Clinical Policy: AbobotulinumtoxinA (Dysport)

Reference Number: CP.PHAR.230
Effective Date: 07.01.16
Last Review Date: 05.23
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

AbobotulinumtoxinA (Dysport®) is an acetylcholine release inhibitor and a neuromuscular blocking agent.

FDA Approved Indication(s)

Indication	Adults	Pediatrics	Treatment	Prophylaxis
Cervical dystonia (focal dystonia)	X		X	
Upper/lower limb spasticity (includes CP)	X	X	X	
Off-Label Uses				
Overactive bladder (OAB)	X		X	
Urinary incontinence	X		X	
Migraine	X			X
Axillary hyperhidrosis	X		X	
Blepharospasm (focal dystonia)	X		X	
Strabismus	X		X	
Sialorrhea	X			
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*

Dysport is indicated:

- For the treatment of cervical dystonia (CD) in adults
- For the treatment of spasticity in patients 2 years of age and older
- For temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adult patients < 65 years of age [*benefit exclusion*]

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 Dysport is **medically necessary** when one of the following criteria are met:

I. Initial Approval Criteria

A. 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 ≥ 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, shoulders or head;
5. Contractions are causing pain and functional impairment;
6. Dysport 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 500 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 months

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 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. Dysport 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 (i, ii, or iii):
      i. Upper limb spasticity: Dose does not exceed 1,000 Units per treatment session;
      ii. Lower limb spasticity: Dose does not exceed 1,500 Units per treatment session;
      iii. Upper and lower limb spasticity: Dose does not exceed 1,500 Units per treatment session staying within per limb dosing guidelines;
   b. Age ≥ 2 years to < 18 years (i, ii, or iii):
      i. Upper limb spasticity: Dose does not exceed the lower of 16 Units/kg or 640 Units;
      ii. Lower limb spasticity: Dose does not exceed the lower of 15 Units/kg (one limb), 30 Units/kg (two limbs), or 1,000 Units per treatment session;
      iii. Upper and lower limb spasticity: Dose does not exceed the lower of 30 Units/kg or 1,000 Units per treatment session staying within per limb dosing guidelines.

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

C. 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 one of the following (a or b), each used for at least 30 days, unless clinically significant adverse effects are experienced or all are contraindicated *(see Appendix B)*;
   a. Two anticholinergic agents;
   b. One oral beta-3 agonist medication;
5. Dysport 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 250 Units per treatment session.

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

D. 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. Dysport is not prescribed concurrently with injectable calcitonin gene-related peptide (CGRP) inhibitors (e.g., Aimovig®, Ajovy®, Emgality®);
6. Dysport 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 250 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)* (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. Dysport 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 200 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)* (off-label) (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. Dysport 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 120 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)* (off-label) (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. Dysport 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. Dose does not exceed 20 Units per treatment session.

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

H. 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. Dysport 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. Dose does not exceed 250 Units per treatment session;

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

I. 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 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. Dysport 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, b, or c):
   a. Laryngeal dystonia: Dose does not exceed 45 Units per treatment session;
   b. OMD: Dose does not exceed 100 Units per treatment session;
   c. 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 16 Units/kg body weight or 640 Units for pediatrics, or 1,000 Units for adults*).

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

J. 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. Dysport 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 250 Units per treatment session.

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

K. 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. Dysport is prescribed for constipation post-surgery;
   b. Internal anal sphincter (IAS) achalasia;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 3 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. Dysport 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 200 Units per treatment session.

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

L. 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. Dysport 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 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 Dysport treatment sessions, member has experienced and maintained a 30% reduction in monthly migraine headache frequency from baseline;
3. Dysport is not prescribed concurrently with injectable CGRP inhibitors (e.g., Aimovig, Ajovy, Emgality);
4. Dysport 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 250 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. Dysport 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 Dysport 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 250 Units per treatment session.

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

C. Cervical Dystonia and Upper/Lower Limb Spasticity (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. Dysport 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 or b):
   a. Age ≥ 18 years (i, ii, iii, or iv):
      i. CD: Dose does not exceed an increase of 250 Units per treatment session up to a total of 1,000 Units per treatment session;
      ii. Upper limb spasticity: Dose does not exceed 1,000 Units per treatment session;
      iii. Lower limb spasticity: Dose does not exceed 1,500 Units per treatment session;
      iv. Upper and lower limb spasticity: Dose does not exceed 1,500 Units per treatment session staying within per limb dosing guidelines;
   b. Age ≥ 2 years to < 18 years (i, ii, or iii):
      i. Upper limb spasticity: Dose does not exceed the lower of 16 Units/kg or 640 Units;
      ii. Lower limb spasticity: Dose does not exceed the lower of 15 Units/kg (one limb), 30 Units/kg (two limbs), or 1,000 Units per treatment session;
      iii. Upper and lower limb spasticity: Dose does not exceed the lower of 30 Units/kg or 1,000 Units per treatment session staying within per limb dosing guidelines.

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

D. All Other Indications in Section I (off-label) (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. Dysport 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. OAB/urinary incontinence, sialorrhea: Dose does not exceed 250 Units per treatment session;
   b. Axillary hyperhidrosis, HD, IAS achalasia: Dose does not exceed 200 Units per treatment session;
   c. Blepharospasm: Dose does not exceed 120 Units per treatment session;
   d. Strabismus: Dose does not exceed 20 Units per treatment session;
   e. Laryngeal dystonia: Dose does not exceed 45 Units per treatment session;
   f. OMD, 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

E. 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 30 Units/kg body weight or 1,000 Units for pediatrics and 1,500 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
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
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
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
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
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

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 excipients
  - Hypersensitivity to cow's milk protein
  - Infection at the proposed injection site
- Boxed warning(s): distant spread of toxin effect

Appendix D: Botulinum Toxin Product Interchangeability

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

Indication	Guideline
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

Indication	Dosing Regimen	Maximum Dose
CD	Divided among affected muscles every 12 weeks: Up to 1,000 Units IM	See dosing regimens for maximum dose Frequency: • Esophageal achalasia: one treatment session every 24 weeks. • All other indications: one treatment session every 12 weeks.
Adult upper and lower limb spasticity	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	
Pediatric upper and lower limb spasticity	Divided among affected muscles every 12 weeks: • Upper limb: Up to the lower 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/kg IM or 1,000 Units IM Upper and lower limbs: Up to the lower of 30 Units/kg IM or 1,000 Units IM staying within per limb guidelines	
Off-label uses		
Adults: OAB/ urinary incontinence associated with neurologic condition	Up to 250 Units IM in the detrusor muscle per treatment session. *(Off-label - Irwin 2013)*	
Adults: chronic migraine	Up to 250 Units IM per treatment session. *(Off-label - Alipour 2016, Menezes 2007)*	

Indication	Dosing Regimen	Maximum Dose
Adults: axillary hyperhidrosis	Up to 200 Units IM per treatment session. *(Off-label - Clinical Pharmacology, Heckmann 2001)*	
Adults: blepharospasm	Up to 120 Units SC per treatment session. *(Off-label - Hallet 2009, Micromedex, Truong 2008)*	
Adults: strabismus	Up to 20 Units IM per treatment session. *(Off-label - Bunting 2013, Talebnejad 2008)*	
Adults: chronic sialorrhea	Up to 250 Units IM per treatment session. *(Off-label - Guidubaldi 2011)*	
Adults: laryngeal dystonia	Up to 45 Units IM per treatment session. *(Off-label - Truong 2006, Guglielmino 2018)*	
Adults: OMD	Up to 100 Units IM per treatment session. *(Off-label - Hallet 2009)*	
Adults and pediatrics: UE dystonia Adults: 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 16 Units/kg body weight or 640 Units IM for pediatrics, or 1,000 Units IM for adults).	
Adults: esophageal achalasia	Up to 250 Units IM per treatment session. *(Off-label - Annese 1999)*	
Adults and pediatrics: HD, IAS achalasia	Up to 200 Units IM per treatment session. *(Off-label - Han-Geurts 2014, Roorda 2019)*	
Adults: chronic anal fissure	Up to 100 Units IM per treatment session. *(Off-label - Pilkington 2018)*	

VI. Product Availability

Vials: 300 units, 500 units

VII. References

1. Dysport Prescribing Information. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; July 2020. Available at: www.dysport.com. Accessed February 1, 2023.
2. AbobotulinumtoxinA. In: Micromedex. Ann Arbor, MI: Truven Health Analytics; 2020. Available from: www.micromedexsolutions.com. Accessed February 1, 2023.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Assessed February 1, 2023.

Migraine, Spasticity, Dystonia, Tremor

4. Albanese A, Bhatia K, Bressman SB, et al. Phenomenology and classification of dystonia: a consensus update. Mov Disord. June 15, 2013; 28(7): 863-873.
5. Alipour A, Homam SM, Khorashadizadeh M, et al. The effect of abobotulinum toxin A in the prophylactic treatment of refractory migraine. Turk J Neurol. 2016;22:156-160.

6. Bunting HJ, Dawson ELM, Lee JP, Adams GGW. Role of inferior rectus botulinum toxin injection in vertical strabismus resulting from orbital pathology. Strabismus. 2013 Sep;21(3):165-168.
7. Cloud LJ, Jinnah HA. Treatment strategies for dystonia. Expert Opin Pharmacother 2010; 11(1):5-15.
8. France K, Stoopler ET. The American Academy of Oral Medicine clinical practice statement: Oromandibular dystonia. Oral Med Oral Pathol Oral Radiol, April 2018; 125 (4), 283-285.
9. Guglielmino G, Teixeira de Moraes B, Villanova LC, et al. Comparison of botulinum toxin and propranolol for essential and dystonic vocal tremors. Clinics (Sao Paulo). 2018 Jul 16;73:e87.
10. Hallett M, Benecke R, Biltzer A et al. Treatment of focal dystonias with botulinum neurotoxin. Toxicon., October 2009;54(5):628-633.
11. Menezes C, Rodrigues B, Magalhaes E, Melo A. Botulinum toxin type A in refractory chronic migraine: an open-label trial. Arq Neuropsiquiatr. 2007;65(3-A):596-598.
12. Silberstein SD, Holland S, Freitag F et al. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012; 78(17): 1337-1345.
13. Ailani J, Burch RC, Robbins MS et al. The American Headache Society Consensus Statement: update on integrating new migraine treatments into clinical practice. Headache 2021;61:1021-1039
14. Simpson DM, Hallett M, Ashman EJ et al. Practice guideline update summary: botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2016; 86(19): 1818-1826.
15. Stachler RJ, Francis DO, Schwartz SR, Damask CC, et al. Clinical practice guidelines: Hoarseness (Dysphonia) (Update). American Academy of Otolaryngology–Head and Neck Surgery Foundation 2018. 1-42. https://doi.org/10.1177/0194599817751030
16. Position statement: botulinum toxin treatment. American Academy of Otolaryngology-Head and Neck Surgery. April 21, 2021. Available at: https://www.entnet.org/resource/position-statement-botulinum-toxin-treatment/. Accessed February 8, 2023.
17. Talebnejad MR, Sharifi M, Nowroozzadeh MH. The role of botulinum toxin in management of acute traumatic third-nerve palsy. J AAPOS. 2008;12(5):510-513.
18. Truong D, Comella C, Fernandez HH, et al: Efficacy and safety of purified botulinum toxin type A (Dysport) for the treatment of benign essential blepharospasm: a randomized, placebo-controlled, phase II trial. Parkinsonism Relat Disord. 2008;14(5):407-414.
19. Zesiewiz TA, Elbe RJ, Louis ED et al. Evidence-based guideline update: Treatment of essential tremor. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology Nov 2011, 77 (19) 1752-1755

Sialorrhea

20. AACPDM Sialorrhea Care Pathway Team: L Glader (team lead), C Delsing, A Hughes, J Parr, L Pennington, D Reddihough, K van Hulst, J van der Burg. Sialorrhea in cerebral palsy. Available at: https://www.aacpdm.org/publications/care-pathways/sialorrhea. Last updated June 4, 2018. Accessed February 1, 2023.

21. Guidubaldi A, Fasano A, Ialongo T, et al. Botulinum toxin A versus B in sialorrhea: a prospective, randomized, double-blind, crossover pilot study in patients with amyotrophic lateral sclerosis or Parkinson's disease. Movement Disorders. 2011;26(2):313-319.
22. Lakraj AA, Moghimi, Jabbari B. Sialorrhea: Anatomy, pathophysiology and treatment with emphasis on the role of botulinum toxins. Toxins 2013, 5, 1010-1031;
23. Seppi K, Chahine L, Chaudhuri R et al. Update on treatments for nonmotor symptoms of parkinson's disease-an evidence-based medicine review. Mov Disord. 2019 Feb;34(2):180-198.
24. Sridharan K, Sivaramakrishnan G. Pharmacological interventions for treating sialorrhea associated with neurological disorders: A mixed treatment network meta-analysis of randomized controlled trials. Journal of Clinical Neuroscience 51 (2018) 12–17.
25. Young CA, Johnson EC, et al. Treatment for sialorrhea (excessive saliva) in people with motor neuron disease/amyotrophic lateral sclerosis. Cochrane Database Syst Rev. 2011 May 11;(5):CD006981.

Overactive Bladder, Urinary Incontinence

26. Lightner DJ, Gomelsky A, Souter L, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline amendment 2019. J Urol 2019; 202: 558.
27. Irwin P, Somov P, Ekwueme K. Patient reported outcomes of abobotulinumtoxinA injection treatment for idiopathic detrusor overactivity: a pragmatic approach to management in secondary care. Journal of Clin Urol. 2013;6:1.

Primary Axillary Hyperhidrosis,

28. Heckmann M, Ceballos-Baumann AO, Plewig G. Botulinum toxin A for axillary hyperhidrosis (excessive sweating). N Engl J Med. 2001;344:488-493.
29. Pariser DM, Ballard A. Topical therapies in hyperhidrosis care. Dermatol Clin. October 2014; 32(4): 485-90.
30. Cefolio RJ, Milanez De Campos RJ, Bryant AS et al. The Society of Thoracic Surgeons expert consensus for the surgical treatment of hyperhidrosis. Ann Thorac Surg 2011;91:1642-8.

Esophageal Achalasia

31. Annese V, Bassotti G, Coccia G, et al. Comparison of two different formulations of botulinum toxin A for the treatment of esophageal achalasia. Aliment Pharmacol Ther. 1999;13:1347-1350.
32. Vaezi MF, Pandolfino JE, Yadlapati RH. American College of Gastroenterology clinical guideline: Diagnosis and management of achalasia. Am J Gastroenterol. 2020; 115(9): 1393-1411.

Hirschsprung Disease, Internal Anal Sphincter Achalasia

33. Han-Geurts IJM, Hendrix VC, de Blaauw I, et al. Outcome after anal intrasphincteric Botox injection in children with surgically treated Hirschsprung disease. JPGN. November 2014;59(5):604-607.
34. Langer JC, Rollins, MD, Levitt M. Guidelines for the management of postoperative obstructive symptoms in children with Hirschsprung disease. Pediatr Surg Int, 2017; 33:523-526.
35. Roorda D, Abeln ZAM, Oosterlaan J, et al. Botulinum toxin injections after surgery for Hirschsprung disease: Systematic review and meta-analysis. World J Gastroenterol. 2019 July 7;25(25):3268-3280.

Chronic Anal Fissure

36. Pilkington SA, Bhome R, Welch RE et al. Bilateral versus unilateral botulinum toxin injections for chronic anal fissure: a randomised trial. Techniques in Coloproctology. 2018;22:545-551.
37. Wald A, Bharucha AE, Limketkai B, et al. American College of Gastroenterology clinical guideline: Management of benign anorectal disorders. Am J Gastroenterol 2021; 116(10): 1987-2008.

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
J0586	Injection, abobotulinumtoxinA, 5 units

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.15.19	05.19
RT4: added use for pediatric upper limb spasticity and updated dosing per updated Dysport prescribing information; references reviewed and updated.	11.06.19	
2Q 2020 annual review: cerebral palsy included in spasticity criteria set without restriction; 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 limited to upper/lower limb spasticity (Section III); references reviewed and updated.	03.02.20	05.20
RT4: updated FDA approved indication for spasticity which now includes cerebral palsy for upper limb spasticity in pediatric patients.	07.15.20	
2Q 2021 annual review: 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 (OAB/urinary incontinence, migraine, AH, blepharospasm, strabismus, sialorrhea, LD, OMD, UE dystonia, UE essential tremor; EA, HD, IAS achalasia, CAF; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	01.14.21	05.21
Revised continued therapy max dose for chronic migraine from 155 units to 250 units; allowed continued approval of sialorrhea from 12 weeks to 16 weeks to match initial approval duration; clarified continued approval duration for esophageal achalasia for 2nd dose vs beyond.	09.23.21	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2022 annual review: revised max dose for blepharospasm from 60 units to 120 units per literature review; 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"; removal of the statement "**The treatment of hyperhidrosis is a benefit exclusion for HIM;*" references reviewed and updated.	02.01.22	05.22
Spelling corrected for "medial" for strabismus in section I.	05.05.22	
Template changes applied to other diagnoses/indications and continued therapy section.	10.07.22	
2Q 2023 annual review: per February SDC, for overactive bladder updated criteria to require use of two anticholinergic agents or one oral beta-3 agonist medication (previously both were required), revised Medicaid and HIM approval durations to 12 months; references reviewed and updated.	03.30.23	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.