Clinical Policy: IncobotulinumtoxinA (Xeomin)
Reference Number: CP.PHAR.231
Effective Date: 07.01.16
Last Review Date: 05.21
Line of Business: Commercial, HIM, Medicaid

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

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

FDA Approved Indication(s)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Adults</th>
<th>Pediatrics</th>
<th>Treatment</th>
<th>Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sialorrhea</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Upper limb spasticity (includes CP)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Cervical dystonia (focal dystonia)</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Blepharospasm (focal dystonia)</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

**Off-Label Uses**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Adults</th>
<th>Pediatrics</th>
<th>Treatment</th>
<th>Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower limb spasticity*</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Overactive bladder</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Migraine</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Axillary hyperhidrosis</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oromandibular dystonia**</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Upper extremity dystonia**</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Upper extremity essential tremor**</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

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

Xeomin is indicated for the treatment or improvement of:
- Chronic sialorrhea in patients 2 years of age and older
- Upper limb spasticity in adults
- Upper limb spasticity in pediatric patients 2 to 17 years of age, excluding spasticity caused by cerebral palsy
- Cervical dystonia in adults
- Blepharospasm in adults
- Temporary improvement in the appearance of moderate to severe glabellar lines with corrugator and/or procerus muscle activity in adults

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

I. Initial Approval Criteria
   A. Chronic Sialorrhea (must meet all):
      1. Diagnosis of chronic sialorrhea for at least the last three months due to one of the following (a or b):
         a. Underlying neurologic disorder (e.g., Parkinson disease, atypical parkinsonism, stroke, traumatic brain injury, cerebral palsy, amyotrophic lateral sclerosis);
         b. Craniofacial abnormality (e.g., Goldenhar syndrome);
      2. Prescribed by or in consultation with a neurologist or physiatrist;
      3. Age ≥ 2 years;
      4. Failure of at least one anticholinergic drug (see Appendix B), unless clinically significant adverse effects are experienced or all are contraindicated;
      5. Member meets both of the following (a and b):
         a. Xeomin is not prescribed concurrently with other botulinum toxin products;
         b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 16 weeks;
      6. Treatment plan provided detailing number of Units per indication and treatment session;
      7. Request is for one of the following (a or b):
         a. For age ≥ 18 years, dose does not exceed 30 Units per parotid gland, 20 Units per submandibular gland, 100 Units per treatment session;
         b. For age ≥ 2 years, dose does not exceed any of the following (i, ii, iii, iv, v, or vi):

II. Continued Approval Criteria
   A. Chronic Migraine
   B. All Other Indications in Section I
   C. Other diagnoses/indications

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

IV. Appendices

V. Dosage and Administration

VI. Product Availability

VII. References

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

I. Initial Approval Criteria
   A. Chronic Sialorrhea (must meet all):
      1. Diagnosis of chronic sialorrhea for at least the last three months due to one of the following (a or b):
         a. Underlying neurologic disorder (e.g., Parkinson disease, atypical parkinsonism, stroke, traumatic brain injury, cerebral palsy, amyotrophic lateral sclerosis);
         b. Craniofacial abnormality (e.g., Goldenhar syndrome);
      2. Prescribed by or in consultation with a neurologist or physiatrist;
      3. Age ≥ 2 years;
      4. Failure of at least one anticholinergic drug (see Appendix B), unless clinically significant adverse effects are experienced or all are contraindicated;
      5. Member meets both of the following (a and b):
         a. Xeomin is not prescribed concurrently with other botulinum toxin products;
         b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 16 weeks;
      6. Treatment plan provided detailing number of Units per indication and treatment session;
      7. Request is for one of the following (a or b):
         a. For age ≥ 18 years, dose does not exceed 30 Units per parotid gland, 20 Units per submandibular gland, 100 Units per treatment session;
         b. For age ≥ 2 years, dose does not exceed any of the following (i, ii, iii, iv, v, or vi):
i. For body weight 12 kg to < 15 kg, 6 Units per parotid gland, 4 Units per submandibular gland, 20 Units per treatment session;
ii. For body weight 15 kg to < 19 kg, 9 Units per parotid gland, 6 Units per submandibular gland, 30 Units per treatment session;
iii. For body weight 19 kg to < 23 kg, 12 Units per parotid gland, 8 Units per submandibular gland, 40 Units per treatment session;
iv. For body weight 23 kg to < 27 kg, 15 Units per parotid gland, 10 Units per submandibular gland, 50 Units per treatment session;
v. For body weight 27 kg to < 30 kg, 18 Units per parotid gland, 12 Units per submandibular gland, 60 Units per treatment session;
vi. For body weight ≥ 30 kg, 22.5 Units per parotid gland, 15 Units per submandibular gland, 75 Units per treatment session.

Approval duration:
Medicaid/HIM – 16 weeks (single treatment session)
Commercial – 6 months

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

Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months

C. Cervical Dystonia (must meet all):
1. Diagnosis of CD;
2. Prescribed by or in consultation with a neurologist, orthopedist, or physiatrist;
3. Age ≥ 18 years;
4. Member is experiencing involuntary contractions of the neck and shoulder muscles (e.g., splenius, sternocleidomastoid, levator scapulae, scalene, trapezius, semispinalis capitis) resulting in abnormal postures or movements of the neck, shoulder or head;
5. Contractions are causing pain and functional impairment;
6. Member meets both of the following (a and b):
   a. Xeomin is not prescribed concurrently with other botulinum toxin products;
b. 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 one of the following (a or b):
   a. Treatment-naïve: 120 Units per treatment session;
   b. Treatment-experienced: 300 Units per treatment session.

Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months

D. Blepharospasm \textit{(a focal dystonia)} (must meet all):
1. Diagnosis of blepharospasm;
2. Prescribed by or in consultation with a neurologist or ophthalmologist;
3. Age \(\geq 18\) years;
4. Member is experiencing significant disability in daily functional activities due to interference with vision;
5. Member meets both of the following (a and b):
   a. Xeomin is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan provided detailing number of Units per indication and treatment session;
7. Dose does not exceed 50 Units per eye per treatment session.

Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months

E. Overactive Bladder and Urinary Incontinence \textit{(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 \(\geq 18\) years;
4. Failure of a trial of at least two anticholinergic agents and one oral beta-3 agonist medication \textit{(see Appendix B)}, each used for at least 30 days, unless clinically significant adverse effects are experienced or all are contraindicated;
5. Member meets both of the following (a and b):
   a. Xeomin is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan provided detailing number of Units per indication and treatment session;
7. Dose does not exceed 200 Units per treatment session.
Approval duration:
Medicaid/HIM – 12 weeks (single treatment session)
Commercial – 6 months or to member’s renewal date, whichever is longer

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

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

G. Primary Axillary Hyperhidrosis (excessive underarm sweating) (off-label) (must meet all):
*The treatment of hyperhidrosis is a benefit exclusion for HIM
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. Member meets both of the following (a and b):
   a. Xeomin is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;
6. Treatment plan provided detailing number of Units per indication and treatment session;
7. Dose does not exceed 100 Units per treatment session.

Approval duration:
Medicaid – 12 weeks (single treatment session)
HIM – Benefit Exclusion (Not Approvable)
Commercial – 6 months or to member’s renewal date, whichever is longer

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

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

I. Other diagnoses/indications
   1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
      2. If receipt of ≥ 2 Xeomin treatment sessions, member has experienced and maintained a 30% reduction in monthly migraine headache frequency from baseline;
      3. Member meets all of the following (a, b, and c):
a. Xeomin is not prescribed concurrently with injectable CGRP inhibitors (e.g., Aimovig, Ajovy, Emgality);
b. Xeomin is not prescribed concurrently with other botulinum toxin products;
c. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 weeks;

4. Treatment plan details number of Units per indication and treatment session;

5. If request is for a dose increase, new dose does not exceed 155 Units per treatment session.

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

B. All Other Indications in Section I (must meet all):
*The treatment of hyperhidrosis is a benefit exclusion for HIM.
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Member meets both of the following (a and b):
   a. Xeomin is not prescribed concurrently with other botulinum toxin products;
   b. Botulinum toxin therapy for cosmetic or medical conditions has not been administered within the last 12 week (16 weeks if sialorrhea);
4. If request is for a dose increase, new dose does not exceed the following indication-specific maximums (a, b, c, d, e, f, or g):
   a. Chronic sialorrhea:
      i. For age ≥ 18 years, dose does not exceed 30 Units per parotid gland, 20 Units per submandibular gland, 100 Units per treatment session;
      ii. For age ≥ 2 years, dose does not exceed any of the following (a, b, c, d, e, or f):
         a) For body weight 12 kg to < 15 kg, 6 Units per parotid gland, 4 Units per submandibular gland, 20 Units per treatment session;
         b) For body weight 15 kg to < 19 kg, 9 Units per parotid gland, 6 Units per submandibular gland, 30 Units per treatment session;
         c) For body weight 19 kg to < 23 kg, 12 Units per parotid gland, 8 Units per submandibular gland, 40 Units per treatment session;
         d) For body weight 23 kg to < 27 kg, 15 Units per parotid gland, 10 Units per submandibular gland, 50 Units per treatment session;
         e) For body weight 27 kg to < 30 kg, 18 Units per parotid gland, 12 Units per submandibular gland, 60 Units per treatment session;
         f) For body weight ≥ 30 kg, 22.5 Units per parotid gland, 15 Units per submandibular gland, 75 Units per treatment session.
   b. Upper/lower limb spasticity, UE dystonia, UE essential tremor: 400 Units per treatment session;
   c. OMD: 25 Units per treatment session;
   d. CD (a or b):
      a) Treatment-naïve: 120 Units per treatment session;
      b) Treatment-experienced: 300 Units per treatment session;
e. Blepharospasm: 50 Units per eye per treatment session;
f. OAB/urinary incontinence: 200 Units per treatment session;
g. Axillary hyperhidrosis: 100 Units per treatment session.

Approval duration:
Medicaid/HIM – 16 weeks for sialorrhea (single treatment session), 12 weeks for all other indications (single treatment session)
Commercial – 12 months

C. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CD: cervical dystonia
FDA: Food and Drug Administration
MS: multiple sclerosis
OAB: overactive bladder
OMD: oromandibular dystonia
SCI: spinal cord injury
UE: upper extremity

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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sialorrhea: examples of anticholinergic drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>glycopyrrolate (Glycate® oral tablets, Cuvposa® oral solution)</td>
<td>• Adults: 1 mg PO TID</td>
<td>See regimen information</td>
</tr>
<tr>
<td></td>
<td>(Off-label: Lakraj 2013)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pediatrics: chronic drooling:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>children ≥ 3 years and adolescents</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤ 16 years:</td>
<td></td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/ Maximum Dose</td>
</tr>
<tr>
<td>-----------</td>
<td>----------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>IncobotulinumtoxinA</td>
<td>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)</td>
<td></td>
</tr>
<tr>
<td>benztrpine mesylate (oral tablets - 0.5 mg, 1 mg, 2 mg)</td>
<td>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)</td>
<td>See regimen information</td>
</tr>
<tr>
<td>Overactive bladder, urinary incontinence</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 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 |
| Chronic migraine | Examples of oral migraine preventive therapies -  
• Anticonvulsants: divalproex (Depakote®), topiramate (Topamax®)  
• Beta blockers: propranolol (Inderal®), metoprolol (Lopressor®), timolol  
• Antidepressants/tricyclic antidepressants: | Refer to prescribing information for dosing regimens. Refer to prescribing information |
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>amitriptyline (Elavil®), venlafaxine (Effexor®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Primary axillary hyperhidrosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drysol® (aluminum chloride)</td>
<td>Apply topically once daily</td>
<td>One application/day</td>
</tr>
<tr>
<td><strong>Dystonia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>carbidopa/levodopa (Sinemet®, Duopa®, Rytary®)</td>
<td>25 mg/100 mg PO QD, and increase by 1 tablet every 3 to 5 days.</td>
<td>1,200 mg/day of levodopa</td>
</tr>
<tr>
<td>trihexyphenidyl</td>
<td>30 mg PO QD</td>
<td>30 mg/day</td>
</tr>
</tbody>
</table>

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

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

**Appendix D: Botulinum Toxin Product Interchangeability**
- Potency Units of Xeomin are not interchangeable with other botulinum toxin product preparations (e.g., Dysport®, Botox®, Myobloc®).

**Appendix E: Guideline Support for Botulinum Toxin Use**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><em>Focal Dystonia</em> and Essential Tremor, and Headache</em>*</td>
<td></td>
</tr>
<tr>
<td>Blepharospasm, cervical dystonia, adult spasticity, and headache</td>
<td>Academy of Neurology (2016)</td>
</tr>
<tr>
<td>Focal limb dystonia - UE**</td>
<td>American Academy of Neurology (2008)</td>
</tr>
<tr>
<td>Sialorrhea</td>
<td>American Academy of Cerebral Palsy and Developmental Medicine (AACPDM, 2018); International Parkinson and Movement Disorder Society (2018)</td>
</tr>
<tr>
<td>Indication</td>
<td>Guideline</td>
</tr>
<tr>
<td>-------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Gastrointestinal Conditions (see guidelines for required oral medication information)</td>
<td></td>
</tr>
<tr>
<td>Esophageal achalasia</td>
<td>American College of Gastroenterology (2013)</td>
</tr>
<tr>
<td>HD and IAS achalasia</td>
<td>American Pediatric Surgical Association (2017)</td>
</tr>
<tr>
<td>Chronic anal fissure</td>
<td>American College of Gastroenterology (2014)</td>
</tr>
</tbody>
</table>

*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>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
</table>
| Chronic sialorrhea | • Adults: up to 30 Units IM per parotid gland, 20 Units IM per submandibular gland, and 100 Units IM per treatment session every 16 weeks.  
• Pediatrics (by body weight):  
  o 12 kg to < 15 kg, 6 Units per parotid gland, 4 Units per submandibular gland, 20 Units per treatment session;  
  o 15 kg to < 19 kg, 9 Units per parotid gland, 6 Units per submandibular gland, 30 Units per treatment session;  
  o 19 kg to < 23 kg, 12 Units per parotid gland, 8 Units per submandibular gland, 40 Units per treatment session;  
  o 23 kg to < 27 kg, 15 Units per parotid gland, 10 Units per submandibular gland, 50 Units per treatment session;  
  o 27 kg to < 30 kg, 18 Units per parotid gland, 12 Units per submandibular gland, 60 Units per treatment session;  
  o ≥ 30 kg, 22.5 Units per parotid gland, 15 Units per submandibular gland, 75 Units per treatment session. | Adults: 100 Units/16 weeks  
Pediatrics: 75 Units/16 weeks |
| CD            | Up to 120 Units IM per treatment session every 12 weeks for treatment-naïve patients. | 300 Units/12 weeks    |
### Indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blepharospasm</td>
<td>Up to 50 Units IM per eye per treatment session every 12 weeks.</td>
<td>100 Units/12 weeks</td>
</tr>
<tr>
<td>Upper limb spasticity</td>
<td>Up to 400 Units IM per treatment session every 12 weeks.</td>
<td>400 Units/12 weeks</td>
</tr>
<tr>
<td><strong>Off-label uses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults: Lower limb spasticity</td>
<td>Up to 400 Units IM per treatment session every 12 weeks.</td>
<td>400 Units/12 weeks</td>
</tr>
<tr>
<td>Adults: OAB/urinary incontinence associated with neurologic condition</td>
<td>Up to 200 Units IM in the detrusor muscle per treatment session every 12 weeks.</td>
<td>200 Units/12 weeks</td>
</tr>
<tr>
<td>Adults: chronic migraine</td>
<td>Up to 155 Units IM per treatment session every 12 weeks.</td>
<td>155 Units/12 weeks</td>
</tr>
<tr>
<td>Adults: axillary hyperhidrosis</td>
<td>Up to 100 Units IM per treatment session every 12 weeks.</td>
<td>100 Units/12 weeks</td>
</tr>
<tr>
<td>Adults: OMD</td>
<td>Up to 25 Units IM per treatment session every 12 weeks.</td>
<td>25 Units/12 weeks</td>
</tr>
<tr>
<td>UE dystonia</td>
<td>Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use and member age (prescriber must submit supporting evidence; number of Units per treatment session does not exceed 400 Units IM per treatment session every 12 weeks).</td>
<td>400 Units/12 weeks</td>
</tr>
</tbody>
</table>

### VI. Product Availability

Vial: 50 Units, 100 Units, 200 Units

### VII. References


### Sialorrhea

2. 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. Available at:


Overactive Bladder, Urinary Incontinence


Migraine, Spasticity, Dystonia, Tremor


**Primary Axillary Hyperhidrosis**

**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.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0588</td>
<td>Injection, incobotulinumtoxinA, 1 unit</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD and upper limb spasticity are split into separate criteria sets. Added to CD a definition and requirement of pain and functional</td>
<td>06.17</td>
<td>07.17</td>
</tr>
<tr>
<td>Reviews, Revisions, and Approvals</td>
<td>Date</td>
<td>P&amp;T Approval Date</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Impairment. CD dose reduced from 400 to 120 units per treatment session per PI.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blepharospasm definition is added; “focal dystonia” parenthetical is added clarifying it as a dystonia. Added examples of muscle groups and an informational footnote to upper limb spasticity. Efficacy statement added under continuation criteria. Removed safety information. Dystonia information is added at Appendix B. “Non-cosmetic” parenthetical added to the background FDA indication section; cosmetic coverage restriction reworded under the “Other Diagnoses/Indications” section to include notation of glabellar lines.</td>
<td>04.24.18</td>
<td>05.18</td>
</tr>
<tr>
<td>2Q 2018 annual review: added physical medicine and rehabilitation specialist for cervical dystonia and upper limb spasticity; combined Medicaid and Commercial lines of business; added HIM; intent of therapy language removed from upper limb spasticity indication; Commercial: approval durations changed from length of benefit to 6 months initial and 12 months continued approval; references reviewed and updated.</td>
<td>08.21.18</td>
<td>02.19</td>
</tr>
<tr>
<td>Criteria added for new FDA indication: chronic sialorrhea; references reviewed and updated.</td>
<td>02.05.19</td>
<td>05.19</td>
</tr>
<tr>
<td>2Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>06.25.19</td>
<td>11.19</td>
</tr>
<tr>
<td>Criteria updated for new FDA approved indication: first-line treatment for blepharospasms; references reviewed and updated.</td>
<td>10.08.19</td>
<td>02.20</td>
</tr>
<tr>
<td>Added requirement for trial of anticholinergic agents for chronic sialorrhea.</td>
<td>03.02.20</td>
<td>05.20</td>
</tr>
<tr>
<td>2Q 2020 annual review: HIM nonformulary language removed; sialorrhea medical trial added; rehabilitation specialist incorporated under physiatrist; previous (last 12 weeks) or concurrent toxin product use restriction added to all initial/continuation criteria; dosing updated per package insert; same-visit treatment for multiple indications is excluded (Section III); references reviewed and updated.</td>
<td>10.15.20</td>
<td></td>
</tr>
<tr>
<td>Updated max dosing for treatment-experienced patients for CD up to 300 Units per prior clinical guidance.</td>
<td>12.04.20</td>
<td></td>
</tr>
<tr>
<td>RT4: updated lower age limit from 18 years to 2 years for upper limb spasticity.</td>
<td>01.14.21</td>
<td>05.21</td>
</tr>
<tr>
<td>2Q 2021 annual review: chronic sialorrhea age updated to include pediatrics per FDA label; treatment plan requirement detailing number of Units per site and treatment session is changed to per indication and treatment session; treatment of multiple indications restriction removed and replaced with total treatment dose limitation (Section III); off-label uses added as follows per</td>
<td>12.04.21</td>
<td>05.21</td>
</tr>
</tbody>
</table>
Reviews, Revisions, and Approvals

| previously approved clinical guidance: adults (lower limb spasticity, OAB/urinary incontinence, migraine, AH, OMD, UE dystonia, UE essential tremor; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated. | Date | P&T Approval Date |

**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.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.