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Policy Number: C8755-A

Botulinum Toxin

PRODUCTS AFFECTED

Botox (onabotulinumtoxinA), Daxxify (daxibotulinumtoxinA-lanm), Dysport (abobotulinumtoxinA), Myobloc (rimabotulinumtoxinB), Xeomin (incobotulinumtoxinA)

Requests for Jeuveau™ (prabotulinumtoxinA-xvfs) or Botox Cosmetic (onabotulinumtoxinA [Cosmetic]): Jeuveau™ (prabotulinumtoxinA-xvfs) is indicated for the temporary improvement in the appearance of moderate to severe glabellar (frown) lines between the eyebrows in adults. Botox Cosmetic (onabotulinumtoxinA [Cosmetic]) is indicated for the temporary improvement in the appearance of glabellar lines, lateral canthal lines (crow's feet), and forehead lines. Currently, Jeuveau and Botox Cosmetic are FDA approved only for cosmetic use; they have no other indications.
Cosmetic use is excluded from coverage and therefore Jeuveau™ (prabotulinumtoxinA-xvfs) and Botox Cosmetic (onabotulinumtoxinA [Cosmetic]) are excluded from coverage.

Requests for Daxxify (daxibotulinumtoxinA-lanm), Dysport (abobotulinumtoxinA), Xeomin (incobotulinumtoxinA) for glabellar lines, requests for Xeomin (incobotulinumtoxinA) for appearance of upper facial lines:
Daxxify (daxibotulinumtoxinA-lanm) is also indicated for the temporary improvement in the appearance of moderate to severe glabellar (frown) lines. Dysport (abobotulinumtoxinA) is also indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adults < 65 years of age. Xeomin (incobotulinumtoxinA) is also indicated for the temporary improvement in the appearance of upper facial lines in adults including moderate to severe glabellar lines with corrugator and/or procerus muscle activity, moderate to severe horizontal forehead lines associated with frontalis muscle activity, and moderate to severe lateral canthal lines associated with orbicularis oculi muscle activity.
Cosmetic use is excluded from coverage and therefore Daxxify (daxibotulinumtoxinA-lanm), Dysport (abobotulinumtoxinA), Xeomin (incobotulinumtoxinA) for glabellar lines, and Xeomin (incobotulinumtoxinA) for appearance of upper facial lines 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, Adjunct to surgical larynx closure procedure for chronic aspiration, Organic voice tremor, Spasm of pharyngoesophageal segment following total laryngectomy, Spastic dysphonia

REQUIRED MEDICAL INFORMATION:

NOTE: PRIOR TO ANY REVIEW FOR EXCEPTION, REVIEWER SHOULD VERIFY THERAPY ELIGIBILITY FOR BENEFIT EXCLUSION (i.e., COSMETIC USE)

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. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. FOR ALL INDICATIONS:

1. Prescriber attests to, or the clinical reviewer has found, 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
   MOLINA REVIEWER NOTE: If not supplied, FDA or compendial limit per indication will be approved
   AND
3. Prescribed product has an FDA labeled or compendia supported indication for member's age (see Appendix for guidance on FDA label/compendia and quantity limits)

B. 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 and ineffectiveness/failure after 2 months or serious side effects or contraindication to TWO 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. Documentation that botulinum toxin will NOT be used in combination with prophylaxis CGRP agents (e.g., Aimovig, Ajovy, Emgality, Vyepti)
   MOLINA REVIEWER NOTE: Dual therapy with CGRP may be considered if the member is refractory to at least two preventative treatments and has experienced a partial response to Botox. See Background.
   AND
4. Documentation of baseline (prior to start of requested therapy) monthly migraine days (MMD) [DOCUMENTATION REQUIRED]

C. 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

D. CHRONIC ANAL FISSURE:
NOTE: Use of botulinum toxin for this indication is not supported with sphincterotomy procedure.
1. Member has documented 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

E. AXILLARY HYPERHIDROSIS:
1. Documented diagnosis of primary axillary hyperhidrosis (excessive underarm sweating)
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. Documentation of presence of medical complications of hyperhidrosis, including skin maceration with secondary infection or significant functional impairment

F. 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. Documentation of treatment failure, serious side effects, clinical contraindication, or unable to receive baclofen
AND
3. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., impact on activities of daily living, etc.)

G. STRABISMUS:
1. Documented diagnosis of ONE of the following:
a) Vertical strabismus (superior and inferior rectus muscles, superior and inferior oblique muscles)
OR
b) Horizontal strabismus (medial and lateral rectus muscles) as evidenced by one of the following:
i. Horizontal strabismus < 20 prism diopters
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

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

I. SIALORRHEA:
1. Documentation member has sialorrhea (excessive drooling) due to conditions such as Parkinson's disease or motor neuron disease (cerebral palsy)
AND
2. Documentation of treatment failure, serious side effects, clinical contraindication, or unable to receive glycopyrrolate

J. 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 dysraphism, multiple sclerosis neurogenic detrusor overactivity or overactive bladder)
AND
2. Documented inadequate response to or serious side effect to at least TWO anticholinergic agents (e.g., 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 member has no evidence of current urinary tract infection, or urinary retention

K. CERVICAL DYSTONIA:
1. Documented diagnosis of cervical dystonia
AND
2. 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
3. Contractions are causing pain and functional impairment

L. ALL REMAINING INDICATIONS (Adjunct to surgical larynx closure procedure for chronic aspiration, Organic voice tremor, Spasm of pharyngoesophageal segment following 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 no evidence of intolerable adverse effects or drug toxicity (e.g., 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. Botulinum toxin will not be used in combination with prophylaxis CGRP agents (e.g., Aimovig, Ajovy, Emgality, Vyepti).
   MOLINA REVIEWER NOTE: Dual therapy with CGRP may be considered if the member is refractory to at least two preventative treatments and has experienced a partial response to Botox. See Background.

B. ALL OTHER INDICATIONS:
1. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms
   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 no evidence of intolerable adverse effects or drug toxicity (e.g., 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:
Chronic Anal Fissure, Adjunct to surgical larynx closure procedure: Initial authorization: 1 treatment, Continuation of Therapy: NA
All other indications: Initial authorization: 12 months, Continuation of Therapy: 12 months

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:
Upper limb spasticity, Lower limb spasticity: 2 years of age and older
Severe axillary hyperhidrosis, Cervical dystonia, overactive bladder, chronic migraine, esophageal achalasia, chronic anal fissure: 18 years of age and older
Neurogenic detrusor overactivity (NDO): 5 years of age and older
Blepharospasm associated with dystonia, Strabismus: 12 years of age and older

Xeomin:
Cervical Dystonia, Blepharospasm: 18 years of age and older
Chronic Sialorrhea, Upper Limb Spasticity: 2 years of age and older

Dysport:
Cervical Dystonia, Blepharospasm, Hemifacial spasm: 18 years of age and older
Spasticity: 2 years of age and older

Myobloc:

Cervical Dystonia, Chronic Sialorrhea: 18 years of age and older

Daxxify:
Cervical Dystonia: 18 years of age and older

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

Daxxify – up to 250 units every 3 months (max); in 50 or 75 unit increments, units up to the vial size(s) medically necessary for the use
J0589 Injection, daxibotulinumtoxinA-lanm, 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, Intradetrusor, Intradermal, Intraglandular

DRUG CLASS:
Neuromuscular Blocking Agent

FDA-APPROVED USES:
Botox (onabotulinumtoxinA) is indicated for:

- 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
- Treatment of neurogenic detrusor overactivity (NDO) in pediatric patients 5 years of age and older who have an inadequate response to or are intolerant of anticholinergic medication
- Prophylaxis of headaches in 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

Limitations of Use: 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*

Daxxify (daxibotulinumtoxinA-lanm) is indicated for:
- The treatment of cervical dystonia adult patients

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

Myobloc (rimabotulinumtoxinB) is 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

Xeomin (incobotulinumtoxinA) is indicated for the treatment or improvement of:
- 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

COMPENDIAL APPROVED OFF-LABELED USES:
Botox (onabotulinumtoxinA):
Esophageal Achalasia, Adjunct to surgical larynx closure procedure for chronic aspiration, Organic voice tremor, Spasm of pharyngoesophageal segment following total laryngectomy, Spastic dysphonia, Chronic anal fissure

Daxxify (daxibotulinumtoxinA-lanm):
None

Dysport (abobotulinumtoxinA):
Blepharospasm, Hemifacial spasm, Chronic anal fissure, Axillary hyperhidrosis, Sialorrhea

Myobloc (rimabotulinumtoxinB):
None

Xeomin (incobotulinumtoxinA):
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 medication
100 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; 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,10 units divided

in 2 sites in corrugator muscle, 5 units in 1 site in procerus muscle, 30 units divided in 6 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, 25 units/any muscle as a single injection and 0.15 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)**

Adjunct to surgical larynx closure 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 following 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); [J0586 Injection, abobotulinumtoxinA, 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

Daxxify – up to 250 units every 3 months (max); [J3590]

FDA Indication and Dose- labeled
Cervical Dystonia:
125 to 250 Units IM divided among affected muscles

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. Contraindications to botulinum toxins include: hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation, infection at the proposed injection site. For intradetrusor injections only: current urinary tract infection or urinary retention. For Dysport only: hypersensitivity to cow's milk protein.

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 eyebrows in 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
- Chronic constipation
- 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

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

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
J0589	Daxxify - Injection, daxibotulinumtoxina-lanm, 1 unit

AVAILABLE DOSAGE FORMS: Botox SOLR 100UNIT
Botox SOLR 200UNIT
Daxxify SOLR 100UNIT
Dysport SOLR 300UNIT
Dysport SOLR 500UNIT
Myobloc SOLN 10000UNIT/2ML Myobloc SOLN 2500UNIT/0.5ML
Myobloc SOLN 5000UNIT/ML
Xeomin SOLR 100UNIT
Xeomin SOLR 200UNIT
Xeomin SOLR 50UNIT

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4. Xeomin (IncobotulinumtoxinA) for injection, for intramuscular or intraglandular use [prescribing information] Raleigh, NC: MerzPharmaceuticals LLC; July 2024.
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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy References	Q4 2025
REVISION- Notable revisions: Coding/Billing Information Template Update Products Affected Required Medical Information Age Restrictions Compendial Approved Off-Labeled Uses Contraindications/Exclusions/Discontinuation Coding/Billing Information Available Dosage Forms	Q4 2024
REVISION- Notable revisions: Contraindications/Exclusions/Discontinuation	Q1 2024
REVISION- Notable revisions: Products Affected Diagnosis Required Medical Information Continuation of Therapy Duration of Approval Age Restrictions	Q4 2023

Compendial Approved Off-Labeled Uses Appendix Contraindications/Exclusions/Discontinuation Available Dosage Forms References	
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