Clinical Policy: IncobotulinumtoxinA (Xeomin)
Reference Number: ERX.SPA.194
Effective Date: 01.11.17
Last Review Date: 11.18

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 the treatment or improvement of adult patients with:
- Chronic sialorrhea
- Upper limb spasticity
- Cervical dystonia (CD) in both botulinum toxin-naïve and previously treated patients
- Blepharospasm in adults previously treated with onabotulinumtoxinA (Botox®)
- 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 Envolve Pharmacy Solutions™ 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 an underlying neurologic disorder or craniofacial abnormality *(see Appendix D)*;
      2. Prescribed by or in consultation with a neurologist, physiatrist, or physical medicine and rehabilitation specialist;
      3. Age ≥ 18 years;
      4. Provider submits treatment plan detailing the quantity (in units) of Xeomin to be injected in each gland, anticipated frequency of injection(s), and total dose per visit;
      5. Dose does not exceed 100 units per treatment session.
   Approval duration: 16 weeks (single treatment session)

   B. Cervical Dystonia (must meet all):
      1. Diagnosis of CD *(see Appendix E)*;
      2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;
      3. Age ≥ 18 years;
      4. 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. Provider submits treatment plan detailing the quantity (in units) of Xeomin to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
      7. Dose does not exceed 120 units per treatment session.
   Approval duration: 12 weeks (single treatment session)

   C. Blepharospasm *(a focal dystonia)* (must meet all):
      1. Diagnosis of blepharospasm (i.e., abnormal contraction of eyelid muscles);
      2. Prescribed by or in consultation with a neurologist or ophthalmologist;
3. Age ≥ 18 years;
4. Member previously received treatment with onabotulinumtoxinA (Botox);
5. Provider submits treatment plan detailing the quantity (in units) of Xeomin to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
6. Dose does not exceed 35 units per eye per treatment session.

Approval duration: 12 weeks (single treatment session)

D. Upper Limb Spasticity (must meet all):
1. Diagnosis of upper limb spasticity;
2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;
3. Age ≥ 18 years;
4. Provider submits treatment plan detailing the quantity (in units) of Xeomin to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
5. Dose does not exceed 400 units per treatment session.

Approval duration: 12 weeks (single treatment session)

E. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
A. All Indications in Section I (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. It has been at least 12 weeks (16 weeks if sialorrhea) since the last injection of Xeomin;
4. Provider submits treatment plan detailing the quantity (in units) of Xeomin to be injected in each muscle site, anticipated frequency of injection, and total dose per visit;
5. If request is for a dose increase, new dose does not exceed the following indication-specific maximums (a or b):
   a. Chronic sialorrhea: 100 units per treatment session;
   b. CD: 120 units per treatment session;
   c. Upper limb spasticity: 400 units per treatment session;
   d. Blepharospasm: 35 units per eye per treatment session.

Approval duration: 12 weeks, or 16 weeks if sialorrhea (single treatment session)

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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).

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 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>Botox® (onabotulinumtoxinA)</td>
<td><strong>Blepharospasm</strong> 1.25 units to 2.5 units injected into the medial and lateral</td>
<td>5 units per site per treatment session; 200 total units per 30 days. Treatments last approximately three months.</td>
</tr>
<tr>
<td></td>
<td>pre-tarsal orbicularis oculi of the upper lid and into the lateral pre-tarsal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>orbicularis oculi of the lower lid.</td>
<td></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: Examples of Neurologic Disorders and Craniofacial Abnormalities
- Neurologic disorders:
  - Parkinson disease, atypical parkinsonism, stroke, traumatic brain injury, cerebral palsy, amyotrophic lateral sclerosis
- Craniofacial abnormalities:
  - Goldenhar syndrome

Appendix E: Definition and Classification of Dystonia
- Dystonia is defined as a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both.
  - Dystonic movements are typically patterned and twisting, and may be tremulous.
  - Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation.
- Dystonia is classified along two axes:
  - Clinical characteristics: Age at onset, body distribution, temporal pattern, associated features (additional movement disorders or neurological features) - the clinical characteristics fall into several specific dystonia syndromes that help to guide diagnosis and treatment;
  - Etiology: Nervous system pathology, inheritance.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
</table>
| Chronic sialorrhea | Xeomin is injected into the parotid and submandibular glands on both sides (i.e., 4 injection sites per treatment session). The recommended total dose per treatment session is 100 Units. The dose is divided with a ratio of 3:2 between the parotid and submandibular glands. | • One treatment period per 16 weeks
|                  |                                                                                | • 100 units per treatment session
|                  |                                                                                | • Parotid gland(s): 60 units (30 units per side)
<p>|                  |                                                                                | • Submandibular gland(s): 40 units (20 units per side)                        |
| CD               | The usual starting dose is 120 units per treatment session, doses up to 300 units may be used in treatment-experienced patients. Dose, number, and location of injection sites should be based on the number and location of muscles involved, severity of dystonia, and | 120 units per treatment session                                                                 |</p>
<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>response to any previous botulinum toxin injections.</td>
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</tr>
<tr>
<td>Blepharospasm</td>
<td>When initiating Xeomin therapy, the dose, number, and location of injections should be based on the previous dosing of Botox. If the previous dose of Botox is not known, the recommended starting dose is 1.25-2.5 units per injection site.</td>
<td>35 units per eye per treatment session</td>
</tr>
<tr>
<td>Upper limb spasticity</td>
<td>Dosing varies based on location of muscles to be treated (refer to dosing chart in the prescribing information).</td>
<td>400 units per treatment session</td>
</tr>
<tr>
<td>Chronic sialorrhea</td>
<td>Xeomin is injected into the parotid and submandibular glands on both sides (i.e., 4 injection sites per treatment session). The recommended total dose per treatment session is 100 Units. The dose is divided with a ratio of 3:2 between the parotid and submandibular glands.</td>
<td>One treatment period per 16 weeks, 100 units per treatment session, Parotid gland(s): 60 units (30 units per side), Submandibular gland(s): 40 units (20 units per side)</td>
</tr>
</tbody>
</table>

VI. Product Availability

Vials: 50 units, 100 units, 200 units

VII. References

CLINICAL POLICY
IncobotulinumtoxinA


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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</thead>
<tbody>
<tr>
<td>Policy created.</td>
<td></td>
<td>12.01.16</td>
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<tr>
<td>4Q17 Annual Review</td>
<td></td>
<td>10.03.17</td>
</tr>
<tr>
<td>Converted to new template.</td>
<td></td>
<td>01.17</td>
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<tr>
<td>Added requirement for documentation of positive response to therapy, for reauthorization.</td>
<td></td>
<td>11.17</td>
</tr>
<tr>
<td>2Q 2018 annual review: added physical medicine and rehabilitation specialist for relevant indications; broke up cervical dystonia and upper limb spasticity into separate criteria sets; required prescriber submission of treatment plan details for all initial and continued approval indications; references reviewed and updated.</td>
<td>02.09.18</td>
<td>05.18</td>
</tr>
<tr>
<td>Criteria added for new FDA indication: chronic sialorrhea; references reviewed and updated.</td>
<td></td>
<td>08.21.18</td>
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<td>11.18</td>
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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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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