OVERVIEW
Botulinum neurotoxins produced by Clostridium botulinum, a gram-positive anaerobic bacterium, can prevent the release of acetylcholine, carrying chemical denervation and blockage of neuromuscular transmission. Botulinum toxins produce a presynaptic neuromuscular blockage by preventing release of acetylcholine from motor nerve terminals. The resulting chemical denervation of muscle induces local paresis or paralysis and individual muscles can be weakened selectively. Botulinum toxins have the advantage of being potent neuromuscular blocking agents with good selectivity, long duration of action and few side effects.

Of seven known distinct neurotoxins (A-G), onabotulinumtoxinA (Botox®/Botox Cosmetic), abobotulinumtoxinA (Dysport™), rimabotulinumtoxinB (Myobloc®) and incobotulinumtoxinA (Xeomin®) have been approved by the U.S. Food and Drug Administration for clinical use.

POLICY STATEMENT
Prior approval is required for BOTOX, DYSPORT, MYOBLOC and XEOMIN.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of botulinum toxins is recommended in those who meet the following criteria:

I. Gastrointestinal disorders: The Company considers botulinum toxin (BOTOX, DYSPORT, MYOBLOC and XEOMIN) medically necessary and eligible for reimbursement providing that at least one of the following medical criteria is met:
   - Esophageal achalasia and at least one of the following:
     1. High risk for complications associated with pneumatic dilation or surgical myotomy; or
     2. Failure of a prior dilation or myotomy; or
     3. Previous perforation due to pneumatic dilation; or
     4. Epiphrenic diverticulum or hiatal hernia; or
     5. Esophageal varices; or
   - Anal fissure refractory to conventional nonsurgical medical therapy (e.g., nitrate preparations, sitz baths, stool softeners, bulk agents, diet modifications);

II. Headache: The Company considers botulinum toxin (BOTOX, DYSPORT, MYOBLOC and XEOMIN) medically necessary and eligible for reimbursement providing that all of the following medical criteria are met:
   - Chronic migraines†; and
   - Evaluation and treatment of chronic migraines‡ with botulinum toxin must be performed by a board eligible or board certified neurologist, ophthalmologist, pain management specialist or by a physician certified in headache medicine;
Diagnosis of chronic migraines meets the following:

- Meets international Classification of Headache Disorders (ICHD-3) diagnostic criteria for chronic migraine headache (see appendix); and
- Failure, contraindication, or intolerance to at least two different prescription migraine prevention therapies after titration to maximal tolerated doses (e.g., beta-blockers, calcium channel blockers, anticonvulsants, antidepressants).

III. Hyperhidrosis: The Company considers botulinum toxin (BOTOX, DYSPORT, MYOBLOC and XEOMIN) medically necessary and eligible for reimbursement providing that all of the following medical criteria are met:

- Primary focal hyperhidrosis and
- Failure of (trial period of $\geq 1$ month), intolerance to or unable to receive conventional medical therapy for hyperhidrosis, including prescription strength aluminum chloride products and medications (e.g., anti-cholinergics, anti-inflammatories); and
- Presence of medical complications of hyperhidrosis, including skin maceration with secondary infection or significant functional impairment;

IV. Movement disorders: The Company considers botulinum toxin (BOTOX, DYSPORT, MYOBLOC and XEOMIN) medically necessary and eligible for reimbursement providing that the following medical criteria is met:

- Diagnosis of a movement or focal spastic disorder or excessive muscular contractions, including at least one of the following:
  1. Genetic torsion dystonia; or
  2. Acquired torsion dystonia; or
  3. Fragments of torsion dystonia; or
  4. Hereditary spastic paraplegia; or
  5. Multiple sclerosis; or
  6. Other demyelinating diseases of central nervous system; or
  7. Spastic hemiplegia; or
  8. Infantile cerebral palsy; or
  9. Quadriplegia and quadriparesis; or
  10. Paraplegia; or
  11. Diplegia of upper limbs; or
  12. Monoplegia of upper and/or lower limb; or
  13. Unspecified monoplegia; or
  14. Trigeminal nerve disorder; or
  15. Facial nerve disorder(s); or
  16. Spastic entropion; or
  17. Spastic ectropion; or
  18. Strabismus and other disorders of binocular eye movements including blepharospasm; or
19. Hemiplegia/hemiparesis; or
20. Paralysis of vocal cords or larynx; unilateral or bilateral, partial; or
21. Laryngeal spasm; or
22. Torticollis, unspecified (including cervical dystonia); or
23. Spasm of muscle (including upper and lower limb spasticity); or
24. Other musculoskeletal symptoms referable to limbs; or
25. Certain congenital musculoskeletal deformities of sternocleidomastoid muscle; or
26. Abnormal involuntary movements; or
27. Voice and resonance disorder, unspecified; or
28. Dysphonia; or
29. Other voice and resonance disorders; and

- Failure of, intolerance to or unable to receive conventional medical therapy (e.g., physical therapy, medication);

**V. Sialorrhea:** The Company considers botulinum toxin (BOTOX, DYSPORT, MYOBLOC and XEOMIN) medically necessary and eligible for reimbursement providing that all of the following medical criteria are met:

- Disability from sialorrhea due to conditions such as Parkinson’s disease or motor neuron disease; and
- Failure of, intolerance to or unable to receive a trial of conventional medical therapy, including but not limited to, anticholinergics and speech therapy;

**VI. Urinary Incontinence:** The Company considers botulinum toxin (BOTOX, DYSPORT, MYOBLOC and XEOMIN) medically necessary and eligible for reimbursement providing that all of the following medical criteria are met:

- Urinary incontinence due to neurogenic detrusor overactivity or overactive bladder; and
- Failure of, intolerance to or unable to receive anticholinergic therapy;

**NOTE:** Treatment of brow furrows, wrinkles, forehead creases or other skin lines is considered cosmetic and not eligible for reimbursement.

**Approval Duration:** 365 days (1 year)

**Appendix**

**International Headache Society Criteria for Migraine Diagnosis (ICHD-3)**

A. Headache (tension-type-like and/or migraine-like) on \( \geq \) 15 days per month for > 3 months and fulfilling criteria B and C; OR
B. Occurring in a patient who has had at least five attacks fulfilling criteria B-D for 1.1 Migraine without aura and/or criteria B and C for 1.2 migraine with aura; OR

C. On ≥ 8 days per month for > 3 months, fulfilling any of the following:
1. Criteria C and D for 1.1 Migraine without aura; or
2. Criteria B and C for 1.2 Migraine with aura; or
3. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative; OR

D. Not better accounted for by another ICHD-3 diagnosis.

<table>
<thead>
<tr>
<th>Migraine without aura</th>
<th>Migraine with aura</th>
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<tbody>
<tr>
<td>A. At least five attacks fulfilling criteria B–D</td>
<td>A. At least two attacks fulfilling criteria B and C</td>
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<tr>
<td>B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)</td>
<td>B. One or more of the following fully reversible aura symptoms:</td>
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<tr>
<td></td>
<td>1. visual</td>
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<td>2. sensory</td>
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<td>3. speech and/or language</td>
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<td></td>
<td>4. motor</td>
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<td>5. brainstem</td>
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<td></td>
<td>6. retinal</td>
</tr>
<tr>
<td>C. Headache has at least two of the following four characteristics:</td>
<td>C. At least two of the following four characteristics:</td>
</tr>
<tr>
<td>1. unilateral location</td>
<td>1. at least one aura symptom spreads gradually over ≥5 minutes, and/or two or more symptoms occur in succession</td>
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<td>2. pulsating quality</td>
<td>2. each individual aura symptom lasts 5-60 minutes</td>
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<td>3. moderate or severe pain intensity</td>
<td>3. at least one aura symptom is unilateral</td>
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<td>4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)</td>
<td>4. the aura is accompanied, or followed within 60 minutes, by headache</td>
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<tr>
<td>D. During headache at least one of the following:</td>
<td>D. Not better accounted for by another ICHD-3 diagnosis, and transient ischaemic attack has been excluded</td>
</tr>
<tr>
<td>1. nausea and/or vomiting</td>
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<td>2. photophobia and phonophobia</td>
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</tbody>
</table>

References