Clinical Policy: IncobotulinumtoxinA (Xeomin)
Reference Number: CP.PHAR.231
Effective Date: 07.01.16
Last Review Date: 05.20
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)
Xeomin is indicated
- For treatment or improvement of adult patients with:
  - Chronic sialorrhea
  - Upper limb spasticity
  - Cervical dystonia (CD)
  - Blepharospasm
- For temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients

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.

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 ≥ 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. 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 details number of Units per injection site and treatment session;
7. Dose does not exceed 30 Units per parotid gland, 20 Units per submandibular gland, 100 Units per treatment session.

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

**B. Upper Limb Spasticity** (must meet all):
1. Diagnosis of upper limb spasticity;
2. Prescribed by or in consultation with a neurologist, orthopedist, or physiatrist;
3. Age ≥ 18 years;
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 details number of Units per injection site 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 details number of Units per injection site 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 (a focal dystonia)** (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. 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 details number of Units per injection site and treatment session;
7. Dose does not exceed 25 Units per eye per treatment session.

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

E. 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.PHAR.21 for health insurance
   marketplace, and CP.PMN.53 for Medicaid.

II. Continued Approval
A. All Indications in Section I (must meet all):
   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, or d):
      a. Chronic sialorrhea: 30 Units per parotid gland, 20 Units per submandibular gland,
         100 Units per treatment session;
      b. Upper limb spasticity: 400 Units per treatment session;
      c. CD (a or b):
         a. Treatment-naïve: 120 Units per treatment session;
         b. Treatment-experienced: 300 Units per treatment session;
      d. Blepharospasm: 50 Units per eye 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

B. 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
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.PHAR.21 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. Same-visit treatment of multiple indications.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CD: cervical dystonia
FDA: Food and Drug Administration

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>glycopyrrolate (Glycate®)</td>
<td>1 mg PO TID</td>
<td>6 mg/day</td>
</tr>
<tr>
<td>benztropine (Cogentin®)</td>
<td>1 mg PO QD-BID</td>
<td>3.8 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®).

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic sialorrhea</td>
<td>Up to 30 Units IM per parotid gland, 20 Units IM per submandibular gland, and 100 Units IM per treatment session every 16 weeks.</td>
<td>100 Units/16 weeks</td>
</tr>
</tbody>
</table>
### Indication | Dosing Regimen | Maximum Dose
--- | --- | ---
CD | Up to 120 Units IM per treatment session every 12 weeks for treatment-naïve patients. Up to 300 Units IM per treatment session every 12 weeks for treatment-experienced patients. | 300 Units/12 weeks
Blepharospasm | Up to 25 Units IM per eye per treatment session every 12 weeks. | 100 Units/12 weeks
Upper limb spasticity | Up to 400 Units IM per treatment session every 12 weeks. | 400 Units/12 weeks

### VI. Product Availability
Vial: 50 Units, 100 Units, 200 Units

### VII. References

**Sialorrhea**

**Spasticity, Dystonia**

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>Policy split from CP.PHAR.09. Created criteria for new indication of upper limb spasticity per FDA labeling. Added max dosing per FDA labeling. Added prescriber requirement. Removed reauthorization criteria requiring attestation of significant improvement in symptoms and/or health-related quality of life.</td>
<td>05.16</td>
<td>07.16</td>
</tr>
<tr>
<td>CD and upper limb spasticity are split into separate criteria sets. Added to CD a definition and requirement of pain and functional impairment. CD dose reduced from 400 to 120 units per treatment session per PI. 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>06.17</td>
<td>07.17</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>04.24.18</td>
<td>05.18</td>
</tr>
<tr>
<td>Criteria added for new FDA indication: chronic sialorrhea; references reviewed and updated.</td>
<td>08.21.18</td>
<td>02.19</td>
</tr>
<tr>
<td>2Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>02.05.19</td>
<td>05.19</td>
</tr>
</tbody>
</table>
**Clinical Policy**

**IncobotulinumtoxinA**

<table>
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<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria updated for new FDA approved indication: first-line treatment for blepharospasms; references reviewed and updated.</td>
<td>06.25.19</td>
<td>11.19</td>
</tr>
<tr>
<td>Added requirement for trial of anticholinergic agents for chronic sialorrhea.</td>
<td>10.08.19</td>
<td>02.20</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>03.02.20</td>
<td>05.20</td>
</tr>
<tr>
<td>Updated max dosing for treatment-experienced patients for CD up to 300 Units per prior clinical guidance.</td>
<td>10.15.20</td>
<td></td>
</tr>
</tbody>
</table>

**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.

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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.

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