Corporate Medical Policy: Botulinum Toxin Injection **"Notification"** **POLICY EFFECTIVE NOVEMBER 1, 2024**

Restricted Product(s):

- ***abobotulinumtoxinA (Dysport®) intramuscular injection for administration by a healthcare professional
- daxibotulinumtoxinA-lanm (Daxxify®) intramuscular injection for administration by a healthcare professional
- ***incobotulinumtoxinA (Xeomin®) intramuscular or intraglandular injection for administration by a healthcare professional
- letibotulinumtoxinA-wlbg (Letybo®) intramuscular injection for administration by a healthcare professional
- onabotulinumtoxinA (Botox®) intramuscular, intradetrusor, or intradermal injection for administration by a healthcare professional
- rimabotulinumtoxinB (Myobloc®) intramuscular or intraglandular injection for administration by a healthcare professional

***preferred agent(s)**

FDA Approved Use:

- AbobotulinumtoxinA (Dysport®)
  - For the treatment of cervical dystonia in adults
  - For the treatment of spasticity in patients 2 years or older
  - **For temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adults less than 65 years old

- DaxibotulinumtoxinA-lanm (Daxxify®)
  - For the treatment of cervical dystonia in adults
  - **For temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adults

- IncobotulinumtoxinA (Xeomin®)
  - For the treatment of cervical dystonia in adults
  - For the treatment of upper limb spasticity in adults
  - For the treatment of upper limb spasticity in patients 2 to 17 years old, excluding spasticity caused by cerebral palsy
  - For the treatment of chronic sialorrhea in patients 2 years or older
  - For the treatment of blepharospasm in adults
  - **For temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and/or corrugator muscle activity in adults

- **LetibotulinumtoxinA-wlbg (Letybo®)
  - **For temporary improvement in the appearance of moderate to severe glabellar (frown) lines associated with corrugator and/or procerus muscle activity in adult patients

- OnabotulinumtoxinA (Botox®)
  - For the treatment of cervical dystonia in adults to reduce the severity of abnormal head position and neck pain
  - For the treatment of spasticity in patients 2 years or older
    - Limitations of use: Not for improvement of upper extremity functional abilities or range of motion at a joint affected by a fixed contracture
  - For the prophylaxis of headaches in adults with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer)
    - Limitations of use: Not for prophylaxis of episodic migraine (≤14 headache days per month)
  - For the 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
  - For the treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) in adults who have an inadequate response to or are intolerant of an anticholinergic medication
  - For the treatment of neurogenic detrusor overactivity in pediatric patients 5 years or older who have an inadequate response to or are intolerant of an anticholinergic medication
  - For the treatment of blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders, in patients 12 years or older
  - For the treatment of strabismus in patients 12 years or older
  - For the treatment of severe axillary hyperhidrosis in adults that is inadequately managed by topical agents
    - Limitations of use: Not for use in body areas other than axillary
  - **For temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and/or corrugator muscle activity, moderate to severe lateral canthal lines associated with orbicularis oculi activity, and moderate to severe forehead lines associated with frontalis muscle activity in adults

- RimabotulinumtoxinB (Myobloc®)
  - For the treatment of cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia in adults
  - For the treatment of chronic sialorrhea in adults

**The restricted products within this policy may be FDA approved for temporary improvement of the appearance of glabellar (frown) lines in adults; however, use of these products for cosmetic purposes are considered a benefit exclusion and are not addressed in this medical policy. Please refer to the Member's Benefit Booklet for availability of benefits and for the definition of cosmetic and reconstructive services. Member's benefits may vary according to benefit design; therefore, member benefit language should be reviewed before applying the terms of this medical policy. NOTE: LetibotulinumtoxinA-wlbg (Letybo) is FDA approved only for temporary improvement in the appearance of moderate to severe glabellar (frown) lines associated with corrugator and/or procerus muscle activity in adult patients, which is considered use for cosmetic purposes and therefore use of this product is considered a benefit exclusion.

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

Botulinum toxin may be considered medically necessary when the following criteria are met:

1. The patient will NOT be using the requested agent for cosmetic purposes (e.g., glabellar lines, wrinkles); **AND**

2. The patient has a diagnosis of **blepharospasm**; **AND**
    a. The patient is 12 years of age or older; **AND**
    b. If the requested agent is Botox, Daxxify, or Myobloc AND the patient is 18 years of age or older, one of the following:
        i. The patient has tried and had an inadequate response with Xeomin **[medical record documentation required]**; **OR**
        ii. The patient has a clinical contraindication or intolerance to Xeomin **[medical record documentation required]**; **OR**
        iii. The patient's blepharospasm is associated with dystonia or facial nerve (VII) disorders (including benign essential blepharospasm and hemifacial spasm); **OR**

3. The patient has a diagnosis of **hemifacial spasm**; **OR**

4. The patient has a diagnosis of **cervical dystonia** (spasmodic torticollis; applicable whether congenital, due to child birth injury, or traumatic injury); **AND**
    a. The patient is 16 years of age or older; **AND**

b. The patient's cervical dystonia is associated with sustained head tilt or abnormal posturing with limited range of motion in the neck; **AND**
c. The patient has a history of recurrent involuntary contraction(s) of one or more of the muscles of the neck (e.g., sternocleidomastoid, splenius, trapezius, or posterior cervical muscles); **AND**
d. If the requested agent is Botox, Daxxify, or Myobloc, one of the following:
    i. The patient has tried and had an inadequate response with Xeomin AND Dysport **[medical record documentation required]**; **OR**
    ii. The patient has a clinical contraindication or intolerance to BOTH Xeomin AND Dysport **[medical record documentation required]**; **OR**

5. The patient has a diagnosis of **dystonia**; **AND**
    a. The patient is 18 years of age or older; **AND**
    b. The patient has at least ONE of the following focal dystonias:
        i. Focal upper-limb dystonia (e.g., organic writer's cramp);
        ii. Oromandibular dystonia (e.g., orofacial dyskinesia, Meige syndrome);
        iii. Laryngeal dystonia (e.g., adductor spasmodic dysphonia);
        iv. Idiopathic (primary or genetic) torsion dystonia;
        v. Symptomatic (acquired) torsion dystonia; **AND**
    c. The patient's dystonia results in functional impairment (interference with joint function, mobility, communication, nutritional intake) with or without pain; **AND**
    d. The requested agent will NOT be used for treatment of temporomandibular joint (TMJ) disorders; **AND**
    e. If the requested agent is Botox, Daxxify, or Myobloc, one of the following:
        i. The patient has tried and had an inadequate response with Xeomin AND Dysport **[medical record documentation required]**; **OR**
        ii. The patient has a clinical contraindication or intolerance to BOTH Xeomin AND Dysport **[medical record documentation required]**; **OR**

6. The patient has a diagnosis of **spasticity**; **AND**
    a. The patient is 2 years of age or older; **AND**
    b. The patient has at least ONE of the following spastic conditions:
        i. Upper and/or lower limb spasticity;
        ii. Cerebral palsy;
        iii. Spasticity related to stroke;

iv. Acquired spinal cord or brain injury;
v. Hereditary spastic paraparesis;
vi. Spastic hemiplegia;
vii. Neuromyelitis optica;
viii. Multiple sclerosis or Schilder's disease; **AND**

c. The patient's spasticity results in functional impairment (interference with joint function, mobility, communication, nutritional intake) with or without pain; **AND**
d. If the requested agent is Botox, Daxxify, or Myobloc, one of the following:
    i. The patient has tried and had an inadequate response with Xeomin AND Dysport **[medical record documentation required]**; **OR**
    ii. The patient has a clinical contraindication or intolerance to BOTH Xeomin AND Dysport **[medical record documentation required]**; **OR**

7. The patient has a diagnosis of **chronic anal fissure**; **AND**
    a. The patient is 18 years of age or older; **AND**
    b. The patient has a tried and had an inadequate response to ONE of the following conventional therapies: topical nitrates or topical calcium channel blockers (e.g., diltiazem, nifedipine); **OR**
    c. The patient has a clinical contraindication or intolerance to ALL topical nitrates and topical calcium channel blockers (e.g., diltiazem, nifedipine); **OR**

8. The patient has a diagnosis of **chronic migraine headache**; **AND**
    a. The patient is 18 years of age or older; **AND**
    b. The patient has ≥ 15 headache days per month for a minimum of 3 months; **AND**
    c. The patient ≥ 8 migraine headache days per month for a minimum of 3 months; **AND**
    d. The patient will be using the requested agent for chronic migraine prophylaxis; **AND**
    e. The patient has been evaluated for and does NOT have medication overuse headache; **AND**
    f. ONE of the following:
        i. The patient has tried and had an inadequate response to at least TWO agents from different migraine prophylaxis classes (anticonvulsants [i.e., divalproex, valproate, topiramate], beta blockers [i.e., atenolol, metoprolol, nadolol, propranolol, timolol], antidepressants [i.e., amitriptyline, venlafaxine], calcitonin gene-related peptide receptor antagonists [i.e., fremanezumab, galcanezumab, erenumab, eptinezumab]) after an adequate trial as defined by BOTH of the following:
            1. The trial length was at least 6 weeks for each class at generally accepted doses; **AND**
            2. The patient was ≥ 80% adherent to the prophylaxis agent during the trial; **OR**

ii. The patient has a clinical contraindication or intolerance to ALL anticonvulsants, beta blockers, antidepressants, AND prophylactic calcitonin gene-related peptide receptor antagonists listed above; **AND**

g. If the requested agent is Botox, one of the following:
   i. The patient has tried and had an inadequate response to at least one calcitonin gene-related peptide (CGRP) receptor antagonist for chronic migraine headache prophylaxis (e.g., fremanezumab, galcanezumab, erenumab, or eptinezumab) **[medical record documentation required]**; **OR**
   ii. The patient has a clinical contraindication or intolerance to ALL calcitonin gene-related peptide (CGRP) receptor antagonists (e.g., fremanezumab, galcanezumab, erenumab, or eptinezumab) **[medical record documentation required]**; **AND**

h. ONE of the following:
   i. The patient will NOT be using the requested agent in combination with a calcitonin gene-related peptide (CGRP) receptor antagonist for migraine prophylaxis (e.g., fremanezumab, galcanezumab, erenumab, or eptinezumab); **OR**
   ii. The patient will be using the requested agent in combination with a CGRP receptor antagonist for the treatment of chronic migraine; **AND**
      1. The patient is continuing to experience 4 or more migraine headache days per month after treatment with ONE of the following preventative therapies for chronic migraine **[medical record documentation required]**:
         a. At least a 6-month trial (2 injection cycles) with a botulinum toxin agent **[medical record documentation required]**; **OR**
         b. At least a 3-month trial with a calcitonin gene-related peptide (CGRP) receptor antagonist **[medical record documentation required]**; **OR**

9. The patient has a diagnosis of **esophageal achalasia**; **AND**
   a. The patient has NOT responded to dilation therapy; **OR**
   b. The patient is considered a poor surgical candidate; **OR**

10. The patient has a diagnosis of **Hirschsprung disease**; **AND**
   a. The patient has developed obstructive symptoms after a pull-through operation; **OR**

11. The patient has a diagnosis of **overactive bladder (OAB)**; **AND**
   a. The patient is 18 years of age or older; **AND**
   b. The patient has symptoms of urge urinary incontinence, urgency, and frequency; **AND**
   c. The patient has tried and had an inadequate response to ONE anticholinergic agent (e.g., oxybutynin, tolterodine, trospium, darifenacin, solifenacin or fesoterodine); **OR**
   d. The patient has tried and had an inadequate response to a beta-3 adrenergic agonist (e.g., Myrbetriq [mirabegron]); **OR**

e. The patient has a clinical contraindication or intolerance to ALL anticholinergic agents AND beta-3 adrenergic agonists; **OR**

12. The patient has a diagnosis of **urinary incontinence** with detrusor muscle overactivity associated with neurogenic causes (e.g., spinal cord injury, multiple sclerosis); **AND**
    a. The patient is 18 years of age or older; **AND**
    b. The patient has tried and had an inadequate response to ONE anticholinergic agent (e.g., oxybutynin, tolterodine, trospium, darifenacin, solifenacin or fesoterodine); **OR**
    c. The patient has tried and had an inadequate response to a beta-3 adrenergic agonist (e.g., Myrbetriq [mirabegron]); **OR**
    d. The patient has a clinical contraindication or intolerance to ALL anticholinergic agents AND beta-3 adrenergic agonists; **OR**

13. The patient has a diagnosis of **neurogenic detrusor overactivity (NDO)**; **AND**
    a. The patient is 5 years of age or older; **AND**
    b. The patient has tried and had an inadequate response to ONE anticholinergic agent (e.g., oxybutynin, solifenacin); **OR**
    c. The patient has a clinical contraindication or intolerance to ALL anticholinergic agents; **OR**

14. The patient has a diagnosis of chronic **sialorrhea** (drooling); **AND**
    a. The patient is 18 years of age or older; **OR**
    b. If the requested agent is Xeomin, the patient is 2 years of age or older; **AND**
    c. The patient's diagnosis is associated with a neurological disorder (e.g., amyotrophic lateral sclerosis, atypical parkinsonian disorders, cerebral palsy, Parkinson disease, stroke, traumatic brain injury); **AND**
    d. The patient has experienced excessive salivation for ≥ 3 months; **AND**
    e. The patient has tried and had an inadequate response to at least 2 months continuous treatment with at least one conventional agent (e.g., anticholinergics, benztropine, oral hyoscyamine, glycopyrrolate); **OR**
    f. The patient has a clinical contraindication or intolerance to ALL conventional agents above; **AND**
    g. If the requested agent is Botox, Daxxify, or Myobloc, one of the following:
        i. The patient has tried and had an inadequate response with Xeomin **[medical record documentation required]**; **OR**
        ii. The patient has a clinical contraindication or intolerance to Xeomin **[medical record documentation required]**; **OR**

15. The patient has a diagnosis of **strabismus**; **AND**
    a. The patient is 12 years of age or older; **OR**

16. The patient has a diagnosis of **severe primary axillary or palmar hyperhidrosis**; **AND**
    a. The patient is 18 years of age or older; **AND**

b. The patient has focal, visible, excessive sweating of at least 6 months duration without apparent cause with at least TWO of the following characteristics:
    i. Bilateral and relatively symmetric;
    ii. Impairs daily activities;
    iii. Frequency of at least one episode per week;
    iv. Age of onset is less than 25 years;
    v. Positive family history;
    vi. Cessation of focal sweating during sleep; **AND**
c. The patient has one of the following associated medical conditions:
    i. Acrocyanosis of the hands;
    ii. History of recurrent skin maceration with bacterial or fungal infections;
    iii. History of recurrent secondary infections;
    iv. History of persistent eczematous dermatitis despite medical treatments with topical dermatologic or systemic anticholinergic agents; **OR**
d. The patient's hyperhidrosis causes functional impairment (e.g., inability to perform activities of daily living and/or manual tasks in a professional setting); **AND**
e. Potential causes of secondary hyperhidrosis have been ruled out (e.g., hyperthyroidism); **AND**
f. The patient has tried and had an inadequate response with topical agents (e.g., aluminum chloride 20% solution); **OR**
g. The patient has a clinical contraindication or intolerance to ALL topical agents; **OR**

17. The patient has another diagnosis that is an FDA approved indication for botulinum toxins; **AND**
18. The patient will NOT be receiving botulinum toxin more frequently than every 12 weeks, regardless of diagnosis; **AND**
19. The requested quantity does NOT exceed the maximum units/visits allowed for the duration of approval (see table below).

Duration of Approval:

Migraine: 168 days (24 weeks)
All other indications: 336 days (48 weeks)

Continuation Criteria for Approval:

Botulinum toxin may be considered medically necessary when the following criteria are met:

1. The patient will NOT be using the requested agent for cosmetic purposes (e.g., glabellar lines, wrinkles); **AND**
2. The patient was approved through Blue Cross NC initial criteria for approval (above) or would have met initial criteria for approval upon the start of therapy; **AND**
3. The patient has a diagnosis of **chronic migraine headache**; **AND**
    a. ONE of the following:
        i. The patient's migraine headache frequency has been reduced by at least 7 days per month compared to pre-treatment frequency; **OR**
        ii. The patient's migraine headache duration has been reduced by at least 100 hours per month compared to pre-treatment duration; **AND**
    b. ONE of the following:
        i. The patient will NOT be using the requested agent in combination with a calcitonin gene-related peptide (CGRP) receptor antagonist for migraine prophylaxis (e.g., fremanezumab, galcanezumab, erenumab, or eptinezumab); **OR**
        ii. The patient will be using the requested agent in combination with a CGRP receptor antagonist for the treatment of chronic migraine; **AND**
            1. The patient is continuing to experience 4 or more migraine headache days per month after treatment with ONE of the following preventative therapies for chronic migraine **[medical record documentation required]**:
                a. At least a 6-month trial (2 injection cycles) with a botulinum toxin agent **[medical record documentation required]**; **OR**
                b. At least a 3-month trial with a calcitonin gene-related peptide (CGRP) receptor antagonist **[medical record documentation required]**; **OR**
4. The patient is continuing botulinum toxin therapy for one of the indications listed in the initial coverage criteria; **AND**
    a. The patient has had a positive clinical response to botulinum toxin therapy; **AND**
5. The patient will NOT be receiving botulinum toxin more frequently than every 12 weeks, regardless of diagnosis; **AND**
6. The requested quantity does NOT exceed the maximum units/visits allowed for the duration of approval (see table below).

Duration of Approval: 336 days (48 weeks)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
abobotulinumtoxinA (Dysport®) intramuscular (IM) injection	Cervical dystonia in adults Spasticity in patients ≥ 2 years old	<u>Cervical dystonia in adults</u>: Initially 500 units IM divided among affected muscles, titrate by 250 units (up to 1000 units) according to patient response Retreatment no sooner than every 12 weeks <u>Spasticity in patients ≥ 2 years old</u> Adults: • Upper limb: 500 to 1000 units divided among affected muscles • Lower limb: Up to 1500 units divided among affected muscles Max dose upper/lower combined: 1500 units Retreatment no sooner than every 12 weeks 2-17 years old: • Upper limb: 8-16 units/kg per limb; not to exceed 16 units/kg or 640 units, whichever is lower • Lower limb: 10-15 units/kg per limb; not to exceed 15 units/kg (unilateral), 30 units/kg	J0586	4 visits (2 visits for migraine initial)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		(bilateral), or 1000 units, whichever is lower Max total dose in one treatment session is 30 units/kg or 1000 units (whichever is lower) in a 3-month interval Retreatment no sooner than every 12 weeks		
daxibotulinumtoxinA-lanm (Daxxify®) intramuscular injection	Cervical dystonia in adults	Cervical dystonia in adults: 125 to 250 units divided among affected muscles Retreatment no sooner than every 12 weeks	J0589	4 visits (2 visits for migraine initial)
incobotulinumtoxinA (Xeomin®) intramuscular or intraglandular injection	Cervical dystonia in adults Upper limb spasticity in adults Upper limb spasticity in patients 2-17 years old Chronic sialorrhea in patients ≥ 2 years old	Cervical dystonia in adults: Initially 120 units per treatment session; retreatment no sooner than every 12 weeks Max cumulative dose for any indication not to exceed 400 units per treatment session Upper limb spasticity in adults: Total dose is up to 400 units divided among	J0588	4 visits (2 visits for migraine initial)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
	Blepharospasm in adults	affected muscles; retreatment no sooner than every 12 weeks Max cumulative dose for any indication not to exceed 400 units per treatment session <u>Upper limb spasticity in patients 2-17 years old</u>: Total dose is 8 units/kg (max 200 units) per single upper limb or 16 units/kg (max 400 units) in both upper limbs, divided among affected muscles Max cumulative dose for any indication not to exceed 400 units per treatment session <u>Chronic sialorrhea in patients ≥ 2 years old</u> Adults: • 100 units per treatment session; retreatment no sooner than every 16 weeks 2-17 years old: • Weight-based dosing in 3:2 dose ratio parotid:submandibular glands		

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		for patients ≥ 12 kg; retreatment no sooner than every 16 weeks Max cumulative dose for any indication not to exceed 400 units per treatment session <u>Blepharospasm in adults</u>: Previously treated with botulinum toxin: past dose, response, duration of effect, and adverse event history should be considered in dose determination Botulinum toxin naïve: 50 units (25 units per eye) Dose per session not to exceed 100 units (50 units per eye) and retreatment no sooner than every 12 weeks Max cumulative dose for any indication not to exceed 400 units per treatment session		

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
onabotulinumtoxinA (Botox®) intramuscular, intradetrusor, or intradermal injection	Cervical dystonia in adults Spasticity in patients ≥ 2 years Chronic migraine prophylaxis in adults OAB in adults Urinary incontinence due to detrusor overactivity in adults Blepharospasm in patients ≥ 12 years old Strabismus in patients ≥ 12 years old Severe axillary hyperhidrosis in adults	Cervical dystonia in adults: Dosing based on head and neck position, localization of pain, muscle hypertrophy, response, and adverse event history; use lower initial dose in botulinum toxin naïve patients No more than 50 units per site up to a total dose of 400 units divided among affected muscles Maximum cumulative dose not to exceed 400 units in a 3-month interval in patients treated for one or more indication Spasticity in patients ≥ 2 years: Dosing based on affected muscles, severity of muscle activity, prior treatment response, and adverse event history Adults: • Upper limb: Doses ranging from 75 to 400 units, divided among selected muscles • Lower limb: Total dose of 300 to 400 units, divided across ankle and toe muscles	J0585	4 visits (2 visits for migraine initial)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		Maximum cumulative dose not to exceed 400 units in a 3-month interval in patients treated for one or more indication Retreatment no sooner than every 12 weeks 2-17 years old: • Upper limb: Total dose of 3-6 units/kg (max 200 units), divided among affected muscles • Lower limb: Total dose of 4-8 units/kg (max 300 units), divided among affected muscles Maximum cumulative dose not to exceed the lower of 10 units/kg or 340 units in a 3-month interval in patients treated for one or more indication <u>Chronic migraine prophylaxis in adults</u>: Total dose 155 units, as 5-unit (0.1 mL) injections per each site, divided across 7 head/neck muscles Maximum cumulative dose not to exceed 400 units in a 3-month interval		

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		in patients treated for one or more indication Retreatment no sooner than every 12 weeks <u>OAB in adults</u>: Total dose 100 units, as 5-unit (0.5 mL) injections across 20 sites into the detrusor Dose per session not to exceed 100 units Maximum cumulative dose not to exceed 400 units in a 3-month interval in patients treated for one or more indication Retreatment no sooner than every 12 weeks <u>Urinary incontinence due to detrusor overactivity in adults</u>: Total dose 200 units, as ~6.7-unit (1 mL) injections across 30 sites into the detrusor Dose per session not to exceed 200 units		

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		Maximum cumulative dose not to exceed 400 units in a 3-month interval in patients treated for one or more indication Retreatment no sooner than every 12 weeks Blepharospasm in patients ≥ 12 years old: 1.25 to 2.5 units into each of 3 sites per affected eye Maximum cumulative dose in a 30-day period not to exceed 200 units Maximum cumulative dose not to exceed 400 units in a 3-month interval in patients treated for one or more indication Strabismus in patients ≥ 12 years old: Dose based on prism diopter correction or previous response to Botox treatment Initial doses range from 1.25 to 5 units per muscle, subsequent doses at a max dose of 25 units per muscle		

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		Adults: Maximum cumulative dose not to exceed 400 units in a 3-month interval in patients treated for one or more indication Pediatrics: Maximum cumulative dose not to exceed the lower of 10 units/kg or 340 units in a 3-month interval in patients treated for one or more indication <u>Severe axillary hyperhidrosis in adults</u>: 50 units per axilla Maximum cumulative dose not to exceed 400 units in a 3-month interval in patients treated for one or more indication		
rimabotulinumtoxinB (Myobloc®) intramuscular or intraglandular injection	Cervical dystonia in adults Chronic sialorrhea in adults	<u>Cervical dystonia in adults</u>: Previously tolerating botulinum toxin: 2500 to 5000 units divided among affected muscles Botulinum toxin naïve: lower initial dosage	J0587	4 visits (2 visits for migraine initial)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		Retreatment no sooner than every 12 weeks Chronic sialorrhea in adults: 1500 to 3500 units divided among parotid and submandibular glands Retreatment no sooner than every 12 weeks		
***letibotulinumtoxinA-wlbg (Letybo®) intramuscular injection	Temporary improvement in the appearance of moderate to severe glabellar (frown) lines in adults	Temporary improvement in the appearance of moderate to severe glabellar (frown) lines in adults: 4 units into each of 5 sites for a total dose of 20 units	C9399** J3490** J3590**	**N/A**

***Maximum units/visits allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**
*****FDA approved only for temporary improvement in the appearance of glabellar (frown) lines in adults, which is considered use for cosmetic purposes and therefore use of this product is considered a benefit exclusion**

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Ailani J, Burch RC, Robbins MS, Board of Directors of the American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache*. 2021;61:1021-39.
2. Armanious M, Khalil N, Lu Y, et al. Erenumab and onabotulinumtoxinA combination therapy for the prevention of intractable chronic migraine without aura: a retrospective analysis. *J Pain Palliat Care Pharmacother*. 2021;35(1):1-6.
3. Cohen F, Armand C, Lipton RB, et al. Efficacy and tolerability of calcitonin gene-related peptide-targeted monoclonal antibody medications as add-on therapy to onabotulinumtoxinA in patients with chronic migraine. *Pain Med*. 2021;22(8):1857-63.
4. Scuteri D, Tonin P, Nicotera P, et al. Pooled analysis of real-world evidence supports anti-CGRP mAbs and onabotulinumtoxinA combined trial in chronic migraine. *Toxins*. 2022 Aug;14(8):529.
5. Toni T, Tamanaha R, Newman B, et al. Effectiveness of dual migraine therapy with CGRP inhibitors and onabotulinumtoxinA injections: case series. *Neurol Sci*. 2021;42(12):5373-76.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q4 annually.

November 2024: Criteria change: Added criteria under dystonia indication that the requested agent will not be used for treatment of temporomandibular joint (TMJ) disorders. **Policy notification given 9/2/2024 for effective date 11/1/2024**.
June 2024: Criteria update: Added new to market product Letybo (letibotulinumtoxinA-wlbg) FDA approved for temporary improvement in the appearance of moderate to severe glabellar (frown) lines associated with corrugator and/or procerus muscle activity in adult patients, which is considered use for cosmetic purposes and therefore a benefit exclusion.
April 2024: Coding change: Added HCPCS code J0589 for Daxxify to dosing reference table effective 4/1/2024; deleted C9160, J3490, J3590 termed 3/31/2024.
January 2024: Coding change: Added HCPCS code C9160 for Daxxify to dosing reference table effective 1/1/2024; deleted C9399 termed 12/31/2023.
January 2024: Criteria change: For chronic migraine indication: Added the option for use of a botulinum toxin agent in combination with a CGRP receptor antagonist for patients continuing to experience 4 or more migraine headache days per month after treatment with either a 3-month trial of a CGRP receptor antagonist or a 6-month trial (2 injection cycles) of a botulinum toxin agent. References added.
September 2023: Criteria change (Daxxify): Added newly approved covered indication for Daxxify for cervical dystonia in adults, added Daxxify as non-preferred agent, and added associated dosing to FDA label reference table.
November 2022: Criteria update: For chronic migraine prophylaxis indication, changed “chronic migraine headache prophylaxis” to “migraine prophylaxis” within authorization termination language for clarity.

October 2022: Criteria change: Added new to market product Daxxify (daxibotulinumtoxinA-lanm) FDA approved for temporary improvement of the appearance of glabellar (frown) lines in adults, which is considered use for cosmetic purposes and therefore a benefit exclusion.
October 2022: Criteria update: Adjusted duration of approval in initial and continuation sections to 48 weeks, and initial duration of approval for migraine to 24 weeks. **Policy notification given 8/4/2022 for effective date 10/1/2022**.
July 2022: Criteria update: For chronic migraine prophylaxis indication, added authorization termination language to clarify intent of criteria indicating no concurrent use of CGRP receptor antagonists with botulinum toxin agents.
November 2021: Criteria change: Added hemifacial spasm as a covered indication; updated criteria for blepharospasm to include blepharospasm associated with dystonia or facial nerve (VII) disorders (including benign essential blepharospasm and hemifacial spasm) separately without step therapy requirement.
April 2021: Criteria change: Added specific age requirements according to indication where appropriate; Chronic anal fissure: added requirement of trial and failure of one conventional therapy; Chronic migraine: added criteria that patient has been evaluated for and does not have medication overuse headache; Sialorrhea: added requirement that patient has experienced excessive salivation for ≥3 months, and added trial and failure of at least one convention agent, added requirement of trial and failure of preferred Xeomin for Botox/Myobloc requests; OAB/urinary incontinence: added option of trial and failure of a beta-3 adrenergic agonist (Myrbetriq); combined coverage criteria for severe axillary or palmar hyperhidrosis into this policy; added maximum units/visits; medical policy formatting change. **Policy notification given 2/26/2021 for effective date 4/28/2021**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.