantar hyperhidrosis
   q. Temporomandibular dysfunction (TMJ)
   r. Tennis elbow (lateral epicondylitis)
   s. Tension-type headaches
   t. Tics associated with Tourette syndrome
   u. Tremors such as essential (benign) tremor
   v. Voice tremor
   w. Thoracic outlet syndrome

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia

II. Therapeutic Considerations

A. FDA approved indication / Diagnosis
   a. Axillary hyperhidrosis
   b. Cervical dystonia
   c. Chronic migraine
   d. Lower limb spasticity
   e. Overactive bladder
   f. Strabismus and blepharospasm associated with dystonia
   g. Upper limb spasticity
   h. Urinary incontinence due to detrusor overactivity

*Please refer to most recent prescribing information http://www.fda.gov/default.htm

B. Background Information
   a. Botulinum toxin is a neurotoxin that is injected into a muscle to cause temporary paralysis of that muscle through the inhibition of acetylcholine release from peripheral cholinergic nerve endings. There
are three commercial botulinum toxin type A products available: Botox (onabotulinumtoxinA), Dysport (abobotulinumtoxinA), and Xeomin (incobotulinumtoxinA). These agents differ in their manufacturing, isolation and purification processes and utilize different Clostridium batches.

b. At comparable doses, the botulinum toxin A can be considered therapeutically equated. Data are limited and one botulinum toxin A product is not considered superior to the others. Botulinum toxin A products are not interchangeable and require medical expertise to convert patients from one formulation to another.

<table>
<thead>
<tr>
<th>Cross References:</th>
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<tbody>
<tr>
<td>1. Myobloc®, rimabotulinumtoxinB, RegenceRx Medication Policy Manual, Policy drug 006.18</td>
</tr>
<tr>
<td>2. Surgical Treatments for Hyperhidrosis, Regence Medical Policy; Med 165.</td>
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<tr>
<td>3. Cosmetic and Reconstructive Surgery, Surgery Section; Medical Policy No. 12.</td>
</tr>
</tbody>
</table>

C. Efficacy

*Please refer to most recent prescribing information.

D. Medication Safety Considerations

Boxed Warning: Yes

*Please refer to most recent prescribing information.

E. Dosing and Administration

- OnabotulinumtoxinA (Botox) Injection specific dosage and administration recommendations should be followed. In treating adult patients for one or more indications, the maximum cumulative dose should generally not exceed 360 Units in a 3 month interval.[3]
  - Detrusor overactivity: 200 Units total dose as 1 mL (6.7 units) injections across 30 sites into the detrusor
  - Chronic migraine: 155 Units total dose as 0.1mL (5 Units) injections per each site divided across 7 head/neck muscles
  - Upper limb spasticity: Dose selected based on affected muscle
  - Cervical dystonia: Variable based on patient presentation
  - Axillary hyperhidrosis: 50 Units per axilla
  - Blepharospasm: 1.25 – 2.5 Units into each of 3 sites per affected eye
  - Strabismus: 1.25 – 2.5 Units initially in any one muscle
  - Lower Limb Spasticity-adults: Recommended total dose 300 units to 400 units divided across ankle and toe muscles.[3]
  - Pelvic floor spasms: 100-300 Units in tender points

- AbobotulinumtoxinA (Dysport®)[103]
  - Cervical dystonia: 500 Units as a divided dose among affected muscles
  - Lower limb spasticity-pediatrics: The recommended total dose per treatment session is 10 to 15 Units/kg for unilateral lower limb injections or 20 to 30 Units/kg for bilateral lower limb injections or 1000 units, whichever is lower
  - Lower limb spasticity-adults: Dose selected based on affected muscle up to 1500 units divided among selected muscles (up to 500 units per muscle)

- IncobotulinumtoxinA (Xeomin)[104]
  - Cervical dystonia: Recommended initial total dose 120 Units total dose per treatment session
  - Blepharospasm: 1.25 – 2.5 Units per injection site if previous dose of Botox unknown
  - Upper limb spasticity: The recommended total dose up to 400 units no sooner than every 12 weeks

- Dosage Conversion:
  Botulinum toxin A products are not interchangeable and require medical expertise to convert patients from one formulation to another.
• Labels for all products include language that limits the frequency to 12 week intervals or more. Coverage will not be provided when dose frequency is more frequent than every 12 weeks.

*Please refer to most recent prescribing information.

F. How Supplied
   a. Single-use, sterile 50 Units, 100 Units, 200, 300, or 500 Units vacuum-dried powder for reconstitution

Appendix 1: International Headache Society Classification of Chronic Migraine Headache [97]

A. Headache (tension-type or migraine) on 15 or more days per month for at least 3 months.*
B. Occurring in a patient who has had at least 5 attacks fulfilling criteria for a migraine without an aura
C. On 8 or more days per month for at least 3 months headache has fulfilled criteria for pain and associated symptoms of migraine without aura in either or both of criteria 1 or 2 below:
   1. At least two of the following criteria a), b), c) and d) below are met:
      a) Unilateral location
      b) Pulsating quality
      c) Moderate or severe pain intensity
      d) Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
      AND at least one of
   2. Treated and relived by triptan(s) or ergot before the expected development of the above symptoms.
D. No medication overuse and not attributed to another causative disorder

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Appendix 2: Medications for Abortive Migraine Treatment [97]

<table>
<thead>
<tr>
<th>Class</th>
<th>Common Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triptans</td>
<td>Imitrex® (sumatriptan), Maxalt® Zomig®, Amerge® (naratriptan), Axert®, Frova®, Relpax®</td>
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<tr>
<td>Analgesics</td>
<td>Aspirin, acetaminophen</td>
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<td>Non-steroidal Anti-inflammatory Drugs</td>
<td>Motrin® (ibuprofen), Naprosyn® (naproxen), Relafén® (nabumetone), Voltaren® (diclofenac), Orudis® (ketoprofen), Clinon® (sulindac), Toradol® (ketorolac)</td>
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Appendix 3: Medications for Prophylaxis of Migraines [105]

<table>
<thead>
<tr>
<th>Class</th>
<th>Accepted Examples</th>
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<tbody>
<tr>
<td>Anticonvulsants</td>
<td>Depakote® (divalproex), Depakene® (sodium valproate), Topamax® (topiramate), Tegretol® (carbamazepine)</td>
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<td>ACE inhibitor or Angiotensin Receptor Blocker</td>
<td>Zestril® (lisinopril), Atacand® (candesartan)</td>
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<td>Beta Blockers</td>
<td>Inderal® (propranolol), Lopressor® (metoprolol), Tenormin® (atenolol), Corgard® (nadolol), Blocadren® (timolol), Bystolic® (nebivolol), Visken® (pindolol)</td>
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<tr>
<td>Calcium Channel Blockers</td>
<td>Procardia® (nifedipine), Cardizem® (diltiazem), Calan® (verapamil)</td>
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Antidepressants

Elavil® (amitriptyline), Effexor® (venlafaxine)

References
2. Botulinum-A Toxin, BlueCross BlueShield Association Medical Policy #5.01.05, 10/2008.
15. USP DI® and Advice for Patient, Botulinum Toxin Type A, Revised 01/24/2001.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.
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| 1.0  | Effective 11/10/11 | New Policy or Criteria Update  
- Custom/clinical formulary: N/A  
- Part D: Specialty B vs D  
- Part D Formulary Chapter: Central Nervous System: Miscellaneous CNS |
| 1.1  | Effective 11/8/12 | Revised Policy and Updated Criteria Botulinum A and B products separated; Botulinum A products therapeutically |
| 1.2  | Effective 5/2/13  | Updated criteria, extended approval duration                                        |
| 1.3  | Effective 10/24/13 | Updated criteria, (OAB), updated abortive therapies                                 |
| 1.4  | Effective 8/14/2014 | Updated criteria, medication list for prophylactic medications                     |
| 1.5  | Effective 2/12/2015 | Added that the trial of alternatives for migraines needs to be at least 2 months. Changed initial approval for 6 months, renewal to 1 year for migraines. This is in response to a letter from Dr |
| 1.6  | Effective 5/7/2015 | Added language for chronic migraines that conditions that are contributing to chronic migraines must be treated |
| 1.7  | Effective 8/13/2015 | Added new indication of upper limb spasticity                                       |
| 1.8  | Effective 5/5/2016 | Added new indication of lower limb spasticity                                      |
| 1.9  | Effective 11/10/2016 | Annual Review                                                                      |
| 2.0  | Effective 2/9/2017 | Added new indication lower limb spasticity in pediatrics  
Modified Xeomin dosing language in cervical dystonia |
| 2.1  | Effective 2/8/2018 | Added:  
Criteria and dosing for pelvic floor spasms  
Dosing for Xeomin in upper limb spasticity  
Criteria and dosing for Dysport in lower limb spasticity |

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or [http://dailymed.nlm.nih.gov/dailymed/index.cfm](http://dailymed.nlm.nih.gov/dailymed/index.cfm)