Clinical Policy: IncobotulinumtoxinA (Xeomin)

Reference Number: PA.CP.PHAR.231
Effective Date: 01/18
Last Review Date: 04/19

Coding Implications
Revision Log

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
It is the policy of Pennsylvania Health and Wellness® that Xeomin is **medically necessary** when one of 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 cervical dystonia (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 or functional impairment;
6. Provider submits treatment plan detailing the quantity (in units) of Xeomin to be injected in each muscle site;
7. Prescribed dose of Xeomin 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;
6. Prescribed dose of Xeomin does not exceed 50 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;
5. Prescribed dose of Xeomin does not exceed 400 units per treatment session.

Approval duration: 12 weeks (single treatment session)

E. Other diagnoses/indications:
1. Refer to PA.CP.PMN.53 if requested indication is non-cosmetic.

II. Continued Approval

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. Provider submits treatment plan detailing the quantity (in units) of Xeomin to be injected in each muscle site;
4. 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: 50 units per eye per treatment session.

Approval duration: 12 weeks (single treatment session)

B. Other diagnoses/indications (1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
   Approval duration: 12 weeks (single treatment session); or

2. Refer to PA.CP.PMN.53; coverage is not approved for cosmetic use, including for treatment of glabellar frown lines, deep forehead wrinkles and periorbital wrinkles (crow's feet).

III. 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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Botox (onabotulinumtoxinA)	**Blepharospasm** 1.25 units to 2.5 units injected into the medial and lateral pre-tarsal orbicularis oculi of the upper lid and into the lateral pre-tarsal orbicularis oculi of the lower lid.	5 units per site per treatment session; 200 total units per 30 days. Treatments last approximately three months.

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.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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) • 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 response to any previous botulinum toxin injections.	120 units per treatment session
Blepharospasm	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.	50 units per eye per treatment session
Upper limb spasticity	Dosing varies based on location of muscles to be treated (*refer to dosing chart in the prescribing information*).	400 units per treatment session

V. Product Availability

Vials: 50 units, 100 units, 200 units

VI. References

1. Xeomin Prescribing Information. Frankfurt, Germany: Merz Pharmaceuticals, LLC; May 2019. Available at http://xeomin.com/wp-content/uploads/xeomin-full-prescribing-information.pdf. Accessed June 06, 2019.
2. Botox Prescribing Information. Madison, NJ: Allergan USA, Inc.; September 2018. Available at http://www.allergan.com/assets/pdf/botox_pi.pdf. Accessed January 25, 2019.
3. Blitzer A, Freidman A, Michel O, et al. Efficacy and safety of incobotulinumtoxinA for the treatment of sialorrhea in Parkinson's disease (PD) and other neurological conditions:

Results of a Phase III, placebo-controlled, randomized, double-blind study. Poster presented at: MDS 2017 (21st International Congress of Parkinson's Disease and Movement Disorders), Jue 4-8, 2017; Vancouver, BC, Canada. Full Text: https://www.pmrjournal.org/article/S1934-1482(17)31266-2/fulltext (Last accessed: 04 June, 2018.)

4. Seppi K, Chahine L, Chaudhuri R et al. International Parkinson and Movement Disorder Society evidence-based medicine review: Update on treatments for the non-motor symptoms of Parkinson's Disease. 2018. Available at https://www.movementdisorders.org/MDS-Files1/Resources/PDFs/EBM-NMS-Final-Paper-August-2018.pdf.
5. 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.
6. Lakraj AA, Moghimi, Jabbari B. Sialorrhea: Anatomy, pathophysiology and treatment with emphasis on the role of botulinum toxins. Toxins 2013, 5, 1010-1031; doi:10.3390/toxins5051010.
7. Seppi K, Weintraub D, Coelho M, et al. The Movement Disorder Society evidence-based medicine review update: Treatments for the non-motor symptoms of Parkinson's disease. Mov Disord. 2011 October ; 26(0 3): S42–S80.
8. 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. doi: 10.1002/14651858.CD006981.pub2.
9. Miller RG, Jackson CE, Kasarskis EJ, et al. Practice parameter update. The care of the patient with amyotrophic lateral sclerosis: Multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review). Neurology. 2009; 73:1227-1233.
10. Naumann M, So Y, Argoff CE, et al. Assessment: Botulinum neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. May 2008; 70(19): 1707-1714.
11. 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. doi:10.1002/mds.25475.
12. 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.

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
J0588	Injection, incobotulinumtoxinA, 1 unit

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: intent of therapy language removed from upper limb spasticity indication; removed requirement of at least 12 weeks have passed since last treatment; references reviewed and updated.	2.9.18	
2Q 2019 annual review: Criteria added for new FDA indication: chronic sialorrhea; maximum dose for treatment of blepharospasm changed to 50 Units per eye per treatment session. References reviewed and updated.	04/2019	