Clinical Policy: IncobotulinumtoxinA (Xeomin)

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Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

IncobotulinumtoxinA (Xeomin®) is an acetylcholine release inhibitor and a neuromuscular blocking agent.

FDA Approved Indication(s)

Indication	Adults	Pediatrics	Treatment	Prophylaxis
Sialorrhea	X	X	X	
Upper limb spasticity (includes CP)	X	X	X	
Cervical dystonia (focal dystonia)	X		X	
Blepharospasm (focal dystonia)	X		X	
Off-Label Uses				
Lower limb spasticity*	X		X	
Overactive bladder	X		X	
Urinary incontinence	X		X	
Migraine	X			X
Axillary hyperhidrosis	X		X	
Laryngeal dystonia**	X		X	
Oromandibular dystonia**	X		X	
Upper extremity dystonia**	X		X	
Upper extremity essential tremor**	X		X	

Abbreviations: cerebral palsy (CP)
**See criteria set entitled Upper and Lower Limb Spasticity*
***See criteria set entitled Focal Dystonia and Essential Tremor*

Xeomin 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
- The appearance of upper facial lines in adults:
  - Moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity
  - Moderate to severe horizontal forehead lines associated with frontalis muscle activity
  - Moderate to severe lateral canthal lines associated with orbicularis oculi muscle activity

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Index

It is the policy of health plans affiliated with Centene Corporation® that Xeomin is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Sialorrhea (must meet all)**:**

1. Diagnosis of chronic sialorrhea for at least the last three months due to one of the following (a or b):
   a. Underlying neurologic disorder (e.g., Parkinson disease, atypical parkinsonism, stroke, traumatic brain injury, cerebral palsy, amyotrophic lateral sclerosis);
   b. Craniofacial abnormality (e.g., Goldenhar syndrome);
2. Prescribed by or in consultation with a neurologist or physiatrist;
3. Age ≥ 2 years;
4. Failure of at least one anticholinergic drug (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;
5. Xeomin is not prescribed concurrently with other botulinum toxin products;
6. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 16 weeks;
7. Treatment plan provided detailing number of Units per indication and treatment session;

8. Request is for one of the following (a or b):
   a. For age ≥ 18 years, dose does not exceed 30 Units per parotid gland, 20 Units per submandibular gland, 100 Units per treatment session;
   b. For age ≥ 2 years, dose does not exceed any of the following (i, ii, iii, iv, v, or vi):
      i. For body weight 12 kg to < 15 kg, 6 Units per parotid gland, 4 Units per submandibular gland, 20 Units per treatment session;
      ii. For body weight 15 kg to < 19 kg, 9 Units per parotid gland, 6 Units per submandibular gland, 30 Units per treatment session;
      iii. For body weight 19 kg to < 23 kg, 12 Units per parotid gland, 8 Units per submandibular gland, 40 Units per treatment session;
      iv. For body weight 23 kg to < 27 kg, 15 Units per parotid gland, 10 Units per submandibular gland, 50 Units per treatment session;
      v. For body weight 27 kg to < 30 kg, 18 Units per parotid gland, 12 Units per submandibular gland, 60 Units per treatment session;
      vi. For body weight ≥ 30 kg, 22.5 Units per parotid gland, 15 Units per submandibular gland, 75 Units per treatment session.

Approval duration:
Medicaid/HIM – 16 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

B. Upper and Lower Limb Spasticity (*includes cerebral palsy*) (must meet all)**:**
1. Diagnosis of upper limb spasticity or lower limb spasticity (e.g., associated with paralysis, central nervous system demyelinating diseases such as multiple sclerosis, cerebral palsy, stroke);
2. Prescribed by or in consultation with a neurologist, orthopedist, or physiatrist;
3. Member meets one of the following (a or b):
   a. For upper limb spasticity, age ≥ 2 years;
   b. For lower limb spasticity, age ≥ 18 years (off-label);
4. Failure of Botox® and Dysport®, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix B*);
5. Xeomin is not prescribed concurrently with other botulinum toxin products;
6. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
7. Treatment plan provided detailing number of Units per indication and treatment session;
8. Dose does not exceed 400 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

C. Cervical Dystonia (must meet all)**:**
1. Diagnosis of CD;
2. Prescribed by or in consultation with a neurologist, orthopedist , or physiatrist;
3. Age ≥ 18 years;

4. Member is experiencing involuntary contractions of the neck and shoulder muscles (e.g., splenius, sternocleidomastoid, levator scapulae, scalene, trapezius, semispinalis capitis) resulting in abnormal postures or movements of the neck, shoulder or head;
5. Contractions are causing pain and functional impairment;
6. Failure of Botox and Dysport, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix B*);
7. Xeomin is not prescribed concurrently with other botulinum toxin products;
8. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
9. Treatment plan provided detailing number of Units per indication and treatment session;
10. Dose does not exceed one of the following (a or b):
    a. Treatment-naïve: 120 Units per treatment session;
    b. Treatment-experienced: 300 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

D. Blepharospasm *(focal dystonia - abnormal eyelid muscle contraction)* (must meet all)**:**
1. Diagnosis of blepharospasm;
2. Prescribed by or in consultation with a neurologist or ophthalmologist;
3. Age ≥ 18 years;
4. Member is experiencing significant disability in daily functional activities due to interference with vision;
5. Failure of Botox and Dysport, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix B*);
6. Xeomin is not prescribed concurrently with other botulinum toxin products;
7. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
8. Treatment plan provided detailing number of Units per indication and treatment session;
9. Dose does not exceed 50 Units per eye per treatment session.

Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

E. Overactive Bladder and Urinary Incontinence (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a or b):
    a. OAB, and member's history is positive for urinary urgency, frequency, and nocturia with or without incontinence;
    b. Urinary incontinence, and member's history is positive for an associated neurologic condition (e.g., spinal cord injury, multiple sclerosis);
2. Prescribed by or in consultation with a neurologist or urologist;
3. Age ≥ 18 years;

4. Failure of a trial of both of the following (a and b), each used for at least 30 days, unless clinically significant adverse effects are experienced or all are contraindicated *(see Appendix B)*;
   a. At least 2 anticholinergic agents;
   b. Oral beta-3 agonist medication;
5. Failure of Botox and Dysport, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix B*);
6. Xeomin is not prescribed concurrently with other botulinum toxin products;
7. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
8. Treatment plan provided detailing number of Units per indication and treatment session;
9. Dose does not exceed 200 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

F. Chronic Migraine (off-label) (must meet all)**:**
1. Diagnosis of chronic migraine (i.e., ≥ 15 headache days per month for at least 3 months with headache lasting 4 hours a day or longer);
2. Prescribed by or in consultation with a neurologist or pain specialist;
3. Age ≥ 18 years;
4. Failure of at least 2 of the following oral migraine preventative therapies, each for 8 weeks and from different therapeutic classes, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, or c):
   a. Antiepileptics (e.g., divalproex sodium, sodium valproate, topiramate);
   b. Beta-blockers (e.g., metoprolol, propranolol, timolol);
   c. Antidepressants (e.g., amitriptyline, venlafaxine);
5. Failure of Botox and Dysport, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix B*);
6. Xeomin is not prescribed concurrently with injectable calcitonin gene-related peptide (CGRP) inhibitors (e.g., Aimovig®, Ajovy®, Emgality®);
7. Xeomin is not prescribed concurrently with other botulinum toxin products;
8. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
9. Treatment plan provided detailing number of Units per indication and treatment session;
10. Dose does not exceed 155 Units per treatment session.

Approval duration:
Medicaid/HIM – 24 weeks (two 12-week treatment sessions)
Commercial – 6 months or to member's renewal date, whichever is longer

G. Primary Axillary Hyperhidrosis *(excessive underarm sweating)* (off-label) (must meet all)**:**
1. Diagnosis of primary axillary hyperhidrosis;
2. Prescribed by or in consultation with a neurologist or dermatologist;

3. Age ≥ 18 years;
4. Failure of a 6-month trial of topical aluminum chloride, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of Botox and Dysport, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix B*);
6. Xeomin is not prescribed concurrently with other botulinum toxin products;
7. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
8. Treatment plan provided detailing number of Units per indication and treatment session;
9. Dose does not exceed 100 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

H. Focal Dystonia and Essential Tremor (off-label) (must meet all):
1. Diagnosis of one of the following (a, b, c, or d):
   a. Laryngeal dystonia;
   b. Oromandibular dystonia (OMD);
   c. Upper extremity (UE) dystonia;
   d. UE essential tremor;
2. Prescribed by or in consultation with a neurologist, ENT specialist, orthopedist, or physiatrist;
3. Age meets one of the following (a or b):
   a. For upper extremity dystonia: Age ≥ 2 years;
   b. For all other indications: Age ≥ 18 years;
4. For upper extremity dystonia: Failure of a trial of carbidopa/levodopa or trihexyphenidyl *(see Appendix B),* unless clinically significant adverse effects are experienced or both are contraindicated;
5. Failure of Botox and Dysport, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix B*);
6. Xeomin is not prescribed concurrently with other botulinum toxin products;
7. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
8. Treatment plan provided detailing number of Units per indication and treatment session;
9. Request meets one of the following (a or b):
   a. Laryngeal dystonia: Dose does not exceed 25 Units per treatment session;
   b. UE dystonia, UE essential tremor, OMD: Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use and member age (*prescriber must submit supporting evidence; Units per treatment session does not exceed 400 Units per treatment session*).

Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

I. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Approval

A. Chronic Migraine (must meet all):
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. If receipt of ≥ 2 Xeomin treatment sessions, member has experienced and maintained a 30% reduction in monthly migraine headache frequency from baseline;
3. Xeomin is not prescribed concurrently with injectable CGRP inhibitors (e.g., Aimovig, Ajovy, Emgality);
4. Xeomin is not prescribed concurrently with other botulinum toxin products;
5. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan details number of Units per indication and treatment session;
7. If request is for a dose increase, new dose does not exceed 155 Units per treatment session.

Approval duration:
Medicaid/HIM – 24 weeks (two 12-week treatment sessions)
Commercial – 6 months or to member's renewal date, whichever is longer

B. All Other Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

2. Member is responding positively to therapy;
3. Xeomin is not prescribed concurrently with other botulinum toxin products;
4. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 week (16 weeks if sialorrhea);
5. If request is for a dose increase, new dose does not exceed the following indication-specific maximums (a, b, c, d, e, f, or g):
   a. Chronic sialorrhea (i or ii):
      i. For age ≥ 18 years, dose does not exceed 30 Units per parotid gland, 20 Units per submandibular gland, 100 Units per treatment session;
      ii. For age ≥ 2 years, dose does not exceed any of the following (a, b, c, d, e, or f):
         a) For body weight 12 kg to < 15 kg, 6 Units per parotid gland, 4 Units per submandibular gland, 20 Units per treatment session;
         b) For body weight 15 kg to < 19 kg, 9 Units per parotid gland, 6 Units per submandibular gland, 30 Units per treatment session;
         c) For body weight 19 kg to < 23 kg, 12 Units per parotid gland, 8 Units per submandibular gland, 40 Units per treatment session;
         d) For body weight 23 kg to < 27 kg, 15 Units per parotid gland, 10 Units per submandibular gland, 50 Units per treatment session;
         e) For body weight 27 kg to < 30 kg, 18 Units per parotid gland, 12 Units per submandibular gland, 60 Units per treatment session;
         f) For body weight ≥ 30 kg, 22.5 Units per parotid gland, 15 Units per submandibular gland, 75 Units per treatment session.
   b. Upper/lower limb spasticity, UE dystonia, UE essential tremor: 400 Units per treatment session;
   c. Focal dystonia and essential tremor (i and ii):
      i. Laryngeal dystonia: 25 Units per treatment session;
      ii. UE dystonia, UE essential tremor, OMD: Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use and member age;
      (prescriber must submit supporting evidence; Units per treatment session does not exceed 400 Units per treatment session)
   d. CD (i or ii):
      i. Treatment-naïve: 120 Units per treatment session;
      ii. Treatment-experienced: 300 Units per treatment session;
   e. Blepharospasm: 50 Units per eye per treatment session;
   f. OAB/urinary incontinence: 200 Units per treatment session;
   g. Axillary hyperhidrosis: 100 Units per treatment session.

Approval duration:
Medicaid/HIM – 16 weeks for sialorrhea (single treatment session), 12 weeks for all other indications (single treatment session)
Commercial – 6 months or to member's renewal date, whichever is longer

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
B. Cosmetic treatment of hyperfunctional wrinkles of the upper face including glabellar frown lines, deep forehead wrinkles and periorbital wrinkles (crow's feet);
C. Episodic migraine (≤ 14 headache days per month): Safety and efficacy have not been established per the package insert;
D. Total treatment dose per session does not exceed 400 Units.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CD: cervical dystonia
CGRP: calcitonin gene-related peptide
FDA: Food and Drug Administration
MS: multiple sclerosis
OAB: overactive bladder
OMD: oromandibular dystonia
SCI: spinal cord injury
UE: upper extremity

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Sialorrhea: examples of anticholinergic drugs		
glycopyrrolate (Glycate® oral tablets, Cuvposa® oral solution)	• Adults: 1 mg PO TID *(Off-label: Lakraj 2013)*	See regimen information

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	• Pediatrics: chronic drooling: children ≥ 3 years and adolescents ≤ 16 years: oral solution (Cuvposa): 20 mcg/kg/dose 3 times daily, titrate in increments of 20 mcg/kg/dose every 5 to 7 days as tolerated to response up to a maximum dose of 100 mcg/kg/dose 3 times daily; not to exceed 1,500 to 3,000 mcg/dose. *(FDA labeled)*	
benztropine mesylate (oral tablets - 0.5 mg, 1 mg, 2 mg)	Mean doses of 3.8 mg/day have been used in adults and pediatrics ≥ 4 years. Benztropine typically is administered in divided doses titrating up as needed. *(Off-label - Sridharan 2018, Lakraj 2013; Micromedex, package insert)*	See regimen information
Overactive bladder, urinary incontinence		
oxybutynin (Ditropan®/XL, Gelnique®) *(anticholinergic agent)*	• Immediate-release tablets: 5 mg orally two to three times daily • Extended-release tablets: 5-10 mg orally once daily • Topical gel: Apply contents of one sachet topically once daily	• Immediate-release: 20 mg/day • Extended-release: 30 mg/day • Gel: one sachet/day
tolterodine tartrate (Detrol®/LA) *(anticholinergic agent)*	• Immediate-release tablets: 2 mg orally twice daily • Extended-release tablets: 4 mg orally once daily	4 mg/day
Myrbetriq® (mirabegron) *(beta-3 agonist)*	25 mg orally once daily	50 mg/day
Botox (OnabotulinumtoxinA)	<u>OAB:</u> Up to 5 Units IM per injection across up to 20 injection sites in the detrusor muscle for a total of up to 100 Units per treatment session <u>Urinary incontinence associated with neurologic condition:</u> Up to approximately 6.7 Units IM per injection across up to 30 injection sites	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	in the detrusor muscle for a total of up to 200 Units per treatment session	
Dysport (abobotulinumtoxinA)	Up to 250 Units IM in the detrusor muscle per treatment session. *(Off-label - Irwin 2013)*	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks
Chronic migraine		
Examples of oral migraine preventive therapies - • Anticonvulsants: divalproex (Depakote®), topiramate (Topamax®) • Beta blockers: propranolol (Inderal®), metoprolol (Lopressor®), timolol • Antidepressants/tricyclic antidepressants: amitriptyline (Elavil®), venlafaxine (Effexor®)	*Refer to prescribing information for dosing regimens.*	*Refer to prescribing information*
Botox (OnabotulinumtoxinA)	Up to 5 Units IM per injection across up to 7 head/neck muscles for a total of up to 155 Units per treatment session	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks
Dysport (abobotulinumtoxinA)	Up to 250 Units IM per treatment session. *(Off-label - Alipour 2016, Menezes 2007)*	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks
Primary axillary hyperhidrosis		
Drysol® (aluminum chloride)	Apply topically once daily	One application/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Botox (OnabotulinumtoxinA)	Up to 50 Units IM per axilla per treatment session	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks
Dysport (abobotulinumtoxinA)	Up to 200 Units IM per treatment session. *(Off-label - Clinical Pharmacology, Heckmann 2001)*	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks
Dystonia		
carbidopa/levodopa (Sinemet®, Duopa®, Rytary®)	25 mg/100 mg PO QD, and increase by 1 tablet every 3 to 5 days.	1,200 mg/day of levodopa
trihexyphenidyl	30 mg PO QD	30 mg/day
Upper and lower limb spasticity		
Botox (OnabotulinumtoxinA)	Adult: Up to 50 Units IM per injection and up to 400 Units per treatment session Pediatric: • Upper limb spasticity: Up to the lower of 6 Units/kg or 200 Units IM per treatment session • Lower limb spasticity: Up to the lower of 8 Units/kg or 300 Units IM per treatment session • Upper and lower limb spasticity: Up to the lower of 10 Units/kg or 340 Units IM per treatment session	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks
Dysport (abobotulinumtoxinA)	Adult: Divided among affected muscles every 12 weeks: • Upper limb: Up to 1,000 Units IM • Lower limb: Up to 1,500 Units IM Upper and lower limbs: Up to 1,500 Units IM staying within per limb guidelines	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Pediatric: Divided among affected muscles every 12 weeks: • Upper limb: Up to the lowr of 16 Units/kg/limb IM or 640 Units IM • Lower limb: Up to the lower of 15 Units/kg/limb IM or 1,000 Units IM • Bilateral lower limb: Up to the lower of 30 Units IM or 1,000 Units IM Upper and lower limbs: Up to the lower of 30 Units IM or 1,000 Units IM staying within per limb guidelines	
Cervical Dystonia		
Botox® (OnabotulinumtoxinA)	Up to 50 Units IM per injection, 100 Units total in the sternocleidomastoid (SCM) muscle, and 300 Units per treatment session	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks
Dysport (abobotulinumtoxinA)	Divided among affected muscles every 12 weeks: Up to 1,000 Units IM	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks
Blepharospasm		
Botox® (OnabotulinumtoxinA)	• Botox naive: Up to 2.5 Units IM per muscle, 7.5 Units per eye, and 15 Units per treatment session • Botox experienced: Up to 5 Units IM per muscle, 15 Units per eye, and 30 Units per treatment session	See dosing regimens for maximum dose Frequency: One treatment session every 12 weeks
Dysport (abobotulinumtoxinA)	Up to 120 Units SC per treatment session. *(Off-label - Hallet 2009, Micromedex, Truong 2008)*	See dosing regimens for maximum dose

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
		Frequency: One treatment session every 12 weeks

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Known hypersensitivity to the active substance botulinum neurotoxin type A or to any of the excipients
  - Infection at the proposed injection sites
- Boxed warning(s): Distant spread of toxin effect

Appendix D: Botulinum Toxin Product Interchangeability

- Potency Units of Xeomin are not interchangeable with other botulinum toxin product preparations (e.g., Dysport®, Botox®, Myobloc®).

Appendix E: Guideline Support for Botulinum Toxin Use

Indication	Guideline
Focal Dystonia* and Essential Tremor, and Headache	
Blepharospasm, cervical dystonia, adult spasticity, and headache	Academy of Neurology (2016)
Migraine prevention	American Academy of Neurology and the American Headache Society (Neurology 2012, Headache 2021)
Laryngeal dystonia	American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNS, 2018)
Oromandibular dystonia	American Academy of Oral Medicine (2018)
Focal limb dystonia - UE**	American Academy of Neurology (2008)
Essential tremor - UE	American Academy of Neurology (2011)
Sialorrhea	American Academy of Cerebral Palsy and Developmental Medicine (AACPDM, 2018); International Parkinson and Movement Disorder Society (2018)
OAB/urinary incontinence	American Urological Association Society of Urodynamics (2019)
Gastrointestinal Conditions *(see guidelines for required oral medication information)*	
Esophageal achalasia	American College of Gastroenterology (2020)
HD and IAS achalasia	American Pediatric Surgical Association (2017)
Chronic anal fissure	American College of Gastroenterology (2021)

**American Academy of Neurology (AAN) classifies Botox use for hemifacial spasm and motor tics as category C, and notes that data are inadequate to make a recommendation for lower limb dystonia. All other AAN Botox recommendations above are classified as category B - probably effective.*

***Policy criteria requiring failure of oral medication for dystonias are limited to dystonias affecting the limbs (see Cloud and Jinnah, 2010).*

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Chronic sialorrhea	• Adults: up to 30 Units IM per parotid gland, 20 Units IM per submandibular gland, and 100 Units IM per treatment session every 16 weeks. • Pediatrics (by body weight): ○ 12 kg to < 15 kg, 6 Units per parotid gland, 4 Units per submandibular gland, 20 Units per treatment session; ○ 15 kg to < 19 kg, 9 Units per parotid gland, 6 Units per submandibular gland, 30 Units per treatment session; ○ 19 kg to < 23 kg, 12 Units per parotid gland, 8 Units per submandibular gland, 40 Units per treatment session; ○ 23 kg to < 27 kg, 15 Units per parotid gland, 10 Units per submandibular gland, 50 Units per treatment session; ○ 27 kg to < 30 kg, 18 Units per parotid gland, 12 Units per submandibular gland, 60 Units per treatment session; ○ ≥ 30 kg, 22.5 Units per parotid gland, 15 Units per submandibular gland, 75 Units per treatment session.	Adults: 100 Units/16 weeks Pediatrics: 75 Units/16 weeks
CD	Up to 120 Units IM per treatment session every 12 weeks for treatment-naïve patients. Up to 300 Units IM per treatment session every 12 weeks for treatment-experienced patients.	300 Units/12 weeks
Blepharospasm	Up to 50 Units IM per eye per treatment session every 12 weeks.	100 Units/12 weeks
Upper limb spasticity	Up to 400 Units IM per treatment session every 12 weeks.	400 Units/12 weeks
Off-label uses		
Lower limb spasticity	Up to 400 Units IM per treatment session every 12 weeks. *(Off-label - Bensmail 2020, Santamato 2013)*	400 Units/12 weeks
OAB/urinary incontinence associated with neurologic condition	Up to 200 Units IM in the detrusor muscle per treatment session every 12 weeks. *(Off-label - Asafu-Adjei 2020)*	200 Units/12 weeks

Indication	Dosing Regimen	Maximum Dose
Chronic migraine	Up to 155 Units IM per treatment session every 12 weeks. *(Off-label - Salazar 2014, Ion 2018)*	155 Units/12 weeks
Axillary hyperhidrosis	Up to 100 Units IM per treatment session every 12 weeks. *(Off-label - Dressler 2010, Rosell 2013)*	100 Units/12 weeks
Laryngeal Dystonia	Up to 25 Units IM per treatment session *(off-label – Kohli 2022)*	25 Units/12 weeks
UE dystonia, UE essential tremor, OMD	Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use and member age (prescriber must submit supporting evidence; number of Units per treatment session does not exceed 400 Units IM per treatment session every 12 weeks).	400 Units/12 weeks

VI. Product Availability

Vials: 50 Units, 100 Units, 200 Units

VII. References

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Overactive Bladder, Urinary Incontinence

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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0588	Injection, incobotulinumtoxinA, 1 unit

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: HIM nonformulary language removed; sialorrhea medical trial added; rehabilitation specialist incorporated under physiatrist; previous (last 12 weeks) or concurrent toxin product use restriction added to all initial/continuation criteria; dosing updated per package insert; same-visit treatment for multiple indications is excluded (Section III); references reviewed and updated.	03.02.20	05.20
Updated max dosing for treatment-experienced patients for CD up to 300 Units per prior clinical guidance.	10.15.20	
RT4: updated lower age limit from 18 years to 2 years for upper limb spasticity.	12.04.20	
2Q 2021 annual review: chronic sialorrhea age updated to include pediatrics per FDA label; treatment plan requirement detailing number of Units per site and treatment session is changed to per indication and treatment session; treatment of multiple indications restriction removed and replaced with total treatment dose limitation (Section III); off-label uses added as follows per previously approved clinical guidance: adults (lower limb spasticity, OAB/urinary incontinence, migraine, AH, OMD, UE dystonia, UE essential tremor; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	01.14.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2022 annual review: no significant changes; removal of the statement "**The treatment of hyperhidrosis is a benefit exclusion for HIM;"* revised commercial approval duration from "6 months" (or whatever it is now) to the current standard for injectables of "6 months or to member's renewal date, whichever is longer"; references reviewed and updated.	02.07.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.07.22	
2Q 2023 annual review: Per February SDC and prior clinical guidance, added redirection requirement to co-prefer Botox and Dysport for all indications except chronic sialorrhea; references reviewed and updated.	02.21.23	05.23
2Q 2024 annual review: added max dose for laryngeal dystonia (off-label); revised max dose for OMD from "25 units" to standard language "Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use and member age (prescriber must submit supporting evidence; number of Units per treatment session does not exceed 400 Units IM per treatment session every 12 weeks)"; references reviewed and updated.	01.18.24	05.24
RT4: updated FDA approved indications to include horizontal forehead lines and lateral canthal lines per PI with no clinical changes to the criteria as coverage is not authorized for cosmetic usage.	07.18.24	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.