OVERVIEW

Myobloc® (rimabotulinumtoxinB) is indicated for the treatment of patients with cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.¹ There are published studies and case reports supporting the use of botulinum toxin type B for other medical conditions.

Like the botulinum toxin type A products (Botox® and Botox® Cosmetic [onabotulinumtoxinA], Dysport® [abobotulinumtoxinA], and Xeomin® [incobotulinumtoxinA]), Myobloc has also been used to treat cosmetic conditions such as glabellar rhytides, crow’s feet, and platysmal bands, and it has been used in brow lifts.

Albeit rare, repeated injections of botulinum toxin type A products can lead to the formation of neutralizing antibodies which can result in clinical resistance. It is important to note that the presence of botulinum toxin type A antibodies are not equivalent to clinical nonresponse. Myobloc is antigenically distinct from botulinum toxin type A and, therefore, in some cases may be used as an alternative to botulinum toxin type A in type A-resistant patients.² Studies have attempted to establish a conversion ratio between botulinum toxin products, with variable results. In general, conversion ratios of 1:1 for Botox to Xeomin, 1:3 for Botox to Dysport, and 1:50 to 1:100 for Botox to Myobloc have been suggested.³,⁴

Other Uses with Supportive Evidence

Botulinum toxins, including Myobloc, have been studied in a variety of indications outside of FDA-approved uses. Literature is available to support use of Myobloc in the following conditions:

- **Anal Fissures**: Botulinum toxin type B was shown to improve anal fissures in one small, open-label study (using Neurobloc® [European formulation of Myobloc]).⁵ The ACG clinical guideline for the management of benign anorectal disorders (2014) recommends the use of botulinum toxin therapy or surgical internal anal sphincterotomy in patients who do not respond to conservative or topical pharmacologic agents, such as a calcium channel blockers or nitrates.⁵

- **Bladder Dysfunction**: Botulinum toxin type B was shown to be effective in improving symptoms of overactive bladder in one small randomized, double-blind, placebo-controlled study (formulation not specified) in patients unresponsive to oral antimuscarinic agents as well as one small open-label study (using Myobloc) and one case report (using Neurobloc) in quadriplegic patients with clinical resistance to botulinum toxin type A (Dysport and Botox).⁷,⁸,⁹ Oral pharmacologic therapy with antimuscarinic agents is the mainstay of drug therapy in the treatment of overactive bladder.¹⁰,¹¹

- **Blepharospasm**: Botulinum toxin type B was shown to be effective in treating blepharospasm in one small open-label study (formulation not specified), one retrospective study (formulation not specified) in patients with various neurological disorders, and one case report (using Myobloc) in a patient who was clinically resistant to botulinum toxin type A (Dysport and Botox).²,¹²,¹³ Botox is indicated for the treatment of blepharospasm associated with dystonia.¹⁴ While Xeomin is also indicated for blepharospasm, it is only indicated in patients previously treated with Botox.¹⁵ Dysport is not indicated for blepharospasm.¹⁶

- **Hemifacial Spasm**: Botulinum toxin type B was shown to be effective in treating hemifacial spasm in one small open-label study (formulation not specified) and one retrospective study in patients with various neurological disorders (formulation not specified).²,¹² Per American
Academy of Neurology (AAN) guidelines, botulinum toxin is possibly effective and may be considered for hemifacial spasm (Level C).

- **Hyperhidrosis, Palmar or Primary Axillary:** Myobloc was shown to be effective in treating palmar hyperhidrosis in one small, randomized, double-blind, placebo-controlled study and a second prospective, open, single-blind, multicenter study. Botulinum toxin type B was shown to be effective in treating axillary hyperhidrosis in one randomized, double-blind, placebo-controlled trial (using Myobloc) and one small, open-label study (using Neurobloc). There was no significant difference between Botox and Myobloc/Neurobloc in duration of effect in one small comparative study in patients with axillary hyperhidrosis. In a small (n = 10), single-blind, comparative study, botulinum toxin type B (Neurobloc) was significantly more effective than Botox in decreasing sweat weight and area. Topical antiperspirants (e.g., topical aluminum chloride) are recommended first-line therapies for the treatment of primary hyperhidrosis. In the setting of primary axillary hyperhidrosis, Qbrexza, a topical anticholinergic, may also be used first-line. The AAN notes that botulinum toxin therapy is established safe and effective in axillary hyperhidrosis (Level A). AAN guidelines state that botulinum toxins are probably safe and effective and should be considered for palmar hyperhidrosis (Level B).

- **Migraine Headache Prophylaxis in Patients with Chronic Migraine:** Botulinum toxin B (as Myobloc or Neurobloc) has been studied in three small open-label trials in 89 patients with primary headache, showing improvements similar to those described in open-label studies with botulinum toxin A (Botox and Dysport). Neither superiority nor inferiority of one type of the toxins to the other can be inferred at this time.

- **Myofascial Pain:** Botulinum toxin type B was effective in reducing myofascial pain associated with piriformis syndrome in two small open-label studies (one study did not specify the formulation used, the other study used Myobloc).

- **Spasticity (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis, hemifacial spasm):** Botulinum toxin type B was shown to be effective in reducing spasticity in one open-label study (formulation not specified) in children with spastic or dystonic movement disorders and in a randomized, double-blind, placebo-controlled study (n = 24) in hemiparetic patients with disabling elbow flexor overactivity after stroke or traumatic brain injury. In one small, randomized, double-blind, placebo-controlled study in patients with upper-limb post-stroke spasticity (n = 15), Myobloc reduced spasticity at 2 weeks but was not statistically significant at other follow-up visits.

- **Speech/Voice Disorder:** Myobloc was shown to be effective in the treatment of adductor spasmodic dysphonia in one small, open-label study and one case report in a patient clinically resistant to botulinum toxin type A.

**Dosing Considerations**

Definitive dosing has not been established for off-label uses of botulinum toxins, including Myobloc. Recommendations for maximum dosing and frequency for Myobloc are based on a suggested relative conversion of 50:1 between Myobloc and Botox units. Specific dosing considerations by indication are noted below:

- **Bladder Dysfunction:** Botox is indicated for urinary incontinence associated with neurological conditions, up to a maximum dose of 200 units administered not more frequently than once every 12 weeks.

- **Blepharospasm:** Botox is indicated for this use at a maximum dose of 200 units; Botox prescribing information also states that treatments may be repeated once every 3 months.

- **Hemifacial Spasm:** A maximum dose of 220 units of Dysport for this indication is supported. Recommendations for maximum dosing and frequency for Myobloc are based on a suggested relative conversion of 50:1 between Myobloc and Botox units and 3:1 for Dysport to Botox.
• **Hyperhidrosis, Palmar or Primary Axillary**: Botox is indicated for primary axillary hyperhidrosis at a dose of 50 units per axilla, administered not more frequently than once every 3 months.\(^{14}\) Dosing is not established for palmar hyperhidrosis, but in general, the Botox prescribing information states not to exceed a total dose of 400 units in a 3-month interval.

• **Migraine Headache Prophylaxis in Patients with Chronic Migraine**: Botox is indicated for migraine prophylaxis at a dose of 155 units, administered not more frequently than once every 3 months.\(^{14}\)

For other indications addressed in this policy, specific dosing guidance is not available. In these cases, dosing is based on the Botox prescribing information, which states not to exceed a total dose of 400 units in a 3-month interval.\(^{14}\)

**POLICY STATEMENT**

Prior authorization is recommended for medical benefit coverage of Myobloc. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Requests for doses outside the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for 1 year in duration. In cases where the dosing interval is provided in months, 1 month is equal to 30 days. Previous therapy is required to be verified by a clinician when noted in the criteria as [verification of therapies required].

Medical benefit coverage is not recommended for cosmetic conditions.

**RECOMMENDED AUTHORIZATION CRITERIA**

**FDA-Approved Indications**

1. **Cervical Dystonia (Spasmodic Torticollis)**. Approve for 1 year.

   **Dosing.** Approve up to a maximum dose of 5,000 units, administered not more frequently than once every 12 weeks.

2. **Sialorrhea (Salivary Hypersecretion), Chronic.** Approve for 1 year.

   **Dosing.** Approve up to a maximum dose of 3,500 units (1,750 units per side), administered not more frequently than once every 12 weeks.

**Other Uses with Supportive Evidence**

3. **Anal Fissures.** Approve for 1 year.

   **Dosing.** Approve up to a maximum dose of 20,000 units, administered not more frequently than once every 3 months.

4. **Bladder Dysfunction.** Approve for 1 year in patients who meet the following conditions (A and B):
   
   A) Patient has tried at least one other pharmacologic therapy (e.g., oral antimuscarinic agents [for example: oxybutynin, tolterodine tartrate, trospium chloride, Enablex, Toviaz, Vesicare]); AND
   
   B) Myobloc is being prescribed by or after consultation with a urologist.
Dosing. Approve up to a maximum dose of 10,000 units, administered not more frequently than once every 12 weeks.

5. Blepharospasm. Approve for 1 year if the patient has tried Botox.

Dosing. Approve up to a maximum dose of 10,000 units, administered not more frequently than once every 3 months.


Dosing. Approve up to a maximum dose of 4,000 units, administered not more frequently than once every 3 months.

7. Hyperhidrosis, Palmar or Primary Axillary. Approve for 1 year in patients who meet the following conditions (A and B):
   A) Patient has tried at least one topical agent (e.g., topical aluminum chloride, Qbrexa™ [glycopyrronium cloth 2.4% for topical use]); AND
   B) Patient has tried Botox.

Dosing. Approve the following regimens (A or B):
   A) For primary axillary hyperhidrosis: Approve a maximum dose of 2,500 units per axilla, administered not more frequently than once every 3 months.
   B) For palmar hyperhidrosis: Approve a maximum dose of 20,000 units, administered not more frequently than once every 3 months.

8. Migraine Headache Prophylaxis in Patients with Chronic Migraine. Approve for 1 year in patients who meet all of the following criteria (A, B, C, and D):
   A) Patient has ≥ 15 migraine headache days per month with headache lasting 4 hours per day or longer (prior to initiation of botulinum toxin therapy); AND
   B) Patient has tried at least two other prophylactic pharmacologic therapies, each from a different pharmacologic class (e.g., β-blocker, anticonvulsant, tricyclic antidepressant) [verification of therapies required]; AND
   C) Patient meets ONE of the following (i or ii):
      i. Patient has tried at least one triptan therapy (e.g., almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan); OR
      ii. Patient has a contraindication to triptan(s) according to the prescribing physician; AND
   D) Myobloc is being prescribed by or after consultation with a neurologist or headache specialist.

Dosing. Approve up to a maximum dose of 7,750 units, administered not more frequently than once every 3 months.


Dosing. Approve up to a maximum dose of 20,000 units, administered not more frequently than once every 3 months.
10. Spasticity (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis). Approve for 1 year.

Dosing. Approve up to a maximum dose of 20,000 units, administered not more frequently than once every 3 months.


Dosing. Approve up to a maximum dose of 20,000 units, administered not more frequently than once every 3 months.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Myobloc has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Cosmetic Uses (e.g., facial and/or glabellar rhytides [wrinkles, lines], crow’s feet, brow lifts, platysmal bands). Cosmetic use is not recommended for coverage as this indication is excluded from coverage in a typical medical benefit.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES
15. Xeomin® for injection [prescribing information]. Raleigh, NC: Merz Pharmaceuticals; December 2015.

Other References Utilized

HISTORY

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes</th>
<th>Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>New policy</td>
<td>--</td>
<td>08/08/2018</td>
</tr>
<tr>
<td>Selected revision</td>
<td>Changes</td>
<td>Date</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------------------------------------------------------------</td>
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<tr>
<td>Migraine prophylaxis: Change to require verification of specific therapies that have been tried for migraine prophylaxis.</td>
<td>09/19/2018</td>
<td></td>
</tr>
<tr>
<td>Dosing updated throughout policy to simplify maximum approved dosing regimens.</td>
<td>12/05/2018</td>
<td></td>
</tr>
<tr>
<td>Spasticity (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis): Changed to “i.e.” (previously written as “e.g.”).</td>
<td>05/08/2019</td>
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<td>Sialorrhea (Salivary Hypersecretion), Chronic: Moved to FDA-approved indications. “Chronic” added for clarification and to align with product labeling. Dosing updated to reflect FDA-labeled dose.</td>
<td>09/04/2019</td>
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