Original Effective Date: 03/2016
Current Effective Date: 12/08/2022
Last P&T Approval/Version: 10/26/2022
Next Review Due By: 10/2023
Policy Number: C8755-A

Botulinum Toxin

PRODUCTS AFFECTED

Botox/Botox Cosmetic (onabotulinumtoxinA), Dysport (abobotulinumtoxinA), Myobloc (rimabotulinumtoxinB) and Xeomin (incobotulinumtoxinA)

Requests for Jeuveau™ (prabotulinumtoxinA-xvfs)
Jeuveau™ (prabotulinumtoxinA-xvfs) is indicated for the temporary improvement in the appearance of moderate to severe glabellar (frown) lines between the eyebrows in adults. Currently, Jeaveau is FDA approved only for cosmetic use; it has no other indications.
Cosmetic use is excluded from coverage and therefore Jeuveau™ (prabotulinumtoxinA- xvfs) is excluded from coverage

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Chronic migraine, Esophageal achalasia, Anal fissure, Axillary hyperhidrosis, Upper and lower limb spasticity, strabismus, Blepharospasm, Facial palsies, Sialorrhea, Overactive bladder and urinary incontinence, Cervical dystonia, Larynx closure adjunct to surgical procedure, Organic voice tremor, Spasm of pharyngoesophageal segment following total laryngectomy, Spastic dysphonia

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical

governance. Additional information may be required on a case-by-case basis to allow for adequate review

FOR ALL INDICATIONS:

1. Prescriber attests to both of the following: (a) the medication is not prescribed concurrently with other botulinum toxin products; AND (b) Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks.
   AND
2. Prescriber provides documentation of total requested units required for therapy duration. [REVIEWER NOTE: if not supplied- FDA limit per indication will be approved]
   AND
3. Prescribed product has an FDA labeled or compendia supported indication for age (see Appendix for guidance on FDA label/compendia and quantity limits)

A. CHRONIC MIGRAINE HEADACHE

1. Documented diagnosis of chronic migraines (i.e., ≥ 15 headache days per month for at least 3 months with headache lasting 4 hours a day or longer)
   AND
2. Documentation of trial (2 months per agent) and ineffectiveness/failure or clinical intolerance or contraindication to THREE of the following therapeutic classes: beta blockers (propranolol, timolol, atenolol, metoprolol, nadolol), antiepileptics (divalproex sodium, topiramate), antidepressants (amitriptyline, nortriptyline, venlafaxine, duloxetine), antihypertensive (verapamil, lisinopril, candesartan)
   AND
3. Prescriber attests that botulinum toxin will not be used in combination with prophylaxis CGRP agents (e.g., Aimovig, Ajovy, Emgality, Vyepti)
   NOTE TO REVIEWER: Please review evidence in BACKGROUND *for where appropriate combination use has supportive evidence*
   AND
4. Documentation of baseline (prior to start of requested therapy) migraine/headache days per month. [DOCUMENTATION REQUIRED]

B. ESOPHAGEAL ACHALASIA

1. Documented diagnosis of esophageal achalasia
   AND
2. Documentation of ONE of the following:
   a) Member is not a candidate for pneumatic dilation or laparoscopic surgical myotomy (e.g., due to age, comorbidity, member has epiphrenic diverticulum or hiatal hernia, member has esophageal varices)
   b) Member is at high risk for complications (e.g., perforation, recurrent dysphagia, GERD, pneumothorax, bleeding, infection) associated with pneumatic dilation or surgical myotomy
   c) Member has failure of a prior dilation or myotomy;
   d) Member experienced previous perforation due to pneumatic dilation

C. CHRONIC ANAL FISSURE:

1. Member has documentation of chronic anal fissure refractory to conventional nonsurgical medical therapy (e.g., sitz baths, stool softeners, bulk agents, diet modifications)
   AND
2. Documentation of a trial (2 weeks) and failure or absolute contraindication to topical calcium channel blocker (nifedipine or diltiazem) or topical nitroglycerin

D. AXILLARY HYPERHIDROSIS (excessive underarm sweating):

1. Documented diagnosis of primary axillary hyperhidrosis
   AND
2. Documentation of a trial (6 months) and failure of a topical 20% aluminum chloride agent OR oral glycopyrrolate, unless contraindicated or clinically significant adverse reactions were experienced
   AND
3. Presence of medical complications of hyperhidrosis, including skin maceration with secondary infection or significant functional impairment

E. UPPER AND LOWER LIMB SPASTICITY (INCLUDES SPASMS):
1. Diagnosis of ANY of the following upper or lower limb spasticities: Cerebral palsy (including spastic equinus foot deformities, Localized adductor muscle spasticity in multiple sclerosis, Spinal cord injury, Traumatic brain injury, Hereditary spastic paraplegia, Hemifacial spasms
   AND
2. Member has documented failure, serious side effects, or labeled contraindication or unable to receive BOTH preferred first line treatment options: baclofen and ONE formulary benzodiazepine
   AND
3. Prescriber attests that the spasticity causes significant decrease of function or Activities of Daily Living (for example, washing, eating) in pediatric or adult individuals

F. STRABISMUS:
1. Diagnosis of ONE of the following:
   a) Vertical strabismus (superior and inferior rectus muscles, superior and inferior oblique muscles)
      OR
   b) Horizontal strabismus (medical and lateral rectus muscles) (i or ii): i. Horizontal strabismus < 20 prism diopters; OR ii. Horizontal strabismus 20 to 50 prism diopters
      OR
   c) Persistent sixth cranial nerve (VI; abducens nerve) palsy of ≧ at least one month involving the lateral rectus muscle

G. BLEPHAROSPASM OR PALSIES:
1. Diagnosis of blepharospasm OR Seventh cranial nerve palsy (Bell's Palsy) OR Gaze palsies causing persistent pain or vision impairment
   AND
2. Member is experiencing significant disability in daily functional activities due to interference with vision, hyperlacrimation, synkinesis

H. SIALORRHEA:
1. Member has a documented disability due to conditions such as Parkinson's disease or motor neuron disease (cerebral palsy)
   AND
2. Failure of, intolerance to or unable to receive a trial of glycopyrrolate.

I. OVERACTIVE BLADDER AND URINARY INCONTINENCE:
1. Documented diagnosis of urinary incontinence due to EITHER of the following:
   (a) Overactive bladder and member's history is positive for urinary urgency, frequency, and nocturia with or without incontinence
   OR
   (b) Urinary incontinence and member's history is positive for an associated

neurologic condition (e.g., spinal cord injury, spinal dysraphsim, multiple sclerosis neurogenic detrusor over activity or overactive bladder
AND

2. Documented inadequate response to or clinically significant adverse reaction to at least two anticholinergic agents (oxybutynin immediate and extended-release tabs, Oxytrol patch, Gelnique gel, tolterodine immediate and extended release Toviaz, Enablex, Vesicare, trospium immediate and extended release)
AND
3. Prescriber attests to no evidence of current urinary tract infection

J. CERVICAL DYSTONIA:
1. Documented diagnosis of cervical dystonia
AND
2. Prescriber attests: (a) that member is experiencing involuntary contractions of the neck and shoulder muscles (e.g., splenius capitis, sternocleidomastoid, levator scapulae, scalene, trapezius, semispinalis capitis) resulting in abnormal postures or movements of the neck, shoulders, or head AND (b) Contractions are causing pain and functional impairment

K. ALL REMAINING INDICATIONS (Larynx closure, Adjunct to surgical procedure, Organic voice tremor, Spasm of pharyngoesophageal segment -Total laryngectomy, Spastic dysphonia)
1. Documentation of member diagnosis requiring treatment

CONTINUATION OF THERAPY:

A. CHRONIC MIGRAINE:
1. If member has received >2 botulinum toxin treatment sessions, member has experienced and maintained a 30% reduction in monthly migraine frequency (monthly migraine days) from baseline OR stabilization of migraine headaches from baseline with quality-of-life improvement [DOCUMENTATION REQUIRED]
AND
2. Prescriber provides documentation of previous injections as well as the future treatment plan details to include documentation of total units administered and discarded units. [DOCUMENTATION REQUIRED]
AND
3. Prescriber attests to or clinical reviewer has found absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: symptoms of a toxin spread effect (e.g., asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, swallowing/breathing difficulties, etc.), severe hypersensitivity reactions, severe pulmonary effects (e.g., reduced pulmonary function), corneal exposure/ulceration, retrobulbar hemorrhage, bronchitis/upper-respiratory tract infections, autonomic dysreflexia, urinary tract infection, and urinary retention, etc.
AND
4. Prescriber attests that botulinum toxin will not be used in combination with prophylaxis CGRP agents (e.g., Aimovig, Ajovy, Emgality, Vyepti). Reviewer Note: Dual therapy may be considered if the member is refractory to at least two preventative treatments and has experienced a partial response to Botox.

B. ALL OTHER INDICATIONS:
1. Documentation that member is responding positively to therapy
AND
2. Prescriber provides documentation of previous injections as well as the future treatment plan details to include documentation of total units administered and discarded units. [DOCUMENTATION REQUIRED]
AND
3. Prescriber attests to or clinical reviewer has found absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: symptoms of a toxin spread effect (e.g.,

asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, swallowing/breathing difficulties, etc.), severe hypersensitivity reactions, severe pulmonary effects (e.g., reduced pulmonary function), corneal exposure/ulceration, retrobulbar hemorrhage, bronchitis/upper- respiratory tract infections, autonomic dysreflexia, urinary tract infection, and urinary retention, etc.

DURATION OF APPROVAL:
Initial authorization: 24 weeks, Continuation of Therapy: 24 weeks.

PRESCRIBER REQUIREMENTS:
Prescribed by a board eligible or board-certified neurologist, ophthalmologist, pain management specialist, physician certified in headache medicine or specialist in the field that is being treated.

AGE RESTRICTIONS:
BOTOX: Treatment of:
Upper limb spasticity, Lower limb spasticity, Hirschsprung Disease, Internal Anal Sphincter Achalasia, Chronic Anal Fissure: ≥2 years of age
Severe axillary hyperhidrosis, Cervical dystonia, overactive bladder, chronic migraine, esophageal achalasia: ≥18 years of age
Neurogenic detrusor overactivity (NDO): ≥ 5 years of age
Blepharospasm associated with dystonia: ≥ 12 years of age Strabismus : ≥ 12 years of age

Xeomin: Treatment of:
Cervical Dystonia, Blepharospasm: ≥18 years Chronic Sialorrhea, Upper Limb Spasticity: ≥2 years

Dysport: Treatment of:
Cervical Dystonia, Blepharospasm, Hemifacial spasm: ≥18 years Spasticity: ≥2 years

Myobloc: Treatment of:
Cervical Dystonia, Chronic Sialorrhea: ≥18 years

QUANTITY:
Quantity limit approvals are subject to dosing limits in accordance with FDA-approved labeling, accepted compendia and/or evidence-based practice guidelines. (see Appendix for dosage labeled limits)

Botox – up to 400 units every 3 months (max); in 100 or 200-unit increments, units up to the vial size(s)medically necessary for the use
J0585- Injection, onabotulinumtoxinA, 1 unit

Dysport – up to 1500 units every 3 months for adults, 1000 units every 3 months for peds (max); in 300- or 500-unit increments, units up to the vial size(s) medically necessary for the use
J0586 Injection, abobotulinumtoxinA, 5 units

Myobloc – up to 10,000 units every 3 months (max); in 2500, 5000, or 10000 unit increments, units up to the vial size(s) medically necessary for the use
J0587 Injection, rimabotulinumtoxinB, 100 units

Xeomin – up to 400 units every 3 months (max); in 50 or 100 unit increments, units up to the vial size(s)medically necessary for the use
J0588 Injection, incobotulinumtoxinA, 1 unit

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the intramuscular injectable products be administered in a place of service that is a non-hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intramuscular

DRUG CLASS:
Neuromuscular Blocking Agent

FDA-APPROVED USES:
Botox (onabotulinumtoxinA):
- Treatment of 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
- Treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition [e.g., spinal cord injury (SCI), multiple sclerosis (MS)] in adults who have an inadequate response to or are intolerant of an anticholinergic medication
- Prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer)
- Treatment of spasticity in patients 2 years of age and older
- Treatment of cervical dystonia in adult patients, to reduce the severity of abnormal head position and neck pain
- Treatment of severe axillary hyperhidrosis that is inadequately managed by topical agents in adult patients
- Treatment of blepharospasm associated with dystonia in patients 12 years of age and older
- Treatment of strabismus in patients 12 years of age and older
- 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

Important Limitations: Safety and effectiveness of BOTOX 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

Dysport (abobotulinumtoxinA):
Indicated for:
- treatment of cervical dystonia in adults
- treatment of spasticity in patients 2 years of age and older

Xeomin (incobotulinumtoxinA):
indicated for the treatment or improvement of patients with:
- chronic sialorrhea in patients 2 years of age and older
- upper limb spasticity in adults
- upper limb spasticity in pediatric patients 2 to 17 years of age, excluding spasticity caused by cerebral palsy
- cervical dystonia in adults
- blepharospasm in adults

Myobloc (rimabotulinumtoxinB):
indicated for:
- Treatment of cervical dystonia to reduce the severity of abnormal head

position and neck pain associated with cervical dystonia in adults
- Treatment of chronic sialorrhea in adults

COMPENDIAL APPROVED OFF-LABELED USES:
Dysport (abobotulinumtoxinA):
Blepharospasm, Hemifacial spasm

Xeomin (incobotulinumtoxinA):
None

Botox (onabotulinumtoxinA):
Esophageal Achalasia, Spasmodic torticollis, Larynx closure, Adjunct to surgical procedure, Organic voice tremor, Spasm of pharyngoesophageal segment - Total laryngectomy, Spastic dysphonia

Myobloc (rimabotulinumtoxinB):
None

APPENDIX

APPENDIX:
*International Headache Society Criteria for Migraine Diagnosis (ICHD-3) for **Chronic Migraine***
A. Headache (tension-type-like and/or migraine-like) on ≥ 15 days per month for > 3 months and fulfilling criteria B and C;
B. Occurring in a patient who has had at least five attacks fulfilling criteria B-D for 1.1 Migraine without aura and/or criteria B and C for 1.2 migraine with aura;
C. On ≥ 8 days per month for > 3 months, fulfilling any of the following:
1. *Criteria C and D for 1.1 Migraine without aura; or*
2. *Criteria B and C for 1.2 Migraine with aura; or*
3. *Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative; Not better accounted for by another ICHD-3 diagnosis*

Migraine without aura Migraine with aura	Migraine without aura Migraine with aura
A. At least five attacks fulfilling criteria B–D B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) C. Headache has at least two of the following four characteristics: 1. unilateral location 2. pulsating quality 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs) D. During headache at least one of the following: 1. nausea and/or vomiting 2. photophobia and phonophobia E. Not better accounted for by another ICHD-3 diagnosis.	A. At least two attacks fulfilling criteria B and C B. One or more of the following fully reversible aura symptoms: 1. visual 2. sensory 3. speech and/or language 4. motor 5. brainstem 6. retinal C. At least three of the following six characteristics: 1. at least one aura symptom spreads gradually over ≥5 minutes 2. two or more aura symptoms occur in succession 3. each individual aura symptom lasts 5- 60 minutes 4. at least one aura symptom is unilateral 5. at least one aura symptom is positive 6. the aura is accompanied, or followed within 60 minutes, by headache

Migraine without aura Migraine with aura	Migraine without aura Migraine with aura
A. At least five attacks fulfilling criteria B–D B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) C. Headache has at least two of the following four characteristics: 1. unilateral location 2. pulsating quality 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity(e.g., walking or climbing stairs) D. During headache at least one of the following: 1. nausea and/or vomiting 2. photophobia and phonophobia E. Not better accounted for by another ICHD-3 diagnosis	A. At least two attacks fulfilling criteria B and C B. One or more of the following fully reversible aura symptoms: 1. visual 2. sensory 3. speech and/or language 4. motor 5. brainstem 6. retinal C. At least three of the following six characteristics: 1. at least one aura symptom spreads gradually over ≥5 minutes 2. two or more aura symptoms occur in succession 3. each individual aura symptom lasts 5-60 minutes 4. at least one aura symptom is unilateral 5. at least one aura symptom is positive 6. the aura is accompanied, or followed within60 minutes, by headache D. Not better accounted for by another ICHD-3 diagnosis

QUANTITY LIMITS BY INDICATION:

Botox – up to 400 units every 3 months(max); [J0585- Injection, onabotulinumtoxinA, 1unit]

FDA Indication and Dose- labeled-

Axillary hyperhidrosis:
50 units (2 mL of a 2.5 units/0.1 mL reconstituted solution) per axilla injected intradermally divided into 0.1 to 0.2mL aliquots evenly distributed into 10 to 15 sites approximately 1 to 2 cm apart; reinjection may be performed when the benefit of the previous injection lessens

Bladder muscle dysfunction - Overactive, refractory to or intolerant of anticholinergic medication100 units administered as twenty 0.5-mL injections (10 mL of a 10 units/1 mL reconstituted solution) into the detrusor muscle via flexible or rigid cystoscope; i MAX 100 units per treatment (FDA dosage)

Blepharospasm, Associated with dystonia
Initial, 1.25 to 2.5 units (0.05 to 0.1 mL) injected into medial and lateral pretarsal orbicularis oculi muscle of upper lid and into lateral pretarsal orbicularis oculi muscle of lower lid; dose may be increased up to two- fold if the response from the initial treatment is considered insufficient to a max of 5 units per site. treatment may be repeated every 3 months; cumulative MAX, 200 units/30days
may be performed when the benefit of the previous injection lessens

Cervical dystonia (Spasmodic Torticollis):
Treatment naive: Use lower initial dose. Limit total dose administered into sternocleidomastoid muscles to 100units or less to decrease dysphagia occurrence, Patients with history of Botox tolerance: 198 to 300 units (mean, 236 units) divided among affected muscles. Limit total dose administered into sternocleidomastoid muscles to 100 units or less to decrease dysphagia occurrence

Chronic migraine:
155 units (3.1 mL of a 50 unit/mL reconstituted solution) as 5 units (0.1 mL) IM into each of 31 sites divided across 7 specific head/neck muscle areas (20 units divided in 4 sites in frontalis muscle,

10units divided in 2 sites in corrugator muscle, 5 units in 1 site in procerus muscle, 30 units divided in6 sites in occipitalis muscle,40 units divided in 8 sites in temporalis muscle, 30 units divided in 6 sites in trapezius muscle, and 20 units divided in 4 sites in cervical paraspinal muscle group); doses should be evenly distributed bilaterally in all muscles (except for procerus muscle); usual retreatment every 12 weeks

Incontinence due to detrusor instability, Associated with a neurologic condition
Adults and Pediatric Members weighing ≥ 34 kg: 200 units administered as thirty 1-mL (30 mL of a 6.7 units/1 mL reconstituted solution) injections; Median time to retreatment is 42 to 48 weeks, but no sooner than 12 weeks; MAX 200 units per treatment [3].
Pediatric members weighing <34 kg: 6 units/kg administered as twenty 1-mL injections; Median time to retreatment is 30 weeks, but no sooner than 12 weeks

Lower limb spasticity
Start with lowest dose. Total dose of 300 to 400 units. May be repeated when the effects have lessened, but generally no sooner than 12 weeks after the previous injection.

Strabismus
Vertical muscles and horizontal strabismus less than 20 diopters: Initial, 1.25 to 2.5 units injected into any 1 muscle; assess efficacy 7 to 14 days after injection and subsequent doses may be increased up to 2-fold to MAX, 25 units/any muscle as a single injection and
0.15 mL volume per muscle

Horizontal strabismus between 20 to 50 diopters:
Initial, 2.5 to 5 units injected into any 1 muscle; assess efficacy 7 to 14 days after injection and subsequent doses may be increased up to 2-fold to MAX, 25 units/any muscle as a single injection and 0.15 mL volume per muscle
Persistent sixth nerve palsy for at least 1 month: Initial, 1.25 to 2.5 units injected in the medial rectus muscle; assess efficacy 7 to 14 days after injection and subsequent doses may be increased up to 2-fold to MAX, 25units/any muscle as a single injection and0.15 mL volume per muscle

Upper limb spasticity:
Start with lowest dose; usual dosage ranged from 75 to 400 units; MAX 50 units/site; may be repeated when the effects have lessened, but generally no sooner than 12 weeks after the previous injection;

Accepted off-labeled indication
Achalasia
80 to 100 units IM in lower esophageal sphincter (20 to 25 units to each of 4 quadrants in the lower esophageal sphincter) **(off-label dosage)**

Bladder muscle dysfunction: overactive, Refractory to or intolerant of anticholinergic medication[46] Men with no prior prostate surgery: 100 to 300 units intra- detrusor injection (off- label dosage), Men with previous prostate surgery: 100 to 200 units intra- detrusor injection **(off-label dosage)**

Chronic anal fissure: 25 Units per treatment session **(off-label dosage)**

Larynx closure, Adjunct to surgical procedure
200 to 280 units IM into the laryngeal musculature prior to surgery for larynx closure was used in a clinical trial (n=6) (Pototshnig et al, 1996)

Organic voice tremor
0.6 to 5 units IM bilaterally OR 15 units IM unilaterally into affected muscles **(off-label dosage)**

Spasm, Of pharyngoesophageal segment - Total laryngectomy
30 to 100 units IM (off-label dosage)
Initial, 2.5 to 5 units IM and additional injections up to 30 units **(off-label dosage)**

Spastic dysphonia
1.25 to 5 units IM into affected muscles, with doses up to 25 units **(off- label dosage)**

Dysport – up to 1500 units every 3 months for adults, 1000 units every 3 months for peds (max); [J0586Injection, abobotulinumtoxin A, 5 units]

FDA Indication and Dose- labeled-
Cervical dystonia
Initial, 500 units IM, divided among 2 to 4 affected muscles
Maintenance, 250 units to maximum of 1000 units IM total dose in a single treatment, divided among 2 to 4 affected muscles; retreat as needed at least every 12 weeks or longer

Lower limb spasticity
Adult: Total doses of 1000 and 1500 units divided among selected muscles were used in clinical studies for a given treatment session; no more than 1 mL should be injected into any single injection site; MAX dose for upper and lower limb combined is 1500 units-[5]
Gastrocnemius (medial head, lateral head): Initial, 100 to 150 units IM in 1 injection site per muscle
Soleus: Initial, 330 to 500 units IM in 3 injection sites per muscle
Tibialis posterior: Initial, 200 to 300 units IM in 2 injection sites per muscle
Flexor digitorum longus: Initial, 130 to 200 units IM in 1 to 2 injection sites per muscle
Flexor hallucis longus: Initial, 70 to 200 units IM in 1 injection site per muscle;
Pediatric: Total dose per treatment session is 10-15 units/kg for unilateral lower limb injections or 20-30 units/kg for bilateral lower limb injections; MAX 15 units/kg for unilateral lower limb injections or 30 units/kg for bilateral lower limb injections or 1000 units, whichever is lower; When possible the dose should be distributed across more than 1 injection site in any single muscle; Repeat dosage no sooner than 12 weeks after the previous injection.
Gastrocnemius: 6-9 units/kg IM in up to 4 injection sites per muscle
Soleus: 4-6 units/kg IM in up to 2 injections sites per muscle
Total: 10-15 units/kg divided across both muscles IM in up to 6 injection sites per muscle

Upper limb spasticity
Adult: Total doses of 500 and 1000 units divided among certain muscles were used in clinical trials no more than 1 mL should be injected into any single injection site; MAX dose for upper and lower limb combined is 1500 units; ;Repeat dosage no sooner than 12 weeks after the previous injection.
Flexor carpi radialis, flexor carpi ulnaris, flexor digitorum profundus, flexor digitorum superficialis, brachioradialis: Initial, 100 to 200 units IM in 1 to 2 injection sites per muscle;
Pronator teres: Initial, 100 to 200 units IM in 1 injection site per muscle
Brachialis, biceps brachii: Initial, 200 to 400 units IM in 1 to 2 injection sites per muscle
Pediatric: MAX dose of 16 units/kg or 640 units, whichever is lower; no more than 0.5 mL should be injected into any single injection site; Repeat dosage no sooner than 16 weeks after the previous injection Brachialis, Biceps brachii: Initial 3-6 units/kg IM in up to 2 injection sites per muscle
Brachioradialis, Flexor carpi ulnaris (FCU): Initial, 1.5-3 units/kg IM in 1 injection site per muscle Pronator teres, Flexor digitorum profundus (FDP): Initial, 1-2 units/kg IM in 1 injection site per muscle Pronator quadratus: Initial, 0.5-1 unit/kg IM in 1 injection site per muscle
Flexor carpi radialis (FCR): Initial, 2-4 units/kg IM in up to 2 injection sites per muscle
Flexor digitorum superficialis (FDS): Initial, 1.5-3 units/kg IM in up to 4 injection sites per muscle

Accepted off-labeled indication
Blepharospasm
40 units, 80 units, or 120 units per eye subQ in 0.1 mL aliquots into 6 areas of the orbicularis oculimuscle

(0.6 mL total volume/eye) (off-label dosage)

Hemifacial spasm
28 to 220 units subQ per treatment session based on sites and severity of the spasm. Subsequent injections were administered upon recurrence of spasm (off-label dosage)

Anal fissure
90 to 150 units in 2 divided doses injected into the internal anal sphincter on each side of the anterior midline (off-label dosage)

Axillary Hyperhidrosis, primary
100 to 200 units per axilla; injections should be evenly distributed into multiple sites 1 to 2 cm apart (10 to 20 injections). May repeat when clinical effect diminishes. Mean duration of effect ranges from 5.5 months to 8.5 months (off-label dosage)

Sialorrhea
Intraglandular (Ventral) (off-label route): 15 to 75 units injected per gland (submandibular, parotid or both) either unilaterally or bilaterally with intervals of 4 to 6 months between treatments (off-label)

Myobloc – up to 10,000 units every 3 months (max); [J0587 Injection, rimabotulinumtoxinB, 100 units]

FDA Indication and Dose- labeled
Cervical Dystonia
2500 to 5000 Units IM divided among affected muscles

Chronic sialorrhea:
Intraglandular: 1,500 to 3,500 units divided among the parotid (500 to 1,500 units/gland) and submandibular (250 units/gland) glands. Subsequent dosing should be optimized according to patient's response and should generally be repeated no sooner than every 12 weeks

Accepted off-labeled indication
None

Xeomin – up to 400 units every 3 months (max); J0588 Injection, incobotulinumtoxinA, 1 unit

FDA Indication and Dose- labeled-
Blepharospasm
(Treatment-naive members): Initial, 50 units (25 units per eye) Maximum dosage: 100 units per treatment session (50 units per eye)

Retreatment: May repeat based on clinical response, but no more frequently than every 12 weeks

Cervical dystonia
Initial total dose, 120 units divided and injected among affected muscles; repeat treatment no more frequently than every 12 weeks

Excessive salivation, Chronic

Adults: 100 units via intra-salivary gland injection May repeat treatment after no fewer than 16 weeks. Pediatric: weight based dosing in a 3:2 ratio into the parotic and submandibular glands, respectively. May repeat treatment after no fewer than 16 weeks.

Upper limb spasticity
Adult: MAX 400 units/treatment session; frequency of treatments no sooner than every 12 weeks; in previously untreated members, initiate dosing with the low end of the dosing range and titrate as

necessary
Clenched fist (flexor digitorum superficialis or flexor digitorum profundus) 25 to 100 units IM in 2 injection sites per muscle
Flexed wrist (flexor carpi radialis) 25 to 100 units IM in 1 to 2 injection sites per muscle
Flexed wrist (flexor carpi ulnaris) 20 to 100 units IM in 1 to 2 injection sites per muscle
Flexed elbow (biceps) 50 to 200 units IM in 1 to 4 injection sites per muscle
Flexed elbow (brachialis) 25 to 100 units IM in 1 to 2 injection sites per muscle;
Flexed elbow (brachioradialis) 25 to 100 units IM in 1 to 3 injection sites per muscle
Pronated forearm (pronator quadratus) 10 to 50 units IM in 1 injection site per muscle Pronated forearm (pronator teres) 25 to 75 units IM in 1 to 2 injection sites per muscle
Thumb-in-palm (adductor pollicis, flexor pollicis brevis, or opponens pollicis) 5 to 30 units IM in 1 injection site per muscle
Thumb-in-palm (flexor pollicis longus) 10 to 50 units IM in 1 injection site per muscle; untreated member s, initiate dosing with the low end of the dosing range and titrate as necessary -

Pediatric, excluding spasticity caused by cerebral palsy
MAX 8 Units/kg up to a maximum dose of 200 units/single upper limb, if both upper limbs are treated, total dose should not exceed 16 units/kg up to a maximum of 400 units; frequency of treatments no sooner than every 12 weeks
Flexed elbow (biceps) 2-3 units/kg (MAX 75 units) IM in 1 to 3 injection sites per muscle
Flexed elbow (brachialis, brachioradialis) 1-2 units/kg (MAX 50 units) IM in 1 to 2 injection sites per muscle
Flexed wrist (flexor carpi radialis, flexor carpi ulnaris) 1 unit/kg (MAX 25 units) IM in 1 injection site per muscle
Pronated forearm (pronator quadratus) 0.5 unit/kg (MAX 12.5 units) IM in 1 injection site per muscle
Pronated forearm (pronator teres) 1-2 units/kg (MAX 50 units) IM in 1 to 2 injection sites per muscle
Clenched fist (flexor digitorum superficialis or flexor digitorum profundus) 1 unit/kg (MAX 25 units) IM in 1 injection site per muscle
Thumb-in-palm (adductor pollicis, flexor pollicis brevis, or opponens pollicis) 0.5 unit/kg (MAX 12.5 units) IM in 1 injection site per muscle
Thumb-in-palm (flexor pollicis longus) 1 unit/kg (MAX 25 units) IM in 1 injection site per muscle

Accepted off-labeled indication
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Botulinum neurotoxins produced by Clostridium botulinum, a gram-positive anaerobic bacterium, can prevent the release of acetylcholine, carrying chemical denervation and blockage of neuromuscular transmission.
Botulinum toxins produce a presynaptic neuromuscular blockage by preventing release of acetylcholine from motor nerve terminals. The resulting chemical denervation of muscle induces local paresis or paralysis and individual muscles can be weakened selectively. Botulinum toxins have the advantage of being potent neuromuscular blocking agents with good selectivity, long duration of action and few side effects. Of seven known distinct neurotoxins (A-G), onabotulinumtoxinA (Botox®/Botox Cosmetic), abobotulinumtoxinA (Dysport™), rimabotulinumtoxinB (Myobloc®) and incobotulinumtoxinA (Xeomin®) have been approved by the U.S. Food and Drug Administration for clinical use.

Use with CGRP Inhibitors for Migraine

The 2021 American Headache Society Consensus Statement update lists the combo of Botox and CGRP inhibitors as 'probably effective' based on one class IV trial. There are currently only retrospective studies of the combination used in practice. In a retrospective study of 153 patients with chronic migraine treated with onabotulinumtoxinA, 73 percent (111 patients) reported a reduced headache burden after adding a CGRP antagonist. There were no serious adverse events. In another retrospective study of 78 patients with chronic migraine, the addition of erenumab was associated with a reduction of approximately 7 monthly headache days at one month from a baseline of 23 mean monthly headache days on onabotulinumtoxinA alone. These results were sustained at 60 and 90 days.

Safety and efficacy data of combination therapy is limited and not peer reviewed. Further controlled and prospective studies are needed to fully understand the risks and benefits of this approach to therapy. CGRP antagonists may provide additional benefit to patients with chronic migraine with a partial response to onabotulinumtoxinA, who are also refractory to other preventative migraine treatments.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of botulinum toxins are considered experimental/investigational and therefore, will follow Molina's Off-Label policy.

Conditions Not Recommended for Approval:

- Cosmetic Uses (e.g., facial rhytides, frown lines, glabellar wrinkling, horizontal neck rhytides, mid and lower face and neck rejuvenation, platsymal bands, rejuvenation of the periorbital region). Cosmetic use is not recommended for coverage as this indication is excluded from coverage in a typical medical or pharmacy benefit.
- Fibromyalgia. More data are needed to define the place in therapy of botulinum toxin in the treatment of fibromyalgia. A small pilot study involving 16-member s concluded botulinum toxin A injections into fibromyalgia trigger points offered more relief (up to 16weeks minimum) compared with local saline or anesthetic injections; it was concluded Botox is effective in the treatment of fibromyalgia. Other small studies have shown effectiveness of Botox in pain relief post injection. botulinum toxin is not mentioned in guidelines for the treatment of fibromyalgia.
- Gastroparesis. The ACG issued clinical guidelines on the management of gastroparesis (2013). ACG does not recommend the use of botulinum toxin injected into the pylorus as a treatment for gastroparesis. This is based on two double-blind, placebo-controlled studies which did show some improvement in gastric emptying, but no improvement in symptoms compared with placebo.
- Vaginismus. More data are needed to define the place in therapy of botulinum toxin in the treatment of vaginismus. The use of botulinum toxin for the treatment of vaginismus has been evaluated in a few small studies with successful outcomes.
- Requests for Jeuveau™ (prabotulinumtoxinA-xvfs)- Jeuveau™ (prabotulinumtoxinA- xvfs) is indicated for the temporary improvement in the appearance of moderate to severe glabellar (frown) lines between the eyebrowsin adults. Currently, Jeaveau is approved only for cosmetic use; it has no other indications.
- Anismus (pelvic floor dyssynergia)
- Behcet's syndrome
- Brachial Plexus Palsy
- Carpal tunnel syndrome
- Chronic motor tic disorder
- Disorders of the esophagus
- Epicondylitis
- Low back pain
- Myofascial pain syndrome
- Neck pain not related to conditions mentioned above
- Nystagmus
- Parkinson's disease
- Post-mastectomy reconstruction syndrome
- Reynaud's syndrome
- Sphincter of Oddi dysfunction

- Stuttering
- Tics associated with Tourette's Syndrome Tinnitus
- Tourette's Syndrome
- Urinary and anal sphincter dysfunction (except as listed above)
- Vaginismus
- Whiplash related disorders
- Zygomatic Fractures

OTHER SPECIAL CONSIDERATIONS:

Botulinum toxin products are not interchangeable, and dosing units of one product cannot be converted or compared with dosing units of another botulinum toxin product. When treating one or more indications, the maximum cumulative dose of onabotulinumtoxinA should generally not exceed 400 units in a 3-month interval.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J0585	Botox - Injection, onabotulinumtoxinA, 1 unit
J0586	Dysport - Injection, abobotulinumtoxinA, 5 units
J0587	Myobloc - Injection, rimabotulinumtoxinB, 100 units
J0588	Xeomin - Injection, incobotulinumtoxinA, 1 unit

AVAILABLE DOSAGE FORMS:

Dysport 300Unit
Dysport 500Unit
Botox 100Unit
Botox 200Unit
Myobloc 2500Unit/0.5ML
Myobloc 500Unit/ML
Myobloc 1000Unit/2ML
Xeomin 50Unit
Xeomin 100Unit
Xeomin 200Unit

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Background References	Q4 2022
REVISION- Notable revisions: Required Medical Information Age Restrictions FDA Approved Uses Appendix References	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file