Clinical Policy: OnabotulinumtoxinA (Botox)

Reference Number: CP.PHAR.232
Effective Date: 07.01.16
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Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

OnabotulinumtoxinA (Botox®) is an acetylcholine release inhibitor and a neuromuscular blocking agent.

FDA Approved Indication(s)

Indication	Adults	Pediatrics	Treatment	Prophylaxis
Overactive bladder	X		X	
Urinary incontinence	X		X	
Migraine	X			X
Upper/lower limb spasticity (includes CP)	X	X	X	
Cervical dystonia (focal dystonia)	X	X	X	
Axillary hyperhidrosis	X		X	
Blepharospasm (focal dystonia)	X	X	X	
Strabismus	X	X	X	
Off-Label Uses				
Laryngeal dystonia*	X		X	
Oromandibular dystonia*	X		X	
Upper extremity dystonia*	X	X	X	
Upper extremity essential tremor*	X		X	
Esophageal achalasia	X		X	
HD and IAS achalasia	X	X	X	
Chronic anal fissure	X		X	

Abbreviations: cerebral palsy (CP); Hirschsprung disease (HD), internal anal sphincter (IAS) achalasia.
**See criteria set entitled Focal Dystonia and Essential Tremor*

Botox 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
  - Urinary incontinence due to detrusor over-activity 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
  - 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
  - Spasticity in patients 2 years of age and older
  - Cervical dystonia (CD) in adult patients, to reduce the severity of abnormal head position and neck pain

- Severe axillary hyperhidrosis that is inadequately managed by topical agents in adult patients
- Blepharospasm associated with dystonia in patients ≥ 12 years of age
- Strabismus in patients ≥ 12 years of age

- Prophylaxis of headaches in adult patients with chronic migraine (≥ 15 days per month with headache lasting 4 hours a day or longer)

Limitation(s) 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. Weakness of hand muscles and blepharoptosis may occur in patients who receive Botox for palmar hyperhidrosis and facial hyperhidrosis, respectively. Patients should be evaluated for potential causes of secondary hyperhidrosis (e.g., hyperthyroidism) to avoid symptomatic treatment of hyperhidrosis without the diagnosis and/or treatment of the underlying disease.
  - Treatment of axillary hyperhidrosis in pediatric patients under 18 year of age
- Botox has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture.

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.

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VII. References

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

I. Initial Approval Criteria

A. Overactive Bladder and Urinary Incontinence (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, spinal dysraphism, multiple sclerosis);
2. Prescribed by or in consultation with a neurologist or urologist;
3. Age ≥ 5 years;
4. Member meets one of the following, unless clinically significant adverse effects are experienced or all are contraindicated (a or b, *see Appendix B*):
   a. Adult: failure of one of the following, each used for at least 30 days (i or ii):
      i. Two anticholinergic agents;
      ii. One oral beta-3 agonist medication;
   b. Pediatric: failure of at least two anticholinergic agents, each used for at least 30 days;
5. Botox 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 details number of Units per indication and treatment session;
8. Request meets one of the following (a or b):
   a. OAB: Dose does not exceed 100 Units per treatment session;
   b. Urinary incontinence associated with a neurologic condition:
      i. Weight ≥ 34 kg: dose does not exceed 200 Units per treatment session;
      ii. Weight < 34 kg: dose does not exceed 6 units/kg per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

B. Chronic Migraine (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. If currently receiving calcitonin gene-related peptide (CGRP) therapy for migraine prophylaxis and request is for concurrent use of Botox and CGRP therapy (i.e., not switching from one agent to another), all of the following (a, b, and c):
   a. Sufficient evidence is provided from at least two high-quality*, published studies in reputable peer-reviewed journals or evidence-based clinical practice guidelines that provide all of the following (i – iv):
      **Case studies or chart reviews are not considered high-quality evidence*
      i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
      ii. Adequate representation of the prescribed drug regimen;
      iii. Clinically meaningful outcomes such as a reduction in monthly migraine or headache days;
      iv. Appropriate experimental design and method to address research questions (*see Appendix E for additional information*);
   b. Member has experienced and maintained positive response to CGRP monotherapy as evidenced by a reduction in migraine days per month from baseline following at least 6 months for treatments administered quarterly (every 3 months) (e.g., Ajovy®, Vyepti™) or 3 months for treatments administered at least monthly (e.g., Aimovig®, Ajovy®, Emgality®, Nurtec® ODT, Qulipta™);
   c. Despite CGRP monotherapy, member continues to experience chronic migraine (i.e., ≥ 15 headache days per month for at least 3 months with headache lasting 4 hours a day or longer) and/or severe migraine headaches that result in disability and functional impairment;
6. Botox 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 details number of Units per indication and treatment session;
9. Dose does not exceed 155 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

C. Upper and Lower Limb Spasticity *(includes cerebral palsy)* (must meet all)**:**
1. Diagnosis of upper 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. Age ≥ 2 years;
4. Botox 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. Request meets one of the following (a or b):
   a. Age ≥ 18 years: Upper and/or lower limb: Dose does not exceed 400 Units per treatment session;
   b. Age 2 through 17 years (i, ii, and iii):

i. Upper limb: Dose does not exceed the lower of 6 Units/kg body weight or 200 Units per treatment session;
ii. Lower limb: Dose does not exceed the lower of 8 Units/kg body weight or 300 Units per treatment session;
iii. If upper and lower limb spasticity are treated in the same treatment session, number of Units per treatment session does not exceed the lower of 10 Units/kg body weight or 340 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

D. Cervical Dystonia *(focal dystonia)* (must meet all):
1. Diagnosis of CD;
2. Prescribed by or in consultation with a neurologist, orthopedist, or physiatrist;
3. Age ≥ 16 years;
4. 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;
5. Contractions are causing pain and functional impairment;
6. Botox 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 details number of Units per indication and treatment session;
9. Request meets one of the following (a or b):
   a. Age ≥ 18 years: Dose does not exceed 100 Units total in the sternocleidomastoid (SCM) muscle and 300 Units per treatment session;
   b. Age 16 through 17 years: Dose does not exceed 100 Units total in the SCM muscle and the lower of 10 Units/kg body weight or 300 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

E. Primary Axillary Hyperhidrosis *(excessive underarm sweating)* (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. Botox 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 details number of Units per indication and treatment session;
8. Dose does not exceed 100 Units per treatment session.

Approval duration:

Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

F. 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 ≥ 12 years;
4. Member is experiencing significant disability in daily functional activities due to interference with vision;
5. Botox 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 details number of Units per indication and treatment session;
8. Dose does not exceed 2.5 Units per muscle, 7.5 Units per eye, and 15 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

G. Strabismus *(eye misalignment)* (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. Vertical strabismus (superior and inferior rectus muscles, superior and inferior oblique muscles);
   b. Horizontal strabismus (medial and lateral rectus muscles) (i or ii):
      i. Horizontal strabismus < 20 prism diopters;
      ii. Horizontal strabismus 20 to 50 prism diopters;
   c. Persistent sixth cranial nerve (VI; abducens nerve) palsy of ≥ one month involving the lateral rectus muscle;
2. Prescribed by or in consultation with a neurologist or ophthalmologist;
3. Age ≥ 12 years;
4. Botox 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. Request meets one of the following (a, b, or c):
   a. Vertical strabismus, or horizontal strabismus < 20 prism diopters: Dose does not exceed 2.5 Units per muscle and 5 Units per treatment session;
   b. Horizontal strabismus 20 to 50 prism diopters: Dose does not exceed 5 Units per muscle and 10 Units per treatment session;
   c. VI nerve palsy: Dose does not exceed 2.5 Units per treatment session (limited to treatment of one eye).

Approval duration:
Medicaid/HIM – 12 months
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 UE dystonia: Age ≥ 2 years;
   b. For all other indications: Age ≥ 18 years;
4. For UE 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. Botox 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 details number of Units per indication and treatment session;
8. Request meets one of the following (a or b):
   a. Laryngeal dystonia/OMD: Dose does not exceed 25 Units per treatment session;
   b. UE dystonia, UE essential tremor: 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 the lower of 10 Units/kg body weight or 340 Units for pediatrics, or 400 Units for adults*).

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

I. Esophageal Achalasia (off-label) (must meet all)**:**
1. Diagnosis of esophageal achalasia;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Member is not a candidate for pneumatic dilation or laparoscopic surgical myotomy (e.g., due to age, comorbidity);
5. Botox 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 details number of Units per indication and treatment session;
8. Dose does not exceed 100 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

J. Hirschsprung Disease, Internal Anal Sphincter Achalasia (off-label) (must meet all):
1. Diagnosis of one of the following (a or b):

a. Hirschsprung disease (HD) and (i or ii):
   i. Member has an HD subtype known as ultra-short segment HD;
   ii. Botox is prescribed for constipation post-surgery;
b. Internal anal sphincter (IAS) achalasia;

2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 2 years;
4. Failure of a trial of stool softeners and laxatives *(see Appendix B)*, unless clinically adverse effects are experienced or all are contraindicated;
5. Botox 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 details number of Units per indication and treatment session;
8. Dose does not exceed 100 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

K. Chronic Anal Fissure (off-label) (must meet all)**:**

1. Diagnosis of chronic anal fissure;
2. Prescribed by or in consultation with a gastroenterologist or colorectal surgeon;
3. Age ≥ 18 years;
4. Failure of nitroglycerin ointment unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of one of the following (a or b), unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B)*;
   a. Oral/topical nifedipine;
   b. Oral/topical diltiazem;
6. Botox 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 details number of Units per indication and treatment session;
9. Dose does not exceed 25 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

L. Chronic Sialorrhea (off-label) (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 ≥ 18 years;
4. Failure of at least one anticholinergic drug (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;

5. Botox 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 100 Units per treatment session;

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

M. 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 Botox treatment sessions, member has experienced and maintained a 30% reduction in monthly migraine headache frequency from baseline;
3. Botox 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 weeks;
5. Treatment plan details number of Units per indication and treatment session;
6. If request is for a dose increase, new dose does not exceed 155 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months

Commercial – 6 months or to member's renewal date, whichever is longer

B. Esophageal Achalasia (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. Botox 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 weeks;
5. If member has previously received ≥ 2 Botox treatment sessions for esophageal achalasia, it has been at least 24 weeks since the last treatment session;
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 100 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

C. 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. Botox 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 weeks;
5. Treatment plan details number of Units per indication and treatment session;
6. If request is for a dose increase, request meets one of the following (a - i):
   a. OAB: Dose does not exceed 100 Units per treatment session;
   b. Urinary incontinence associated with a neurologic condition: Dose does not exceed 200 Units per treatment session;
   c. Upper/lower limb spasticity (i or ii):
      i. Age ≥ 18 years: Upper and/or lower limb: Dose not exceed 400 Units per treatment session;
      ii. Age 2 through 17 years (a, b, and c):
         a) Upper limb: Dose does not exceed the lower of 6 Units/kg body weight or 200 Units per treatment session;
         b) Lower limb: Dose does not exceed the lower of 8 Units/kg body weight or 300 Units per treatment session;

c) If upper and lower limb spasticity are treated in the same treatment session, number of Units per treatment session does not exceed the lower of 10 Units/kg body weight or 340 Units per treatment session;

d. CD (i or ii):
   i. Age ≥ 18 years: Dose does not exceed 100 Units total in the SCM muscle and 300 Units per treatment session;
   ii. Age 16 through 17 years: Dose does not exceed 100 Units total in the SCM muscle and the lower of 10 Units/kg body weight or 300 Units per treatment session;
e. Primary axillary hyperhidrosis: Dose does not exceed 100 Units per treatment session;
f. Blepharospasm: Dose does not exceed 5 Units per muscle, 15 Units per eye, and 30 Units per treatment session;
g. Strabismus (i or ii):
   i. Vertical and horizontal strabismus: Dose does not exceed the lower of a two-fold increase or 25 Units per muscle and 50 Units per treatment session;
   ii. VI nerve palsy: Dose does not exceed the lower of a two-fold increase or 25 Units per muscle and 25 Units per treatment session;
h. Focal dystonia and essential tremor (i or ii):
   i. Laryngeal dystonia/OMD: Dose does not exceed 25 Units per treatment session;
   ii. UE dystonia, UE essential tremor: 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 the lower of 10 Units/kg body weight or 340 Units for pediatrics, or 400 Units for adults*);
i. HD, IAS achalasia, chronic anal fissure: Dose does not exceed 100 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

D. 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 the lower of 10 Units/kg body weight or 340 Units in a 3-month interval for pediatrics and 400 Units for adults.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CD: cervical dystonia
CGRP: calcitonin gene-related peptide
FDA: Food and Drug Administration
HD: Hirschsprung disease
IAS: internal anal sphincter
MS: multiple sclerosis
NDO: neurogenic detrusor overactivity
OAB: overactive bladder
OMD: oromandibular dystonia
SCI: spinal cord injury
SCM: sternocleidomastoid
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
Overactive bladder, urinary incontinence		
oxybutynin (Ditropan®/XL, Gelnique®) *(anticholinergic agent)*	• Immediate-release tablets (adults and children): 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
solifenacin (Vesicare®) *(anticholinergic agent)*	• Adults and children weighing more than 60 kg: 5 mg PO once daily • Children weighing between 46 to 60 kg: 4 mg PO once daily • Children weighing between 16 to 45 kg: 3 mg PO once daily • Children weighing between 9 to 15 kg: 2 mg once daily	10 mg/day
Myrbetriq® (mirabegron) *(beta-3 agonist)*	25 mg orally once daily	50 mg/day
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*
Primary axillary hyperhidrosis		
Drysol® (aluminum chloride)	Apply topically once daily	One application/day
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
HD, IAS achalasia		
Dulcolax® (bisacodyl)	5 to 15 mg PO or 10 mg PR QD	30 mg/day
MiraLax® (Polyethylene glycol 3350)	17 grams of polyethylene glycol 3350 in 4-8 oz water by mouth once daily	17 grams/day
Colace® (Docusate sodium)	50-200 mg PO QD-QID	200 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Chronic anal fissure		
nitroglycerin 0.2% ointment (Rectiv®)	15 to 30 mg (2.5 to 5 cm as squeezed from the tube, about 1 to 2 inches), applied topically to skin every 8 hours while awake and at bedtime; application frequency may be increased to every 6 hours if needed; alternatively, a regimen providing a 12-hour nitrate-free interval may be used; apply dosage once each morning, then 6 hours later	75 mg (12.5 cm as squeezed from the tube)/day
nifedipine or diltiazem (oral or topical ointment/gel-compounded)	PO: At provider discretion Intra-anal: 0.2% ointment or gel, applied around fissure(s) 2 times daily for 6-8 weeks	Varies
Sialorrhea: examples of anticholinergic drugs		
glycopyrrolate (Glycate® oral tablets, Cuvposa® oral solution)	• Adults: 1 mg PO TID *(Off-label: Lakraj 2013)* • 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)*	See regimen information
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

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 and Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation
  - Infection at the proposed injection site
  - Intradetrusor injections: urinary tract infection or urinary retention
- Boxed warning(s): distant spread of toxin effect

Appendix D: Botulinum Toxin Product Interchangeability

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

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 (2008, 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

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>Adults: OAB</td><td>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</td><td rowspan="2">See dosing regimens for maximum dose

Frequency:
• Esophageal acalasia: one treatment session every 24 weeks.</td></tr>
<tr><td>Pediatric NDO</td><td>• Weight ≥ 34 kg: 200 units
• Weight < 34 kg: 6 units/kg (see table below)
<table>
<tr><th>Body weight (kg)</th><th>Botox (mL)</th><th>Diluent (mL)</th><th>Final dose of Botox in dosing syringe</th></tr>
<tr><td>12 to > 14 kg</td><td>3.6</td><td>6.4</td><td>72 units</td></tr>
<tr><td>14 to < 16 kg</td><td>4.2</td><td>5.8</td><td>84 units</td></tr>
<tr><td>16 to < 18 kg</td><td>4.8</td><td>5.2</td><td>96 units</td></tr>
</table></td></tr>
</table>

Indication	Dosing Regimen				Maximum Dose
	18 to < 20 kg	5.4	4.6	108 units	• All other indications: one treatment session every 12 weeks.
	20 to < 22 kg	6	4	120 units	
	22 to < 24 kg	6.6	3.4	132 units	
	24 to < 26 kg	7.2	2.8	144 units	
	26 to < 28 kg	7.8	2.2	156 units	
	28 to < 30 kg	8.4	1.6	168 units	
	30 to < 32 kg	9	1	180 units	
	32 to < 34 kg	9.6	0.4	192 units	
Adults: urinary incontinence associated with neurologic condition	Up to approximately 6.7 Units IM per injection across up to 30 injection sites in the detrusor muscle for a total of up to 200 Units per treatment session				
Adults: chronic migraine	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				
Adults: upper and lower limb spasticity	Up to 50 Units IM per injection and up to 400 Units per treatment session				
Pediatrics: upper and limb spasticity	• 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				
Adults: CD	Up to 50 Units IM per injection, 100 Units total in the sternocleidomastoid (SCM) muscle, and 300 Units per treatment session				
Pediatrics: CD	Up to 50 Units IM per injection, 100 Units total in the SCM muscle, and the lower of 10 Units/kg body weight or 300 Units per treatment session				
Adults: axillary hyperhidrosis	Up to 50 Units IM per axilla per treatment session				
Adults and pediatrics: blepharospasm	• 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				
Adults and pediatrics: strabismus	• Botox naive: ○ Vertical muscles, or horizontal strabismus < 20 prism diopters: Up to 2.5 Units IM per muscle and 5 Units per treatment session				

Indication	Dosing Regimen	Maximum Dose
	○ Horizontal strabismus 20 to 50 prism diopters: Up to 5 Units IM per muscle and 10 Units per treatment session ○ VI nerve palsy: 2.5 Units IM in the medial rectus muscle and 2.5 Units per treatment session • Botox experienced: ○ Vertical and horizontal strabismus: Up to the lower of a two-fold increase or 25 Units IM per muscle and 50 Units per treatment session ○ VI nerve palsy: Up to the lower of a two-fold increase or 25 Units IM per muscle and 25 Units per treatment session	
Off-label uses		
Laryngeal dystonia	Up to 25 Units IM per treatment session. *(Off-label - Micromedex 2020)*	
UE dystonia UE essential tremor	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 the lower of 10 Units/kg body weight or 340 Units IM for pediatrics, or 400 Units IM for adults).	
OMD	Up to 25 Units IM per treatment session. *(Off-label - Hallet 2009)*	
Esophageal achalasia	Up to 100 Units IM per treatment session. *(Off-label - Vaezi 2013)*	
HD, IAS achalasia	Up to 100 Units IM per treatment session. *(Off-label - Langer 2017)*	
Chronic anal fissure	Up to 100 Units IM per treatment session. *(Off-label – ACG Guidelines 2021)*	

VI. Product Availability

Vials: 100 Units, 200 Units

VII. References

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Hirschsprung Disease, Internal Anal Sphincter Achalasia
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Chronic Anal Fissure
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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
J0585	Injection, onabotulinumtoxinA, 1 unit

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2019 annual review: added requirement that Botox is not prescribed concurrently with injectable CGRP inhibitors; removed coverage for hyperhidrosis for HIM due to benefit exclusion; references reviewed and updated.	01.15.19	05.19
RT4: criteria added for newly FDA approved indication for pediatric extension of upper limb spasticity.	07.23.19	
RT4: criteria added for newly FDA approved indication for pediatric extension of lower limb spasticity; removed 2% specific strength requirement for nitroglycerin ointment due to availability reasons; added disclaimer regarding hyperhidrosis as a benefit exclusion for HIM on continued therapy section.	11.06.19	
2Q 2020 annual review: CP criteria incorporated under upper/lower limb spasticity; rehabilitation specialist incorporated under physiatrist; previous (last 12 weeks) or concurrent toxin product use restriction added to all initial/continuation criteria; off-label uses limited to those with guideline-based support (laryngeal dystonia, OMD, UE dystonia/essential tremor, HD, IAD, esophageal achalasia - Appendix E); dosing updated per package insert/off-label literature (Section V); initial approval duration shortened to 12 weeks for esophageal achalasia and CCB trial added for chronic anal fissure per guidelines;	03.02.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
same-visit treatment for multiple indications is limited to upper/lower limb spasticity (Section III); references reviewed and updated.		
For chronic migraine, clarified requirement for use of two oral migraine preventative therapies that are from different therapeutic classes. RT4: updated FDA approved indication for spasticity which now includes cerebral palsy for lower limb spasticity in pediatric patients.	07.14.20	11.20
Per October SDC and prior clinical guidance, added the following redirections: Xeomin and Dysport for cervical dystonia and limb spasticity, Xeomin for blepharospasm. Ad hoc change: Per-injection dosing limitation removed to support individualized treatment for the following indications: OAB/urinary incontinence, chronic migraine, UE/LE, CD, primary axillary hyperhidrosis; CD continuation pediatric dosing is corrected to reflect 300 rather than 340 Units; for esophageal achalasia continuation criteria, prior toxin therapy is corrected to reflect 12 rather than 24 weeks with addition of a 24-week treatment session limitation after 2 or more sessions.	10.08.20	
2Q 2021 annual review: spasticity step therapy criteria updated; 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); added duration of trial needed for anal fissure; RT4: added newly FDA-approved diagnosis of pediatric detrusor overactivity; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.16.21	05.21
Ad Hoc update: max dose for Xeomin in Appendix B updated to 300 mg for CD per PI.	07.26.21	
Clarified continued approval duration for esophageal achalasia for 2nd dose vs beyond.	09.23.21	
2Q 2022 annual review: no significant changes; WCG.CP.PHAR.232 policy retired per SDC recommendation; removal of required 2 week trial duration of nitroglycerin and nifedipine/diltiazem for chronic anal fissures; adjusted Xeomin blepharospasm dose in Appendix B from 25 units to 50 units per PI; removal of the statement "**The treatment of hyperhidrosis is a benefit exclusion for HIM;*" references reviewed and updated.	02.07.22	05.22
Spelling corrected for "medial" for strabismus in section I and V.	05.05.22	
Added criteria for concurrent use with CGRP therapy requiring supportive evidence from published studies or clinical practice guidelines, positive response with CGRP monotherapy, and continued migraine burden. Template changes applied to other diagnoses/indications and continued therapy section.	07.19.22	11.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Ad Hoc update: max dose for chronic anal fissures updated from 25 units to 100 units per treatment session per ACG guidelines; updated limitation of use for hyperhidrosis per PI.	01.18.23	
2Q 2023 annual review: for chronic anal fissure, revised maximum dosing allowance up to 25 units for initial therapy and 100 units for continued therapy per treatment session; added chronic sialorrhea off-label indication; references reviewed and updated. Per February SDC: removed Dysport and/or Xeomin redirection requirement for upper and lower limp spasticity, cervical dystonia, blepharospasm, overactive bladder, chronic migraine, and axillary hyperhidrosis; for Overactive Bladder, updated criteria for adults to require use of two anticholinergic agents or one oral beta-3 agonist medication (previously both were required); changed Medicaid and HIM approval durations to 12 months.	02.21.23	05.23

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.