

Origination Date: 9/02	Revision Date(s): 7/03, 5/04, 5/05, 5/06, 5/07, 5/08, 12/09, 3/11
Developed By: Medical Criteria Committee	

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Approved: **Robert Neal Mills, MD**

Date: 03/04/11

ODS Rx <sup>1.0</sup> <input type="checkbox"/>	ODS Rx <sup>2.0</sup> <input checked="" type="checkbox"/>	OEBB <input checked="" type="checkbox"/>	OHP <input type="checkbox"/>
NON-SPECIALTY <input type="checkbox"/>	SPECIALTY <input checked="" type="checkbox"/>		
PA <input checked="" type="checkbox"/>	QLL <input type="checkbox"/>	STEP THERAPY <input type="checkbox"/>	

**PURPOSE:** To limit the use of onabotulinumtoxin A (Botox<sup>®</sup>), abobotulinumtoxin A (Dysport<sup>®</sup>), rimabotulinumtoxin B (Myobloc<sup>®</sup>), and incobotulinumtoxin A (Xeomin<sup>®</sup>) to the treatment of FDA approved indications. Prescription benefit coverage of this product is not allowed for cosmetic conditions.

**DESCRIPTION:** Botulinum toxin type A blocks neuromuscular transmission by binding to acceptor sites on motor nerve or sympathetic terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. This inhibition occurs as the neurotoxin cleaves SNAP-25, a protein integral to the successful docking and release of acetylcholine from vesicles situated within nerve endings. When injected IM at therapeutic doses, botulinum toxin type A produces partial chemical denervation of the muscle resulting in a localized reduction in muscle activity. In addition, the muscle may atrophy, axonal sprouting may occur, and extrajunctional acetylcholine receptors may develop. There is evidence that reinnervation of the muscle may occur, thus slowly reversing muscle denervation produced by botulinum toxin type A. When injected intradermally, botulinum toxin type A produces temporary chemical denervation of the sweat gland, resulting in local reduction in sweating.

Rimabotulinumtoxin B, a purified neurotoxin, acts at the neuromuscular junction to produce flaccid paralysis.

The 7 serologically distinct botulinum neurotoxins, designated A through G, share a common structural organization consisting of 1 heavy chain and 1 light chain polypeptide linked by a single disulfide bond. These toxins inhibit acetylcholine release at the neuromuscular junction via a 3-stage process: 1) heavy chain-mediated neurospecific binding of the toxin, 2) internalization of the toxin by receptor-mediated endocytosis, 3) and ATP- and pH-dependent translocation of the light chain to the neuronal cytosol, where it acts as a zinc-dependent endoprotease cleaving polypeptides essential for neurotransmitter release.

Rimabotulinumtoxin B specifically has been demonstrated to cleave synaptic vesicle-associated membrane protein (VAMP, also known as synaptobrevin), which is a component of the protein complex responsible for docking and fusion of the synaptic vesicle to the presynaptic membrane, a necessary step for neurotransmitter release.<sup>1</sup>

**PRODUCT AVAILABILITY:**

- Onabotulinumtoxin A (Botox<sup>®</sup>)
  - 100 units of lyophilized powder for solution, single-use vials
  - 200 units of lyophilized powder for solution, single-use vials
- Abobotulinumtoxin A (Dysport<sup>®</sup>)
  - 500 units of lyophilized powder for solution, single-use vials
- Rimabotulinumtoxin B (Myobloc<sup>®</sup>)

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- 5,000 units/mL in 0.5mL, 1mL, and 2mL single-use vials
- Incobotulinumtoxin A (Xeomin<sup>®</sup>)
  - 50 units of lyophilized powder for solution, single-use vials
  - 100 units of lyophilized powder for solution, single-use vials

**INDICATIONS:**

- Severe primary axillary hyperhidrosis (Botox only):
  - For the treatment of severe primary axillary hyperhidrosis that is inadequately managed with topical agents.
- Cervical dystonia (Botox, Dysport, Xeomin, and Myobloc):
  - For the treatment of cervical dystonia in adults to decrease the severity of abnormal head position and neck pain associated with cervical dystonia in both toxin-naïve and previously treated patients.
- Strabismus and blepharospasm associated with dystonia (Botox and Xeomin):
  - For the treatment of strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and older.
- Focal spasticity, specifically upper limb spasticity (Botox only):
  - For the treatment of upper limb spasticity in adults, to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), and finger flexors (flexor digitorum profundus and flexor digitorum sublimis).
- Chronic migraine (Botox only):
  - For the prophylactic (preventative) treatment of headaches in adults with chronic migraine, a distinct and severe neurological disorder characterized by patients who have a history of migraine and suffer from headaches on 15 or more days per month with headaches lasting four hours a day or longer, in patients 18 years and older.

**POLICY:** Botulinum toxin type A and type B has been used to treat numerous medical conditions. The risk versus benefits should be carefully evaluated before therapy is initiated, as efficacy and safety may not be established in all of these conditions. Payment consideration of botulinum toxin type A and type B will be allowed for non-cosmetic, medical conditions. The following list of medical indications gives examples for which coverage of botulinum toxin type A and type B is recommended. This is not an all-inclusive list. Requests for botulinum toxin type A and type B for indications not included in the following list will be evaluated by a pharmacist and/or a physician on a case-by-case basis to determine a coverage recommendation for the client.

**GUIDELINES FOR USE:**

- 1) **Is the patient 18 years of age or older?**
  - a) **If yes, go to #2**
  - b) **If no, forward to clinical for review**
- 2) **What is the patient's diagnosis?**
  - a) **If blepharospasm, go to #9**
  - b) **If cervical dystonia (torticollis), go to #10**
  - c) **If severe primary axillary hyperhidrosis, go to #3**
  - d) **If chronic migraine headaches, go to #4**
  - e) **If upper limb spasticity, go to #12**
  - f) **If strabismus, go to #13**
  - g) **If none of the above, forward to clinical for review**
- 3) **Has the patient tried and failed aluminum chloride (Drysol) for this condition?**
  - a) **If yes, go to #11**
  - b) **If no, forward to clinical for review**

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- 4) **What is the specialty of the prescribing physician?**
  - a) **If neurology, go to #6**
  - b) **If other, go to #5**
- 5) **Has the patient recently been evaluated by a neurology specialist?**
  - a) **If yes, go to #6**
  - b) **If no, forward to clinical for review**
- 6) **Has the patient failed at least a 90 day trial of another prophylactic migraine therapy regimen (e.g. beta-blockers, calcium channel blockers, Topamax, Depakote, etc.)?**
  - a) **If yes, go to #7**
  - b) **If no, forward to clinical for review**
- 7) **Has the patient experienced migraine headaches during at least 14 of the last 30 days?**
  - a) **If yes, go to #8**
  - b) **If no, forward to clinical for review**

**Chronic Migraine**

- 8) **Approve for duration of 12 weeks with the following quantity limits:**
  - a) **Botox 200 units per 84-day supply** (Copay will need to be manually set for 3 months of medication)

**Blepharospasm**

- 9) **Approve for duration of 12 weeks with the following quantity limits:**
  - a) **Botox 200 units per 84-day supply** (Copay will need to be manually set for 3 months of medication)
  - b) **Xeomin 100 units per 84-day supply** (Copay will need to be manually set for 3 months of medication)

**Cervical Dystonia**

- 10) **Approve for duration of 12 weeks with the following quantity limits:**
  - a) **Botox 300 units per 84-day supply** (Copay will need to be manually set for 3 months of medication)
  - b) **Dysport 1,000 units per 84-day supply** (Copay will need to be manually set for 3 months of medication)
  - c) **Xeomin 200 units per 84-day supply** (Copay will need to be manually set for 3 months of medication)
  - d) **Myobloc 5,000 units per 84-day supply** Copay will need to be manually set for 3 months of medication)

**Primary Axillary Hyperhidrosis**

- 11) **Approve for duration of 12 weeks with the following quantity limits:**
  - a) **Botox 100 units per 84-day supply** (Copay will need to be manually set for 3 months of medication)

**Upper Limb Spasticity**

- 12) **Approve for duration of 12 weeks with the following quantity limits:**
  - a) **Botox 200 units per 84-day supply** (Copay will need to be manually set for 3 months of medication)

**Strabismus**

- 13) **Approve for duration of 12 weeks with the following quantity limits:**
  - a) **Botox 100 units per 84-day supply** (Copay will need to be manually set for 3 months of medication)