oscar

Clinical Guideline

Guideline Number: CG033, Ver. 2

Botulinum Toxin

Disclaimer

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Summary

Botulinum toxins are injectable medications that block the nerves controlling muscle function. Paralysis of the targeted muscles typically occurs within 2 to 5 days and lasts for 2 to 3 months. There are seven different types (A-G) of Botulinum toxin, but only types A and B are approved for clinical use. This medication class can be used to treat muscle spasms or muscle overactivity seen in a number of neurological conditions, such as cerebral palsy, stroke, and spinal cord disorders. Botulinum toxins can also be used for cosmetic purposes, such as for decreasing wrinkles, however cosmetic use is not covered by Oscar. Botulinum toxin preparations must be prescribed and administered by a licensed physician or medical provider.

Definitions

"Botulinum Toxins" refer to the seven serologically distinct neurotoxins derived from the bacterium *Clostridium botulinum*. These agents differ in their synthesis and the specific bacterium strain from which they are isolated. Botulinum toxins function by inhibiting acetylcholine release at the neuromuscular junction to cause flaccid paralysis of muscles. The four preparations that are currently approved for clinical use are:

1. **"AbobotulinumtoxinA" (Dysport)** - a type A botulinum toxin
2. **"OnabotulinumtoxinA" (Botox)** - a type A botulinum toxin
3. **"IncobotulinumtoxinA" (Xeomin)** - a type A botulinum toxin

4. **"RimabotulinumtoxinB" (Myobloc)** - a type B botulinum toxin

"Muscle Spasms" refer to the involuntary contractions of one or more muscles.

"Sialorrhea" (also known as **"Ptyalism"**) refers to excess salivation or drooling.

"Cervical Dystonia" (also known as **"Spasmodic Torticollis"**) refers to painful contraction of the neck muscles causing twisting or tilting of the head to one side.

"Hyperhidrosis" refers to inappropriate, excessive sweating.

"Blepharospasm" refers to uncontrolled blinking or spasms of the eyelids.

"Detrusor Hyperactivity" (also known as **"Bladder Overactivity"**) refers to spasms of the bladder muscles resulting in pain or incontinence.

"Achalasia" is failed relaxation of the lower esophageal sphincter resulting in painful spasms and/or regurgitation of food.

Clinical Indications and Coverage

OnabotulinumtoxinA (Botox) (J0585)

Oscar covers OnabotulinumtoxinA (Botox) for the following indications when the disease-specific criteria below are met:

A. Achalasia, when **ALL** of the following are met:
    a. Confirmed diagnosis with esophageal manometry; ***and***
    b. Presence of progressive dysphagia to solids and liquids; ***and***
    c. Pneumatic dilation or surgical myotomy has been attempted but was unsuccessful, or the member was not a good candidate for the procedure, or the member refused treatment; ***and***
    d. Contraindication or lack of response to appropriate pharmacologic treatment (e.g. calcium channel antagonists, long-acting nitrates); ***and***
    e. Alternative causes of the symptoms (e.g. esophageal stricture, carcinoma, schatzki's ring, or extrinsic compression), have been ruled out by upper endoscopy and/or adequately treated.

B. Chronic anal fissure, when **ALL** of the following are met:
    a. At least 2 months of symptoms, including **ONE** or more of the following:
        i. Nocturnal pain and bleeding; ***or***
        ii. Post-defecation pain.
    b. Failure of topical nitrates or contraindication to their use; ***and***
    c. The member is not a surgical candidate or has refused surgery; ***and***
    d. None of the following features are present:
        i. Anal fistula; ***or***
        ii. Hemorrhoids; ***or***
        iii. HIV; ***or***
        iv. Inflammatory bowel disease; ***or***
        v. Perianal abscess; ***or***
        vi. Perianal cancer; ***or***
        vii. Prior perianal surgical intervention.

C. Blepharospasm, when **ALL** of the following are met:
    a. Documented diagnosis of **ONE** or more of the following:
        i. Benign essential blepharospasm; ***or***
        ii. Blepharospasm associated with dystonia; ***or***
        iii. Blepharospasm associated with facial nerve disorders such as Bell palsy.
    b. Alternative causes of the symptoms have been ruled out or adequately treated, including but not limited to neuromuscular diseases (e.g. myasthenia gravis).

D. Hemifacial spasm, when **ALL** of the following are met:
    a. Documented diagnosis of hemifacial spasm in muscles innervated by the facial nerve (cranial nerve VII); ***and***
    b. Alternative causes of the symptoms have been ruled out or adequately treated, including but not limited to neuromuscular diseases (e.g. myasthenia gravis).

E. Cervical dystonia (i.e. spasmodic torticollis), when **ALL** of the following are met:
    a. Neck pain or abnormal head positioning adversely affects daily functioning; ***and***
    b. There are documented involuntary contractions in the neck muscles (e.g splenius, trapezius, posterior cervical, or sternocleidomastoid); ***and***
    c. Alternative causes of the symptoms have been ruled out or adequately treated, including but not limited to:
        i. Neuromuscular disease (e.g. myasthenia gravis); ***or***
        ii. Chronic neuroleptic treatment; ***or***
        iii. Fixed muscle contractures.
    d. Symptoms have been present for at least 6 months.

F. Axillary hyperhidrosis, when **ALL** of the following are met:
    a. Conservative treatment has failed, is contraindicated, or was not tolerated. Conservative treatment included both topical and oral therapy:
        i. Topical aluminum chloride or extra-strength antiperspirants; ***and***
        ii. Appropriate pharmacotherapy (e.g. beta blockers, anticholinergics, and/or benzodiazepines).
    b. Significant disruption in professional and/or social functioning has occurred because of excessive sweating; ***and***
    c. Alternative causes of the symptoms (e.g. hyperthyroidism, lifestyle factors), have been ruled out or adequately treated.

G. Laryngeal dystonia, when **ALL** of the following are met:
    a. Moderate to severe phonation difficulties; ***and***
    b. Adductor-type spasmodic dysphonia confirmed by fiberoptic laryngoscopy.

H. Migraine headache prophylaxis, when **ALL** of the following are met:
    a. Diagnosis of migraine headache per International Classification of Headache Disorders criteria, defined as meeting **ALL** of the following criteria:
        i. Headache is characterized by at least **TWO** of the following:
            1. Pulsating quality; ***or***
            2. Unilateral; ***or***
            3. Moderate to severe pain; ***or***
            4. Aggravated by physical activity.
        ii. Symptoms are associated with at least **ONE** of the following:
            1. Nausea and/or vomiting; ***or***
            2. Photobobia (sensitivity to light) and phonophobia (sensitivity to sound).
        iii. Other potential causes of headache have been ruled out.
    b. The migraine headaches meet the definition of chronic, defined as occurring for at least 4 hours per day, at a minimum of 15 days per month, and for 3 or more months; ***and***
    c. There is no neuromuscular disease (e.g. myasthenia gravis); ***and***
    d. Failure of at least 3 total medications from two different classes of migraine prophylaxis medications and at least 60 days duration for each medication. Classes include:
        i. Beta blockers
        ii. Tricyclic antidepressants
        iii. Antiepileptics
        iv. Calcium channel blockers
        v. ACE- or ARB-inhibitors.

I. Motor tics, when **ALL** of the following are met:
    a. Failure to respond to conservative therapy with *at least two different* neuroleptics; ***and***
    b. The tics are severe enough to interfere with daily functioning.

J. Neurogenic urinary incontinence, neurogenic detrusor overactivity, or detrusor sphincter dyssynergia, when **ALL** of the following are met:
    a. The condition is secondary to spinal cord injury or neurologic disease (e.g. multiple sclerosis); ***and***
    b. Conservative therapy with *at least one* appropriately dosed anticholinergic medications has failed or was contraindicated; ***and***
    c. Documented failure of behavioral therapy; ***and***
    d. No acute urinary retention unless the patient is receiving intermittent catheterization as part of the overall treatment plan; ***and***
    e. No acute urinary tract infection; ***and***
    f. Balloon sphincter dilation or surgical treatment has been attempted but was unsuccessful, or the member was not a candidate due to comorbidities, or the member refused surgery.

K. Overactive bladder with urge incontinence, when **ALL** of the following are met:
    a. Conservative therapy with *at least three* appropriately dosed, prescription anticholinergic medications has failed or was contraindicated; ***and***
    b. Documented failure of behavioral therapy; ***and***
    c. No acute urinary retention; ***and***
    d. No acute urinary tract infection; ***and***
    e. Urodynamic testing confirms urge urinary incontinence.

L. Raynaud's syndrome, when **ALL** of the following are met:
    a. Non-pharmacologic treatment including behavioral intervention, avoidance of sympathomimetic medications, and smoking cessation have failed to resolve symptoms; ***and***
    b. Medical treatment with an adequate trial oral (e.g. calcium channel blockers, PDE5 inhibitors) and topical agents (e.g. nitrates) has failed to improve symptoms; ***and***
    c. IV prostaglandin therapy has failed to improve symptoms of digital ischemia.

M. Sialorrhea, when **ALL** of the following are met:
    a. Caused by neurological disease (such as Amyotrophic Lateral Sclerosis or Parkinson's disease or Cerebral Palsy); ***and***
    b. Refractory to two months of continuous, appropriate pharmacotherapy (e.g. oral anticholinergics); ***and***

c. Documented complications such as recurrent infection or chronic skin breakdown that have failed treatment with topical agents or lifestyle modifications.

N. Spasticity, when **BOTH** of the following criteria are met:
   a. The member is characterized by **ONE** of the following:
      i. Children greater than the age of 2 with spasticity due to cerebral palsy who are receiving ongoing rehabilitation; ***or***
      ii. Adult members with spasticity secondary to my multiple sclerosis or other demyelinating diseases of the central nervous system; ***or***
      iii. Adults members with post-stroke spasticity of the upper or lower extremity.
   b. The member meets **ALL** of the following:
      i. Documentation of abnormal muscle tone that interferes with daily functioning or is expected to result in joint contracture with further growth; ***and***
      ii. Surgical intervention is the only alternative option; ***and***
      iii. Appropriate non-surgical medical treatment has failed; ***and***
      iv. Treatment is expected to improve functioning and/or allow for further therapeutic rehabilitation.

O. Strabismus, when **ALL** of the following are met:
   a. The deviation is a maximum of 50 prism diopters; ***and***
   b. The strabismus is not primarily due to any of the following:
      i. Duane syndrome with lateral rectus muscle weakness; ***or***
      ii. Restrictive strabismus; ***or***
      iii. Prior surgical over-recession of antagonist orbital musculature.

P. Upper extremity focal dystonia (e.g. writer's cramp), when **ALL** of the following are met:
   a. No prior surgical intervention; ***and***
   b. Conservative therapy and/or lifestyle modification has failed; ***and***
   c. Significant pain and/or abnormal hand or forearm positioning that adversely affects daily functioning.

AbobotulinumtoxinA (Dysport) (J0586)

Oscar covers AbobotulinumtoxinA (Dysport) for the following indications when the disease-specific criteria below are met:

A. Blepharospasm or hemifacial spasms, when **ALL** of the following are met:
   a. Documented diagnosis of **ONE** or more of the following:
      i. Benign essential blepharospasm; ***or***
      ii. Blepharospasm associated with dystonia; ***or***
      iii. Hemifacial spasm involving the orbicularis oculi muscle.

b. Alternative causes of the symptoms have been ruled out or adequately treated, including, but not limited to, neuromuscular diseases (e.g. myasthenia gravis).

B. Cervical dystonia (i.e. spasmodic torticollis) when **ALL** of the following are met:
   a. Neck pain or abnormal head positioning adversely affects daily functioning; ***and***
   b. There are documented involuntary contractions in the neck muscles (e.g splenius, trapezius, posterior cervical, or sternocleidomastoid); ***and***
   c. Alternative causes of the symptoms have been ruled out or adequately treated, including, but not limited to:
      i. Neuromuscular disease (e.g. myasthenia gravis); ***or***
      ii. Chronic neuroleptic treatment; ***or***
      iii. Fixed muscle contractures.
   d. Symptoms have been present for at least 6 months.

C. Axillary hyperhidrosis, when **ALL** of the following are met:
   a. Conservative treatment has failed, is contraindicated, or was not tolerated. Conservative treatment included both topical and oral therapy:
      i. Topical aluminum chloride or extra-strength antiperspirants; ***and***
      ii. Appropriate pharmacotherapy (e.g. beta blockers, anticholinergics, and/or benzodiazepines).
   b. Significant disruption in professional and/or social functioning has occurred because of excessive sweating; ***and***
   c. Alternative causes of the symptoms (e.g. hyperthyroidism, lifestyle factors), have been ruled out or adequately treated.

D. Sialorrhea, when **ALL** of the following are met:
   a. Caused by neurological disease (e.g. Amyotrophic Lateral Sclerosis or Parkinson's disease or Cerebral Palsy); ***and***
   b. Refractory to two months of continuous, appropriate pharmacotherapy (e.g. oral anticholinergics); ***and***
   c. Documented complications such as recurrent infection or chronic skin breakdown that have failed treatment with topical agents and/or lifestyle modifications.

E. Spasticity, when **BOTH** of the following criteria are met:
   a. The member can be characterized into **ONE** of the following:
      i. Children greater than the age of 2 with spasticity due to cerebral palsy who are receiving ongoing rehabilitation; ***or***
      ii. Adult members with spasticity secondary to multiple sclerosis or other demyelinating diseases of the central nervous system; ***or***
      iii. Adults members with post-stroke spasticity of the upper or lower extremity.

b. The member meets **ALL** of the following:
    i. Documentation of abnormal muscle tone that interferes with daily functioning or is expected to result in joint contracture with further growth; ***and***
    ii. Surgical intervention is the only alternative option; ***and***
    iii. Appropriate non-surgical medical treatment has failed; ***and***
    iv. Treatment is expected to improve functioning and/or allow for further therapeutic rehabilitation.

F. Upper extremity focal dystonia (e.g. writer's cramp), when **ALL** of the following are met:
    a. No prior surgical intervention; ***and***
    b. Failure of at least two months of conservative therapy and/or lifestyle modification; ***and***
    c. Significant pain and/or abnormal hand or forearm positioning that adversely affects daily functioning.

RimabotulinumtoxinB (Myobloc) (J0587)

Oscar covers RimabotulinumtoxinB (Myobloc) for the following indications when the disease-specific criteria below are met:

A. Cervical dystonia (i.e. spasmodic torticollis), when **ALL** of the following are met:
    a. Neck pain or abnormal head positioning adversely affects daily functioning; ***and***
    b. There are documented involuntary contractions in the neck muscles (e.g splenius, trapezius, posterior cervical, or sternocleidomastoid); ***and***
    c. Alternative causes of the symptoms have been ruled out or adequately treated, including but not limited to:
        i. Neuromuscular disease (e.g. myasthenia gravis); ***or***
        ii. Chronic neuroleptic treatment; ***or***
        iii. Fixed muscle contractures.
    d. Symptoms have been present for at least 6 months.

B. Sialorrhea, when **ALL** of the following are met:
    a. Caused by neurological disease (e.g. Amyotrophic Lateral Sclerosis or Parkinson's disease or cerebral palsy); ***and***
    b. Refractory to two months of continuous, appropriate pharmacotherapy (e.g. oral anticholinergics); ***and***
    c. Documented complications such as recurrent infection or chronic skin breakdown that have failed treatment with topical agents or lifestyle modifications.

IncobotulinumtoxinA (Xeomin) (J0588)

Oscar covers IncobotulinumtoxinA (Xeomin) for the following indications when the disease-specific criteria below are met:

A. Blepharospasm or hemifacial spasms, when **ALL** of the following are met:
    a. Documented diagnosis of benign essential blepharospasm, dystonia, or hemifacial spasm involving the orbicularis oculi muscle; ***and***
    b. Alternative causes of the symptoms have been ruled out or adequately treated, including but not limited to neuromuscular diseases (e.g. myasthenia gravis).
B. Cervical dystonia (i.e. spasmodic torticollis), when **ALL** of the following are met:
    a. Neck pain or abnormal head positioning adversely affects daily functioning; ***and***
    b. There are documented involuntary contractions in the neck muscles (e.g splenius, trapezius, posterior cervical, or sternocleidomastoid); ***and***
    c. Alternative causes of the symptoms have been ruled out or adequately treated, including but not limited to:
        i. Neuromuscular disease (e.g. myasthenia gravis); ***or***
        ii. Chronic neuroleptic treatment; ***or***
        iii. Fixed muscle contractures.
    d. Symptoms have been present for at least 6 months.
C. Spasticity of the upper limb in adults when **ALL** of the following are met:
    a. Documentation of abnormal muscle tone that interferes with daily functioning; ***and***
    b. Surgical intervention is the only alternative option; ***and***
    c. Appropriate non-surgical medical treatment has failed; ***and***
    d. Treatment is expected to improve functioning and/or allow for further therapeutic rehabilitation.

Continued Care

Criteria for Continuing Treatment After Initial Trial

Continuing treatment with botulinum toxin, except as outlined for specific conditions elsewhere, is considered medically necessary and covered by Oscar when, at the end of the initial trial period:

A. There is a documented positive response in the medical record (the response should generally last 3 months); ***and***
B. The member continues to meet the clinical criteria for the specific botulinum toxin agent; ***and***
C. The prescribing clinician provides an expected duration and frequency of ongoing treatment, which may require ongoing approval (Note: It is generally **NOT** considered medically necessary to provide botulinum toxin treatments more frequently than every 3 months for a covered condition, regardless of diagnosis).

General Recommendations for Time to Retreatment

Assuming all other clinical criteria continue to be met, the following are general recommendations for time to retreatment with botulinum toxin agents. These durations may vary by individual member but should not occur more frequently than every 3 months. Requests for injection frequency more often than specified below should be accompanied with documentation of medical necessity:

1. Botox:
    a. Blepharospasm - 3 months
    b. Cervical dystonia - 3 months
    c. Spasticity in children with cerebral palsy - 3 months
    d. Axillary hyperhidrosis - 4 months
    e. Spasmodic dysphonia - 3 months
    f. Strabismus - 3 months
    g. Upper limb spasticity - 3 months
    h. Chronic migraine - 3 months
    i. Hemifacial spasm - 3 months
    j. Achalasia - 3 months
    k. Focal hand dystonia - 3 months
    l. Sialorrhea - 3 months
    m. Urinary incontinence due to detrusor overactivity secondary to neurologic condition - 6-12 months
    n. Overactive bladder - 3-6 months
2. Dysport:
    a. Cervical dystonia - 3 months
    b. Upper limb spasticity - 3 months
    c. Pediatric lower limb spasticity - 3 months
3. Mybloc
    a. Cervical dystonia - 3-4 months
4. Xeomin
    a. Blepharospasm - 3 months
    b. Upper limb spasticity - 3 months

***Note:** when not specifically mentioned above, frequency should not exceed 3 months regardless of the indication.

Criteria for Discontinuing Treatment

Botulinum toxin treatment is generally no longer covered and should be discontinued, except as outlined for specific conditions elsewhere, when the following criteria are met:

A. Lack of documented clinical response after initial trial; ***or***
B. In cases where initial trial was successful, lack of documented clinical response to two consecutive treatments precludes treatment at that site for a period of at least one year.

For botulinum toxin injection for migraine headaches meeting the above clinical criteria, continuing treatment is considered medically necessary and covered by Oscar when, at the end of the initial trial period:

A. The frequency of migraine headaches was reduced by at least 7 days over a one month period compared to the pre-treatment average; ***or***
B. The duration of migraine headaches was reduced by at least 100 hours total over a one month period compared to the pre-treatment average.

***Note:** the trial period for migraine headaches is defined as 6 months or a maximum of 2 treatments.

Coverage Exclusions

General Exclusions

All botulinum toxin preparations (regardless of type) are considered contraindicated, experimental, investigational, or unproven, and thus not covered, in the following cases:

1. Infection at the proposed injection site
2. Known hypersensitivity to any botulinum toxin preparation or the components in the formulation
3. Retreatment of a condition with the same or different agent after a failed initial trial, regardless of if the member continues to meet clinical criteria. Note: If the member initially failed therapy due to an agent-specific intolerance or reaction, rather than a clinical feature, then this statement may not apply
4. **ALL** cosmetic purposes

Botulinum toxin antibody assays are considered experimental, investigational, or unproven, and thus not covered by Oscar.

AbobotulinumtoxinA (Dysport) (J0586)

The use of AbobotulinumtoxinA (Dysport) for any other indication not listed above is *not covered* by Oscar, as it is considered experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

A. Anal fissure
    a. *Rationale for non-coverage:* A study comparing 100 patients randomized to Dysport/Botox versus topical nitrates for anal fissures demonstrated greater rates of healing in the botulinum toxin group, however the efficacies for the two types of toxins

were not individually reported. The current evidence is insufficient to support Dysport for this indication.[1]

B. Benign prostatic hypertrophy (BPH)
    a. *Rationale for non-coverage:* A 2011 review article on abobotulinumtoxinA for lower urinary tract symptoms related to BPH concluded that the level of evidence is low and further randomized controlled trials are necessary.[2]
C. Charcot-Marie-Tooth disease[3]
D. Chronic musculoskeletal and myofascial pain
    a. *Rationale for non-coverage:* A systematic review of the available randomized trials found lack of efficacy for Dysport in myofascial pain syndromes.[4]
E. Headaches, including migraines, tension headaches, or headaches secondary to cranial neuralgia
    a. *Rationale for non-coverage:* A prospective, multi-center, randomized, double-blind placebo-controlled trial found no significant difference between placebo and Dysport in headache free days (primary outcome) among patients suffering from chronic migraine.[5-6]
F. Hyperhidrosis, other than axillary hyperhidrosis
    a. *Rationale for non-coverage:* An expert review by the American Academy of Neurology concluded that the evidence for Dysport in palmar hyperhidrosis was inadequate to guide clinical decision making.[7]
G. Sialorrhea in children
    a. *Rationale for non-coverage:* A Cochrane review and a separate systematic review on children with excessive salivation/drooling associated with cerebral palsy concluded that the evidence is insufficient to determine the efficacy of AbobotulinumtoxinA in this patient group.[8-9]
H. Lateral epicondylitis[22]
I. Obesity[23]
J. Plantar fasciitis[24]
K. Postnatal brachial plexus injury[25]
L. Refractory interstitial cystitis[26]
M. Shoulder pain
N. Strabismus[27-28]
O. Tardive dyskinesia
P. Carpal tunnel syndrome[29]
Q. Trigeminal neuralgia[30]
R. Achalasia or upper esophageal sphincter dysfunction[31]

S. AbobotulinumtoxinA (Dysport) is contraindicated in members with allergy to cow's milk protein, per FDA guidelines

OnabotulinumtoxinA (Botox) (J0585)

The use of OnabotulinumtoxinA (Botox) for any other indication not listed above is *not covered* by Oscar, as it is considered experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

A. Hyperhidrosis, other than axillary
    a. *Rationale for non-coverage:* An expert review by the American Academy of Neurology concluded that the evidence for Botox in palmar hyperhidrosis was inadequate to guide clinical decision making. For craniofacial hyperhidrosis, an *UpToDate* review on "Primary Focal Hyperhidrosis" highlights an overall lack of randomized evidence for botulinum toxin therapy in craniofacial hyperhidrosis. Further evidence on hyperhidrosis for non-axillary sites is limited and insufficient to guide clinical decision making.[1-12]
B. Sialorrhea in children
    a. *Rationale for non-coverage:* A Cochrane review and a separate systematic review on children with excessive salivation/drooling associated with cerebral palsy concluded that the evidence is insufficient to determine the efficacy of botulinum toxin therapy in this patient group.[13-14]
C. Anal sphincter achalasia
    a. *Rationale for non-coverage:* A 2012 meta-analysis on 16 nonrandomized studies examining Botox for internal anal sphincter achalasia revealed significantly higher rates of non-response and adverse outcomes when compared to myectomy. Further evidence is required to determine a potential benefit of Botox therapy in this patient population.[15]
D. BPH with lower urinary tract symptoms
    a. *Rationale for non-coverage:* A randomized trial on 380 men with BPH and lower urinary tract symptoms who were assigned to either Botox or placebo revealed no significant difference between the two groups. Multiple reviews have found a lack of randomized evidence demonstrating efficacy for this indication.[16-19]
E. Chronic pain, including, but not limited to: myofascial pain syndrome, inflammatory pain, musculoskeletal pain (including acute shoulder and back pain), post-herpetic neuralgia, gynecologic pain syndromes
    a. *Rationale for non-coverage:* Multiple systematic reviews and meta-analyses have concluded that the current evidence is inadequate to support the use of Botox in chronic pain syndromes.[20-27]

F. Club foot (e.g. talipes equinovarus)
    a. *Rationale for non-coverage:* The existing evidence consists of a small (n=20) randomized trial showing no benefit with Botox in reducing cast time, need for further procedural intervention, or risk for relapse. A separate, larger study with 239 patients found some evidence of efficacy for Botox, however the study was designed as a retrospective case series. Further randomized, prospective evidence is needed to determine a potential benefit of Botox for this indication.[28-29]
G. Trigeminal neuralgia
    a. *Rationale for non-coverage:* The current evidence is either uncontrolled or nonrandomized with small patient samples. Review articles have suggested there may be some efficacy for Botox in trigeminal neuralgia but indicate that further study is needed.[30-32]
H. Gastroparesis
    a. *Rationale for non-coverage:* Systematic review and expert consensus has concluded that there is minimal evidence for Botox in gastroparesis.[33-34]
I. Frey Syndrome (i.e. Gustatory sweating)
    a. *Rationale for non-coverage:* A 2013 evidence-based review concluded that the lack of randomized clinical evidence for Botox in Frey's syndrome limits the support for clinical use.[35-36]
J. Migraines or other headaches (e.g. tension, cluster, chronic daily) that do not meet the above criteria
    a. *Rationale for non-coverage:*
        i. A 2012 meta-analysis found that botulinum toxin A was not associated with fewer episodic migraines or chronic tension headaches.[92]
        ii. Per the 2016 American Academy of Neurology guidelines on botulinum neurotoxin for headaches:[11]
            1. No conclusions could be made for chronic daily headache;
            2. "OnaBoNT-A should not be offered as a treatment option for episodic migraine (Level A)." Episodic migraine is defined as fewer than 15 episodes per month.
            3. "OnaBoNT-A should not be considered as a treatment option for tension-type headache (Level B)."
K. Obesity[93-94]
L. Phonic tics[95]
M. Acute and chronic back pain
N. Cosmetic strabismus, defined as adults with congenital strabismus without binocular fusion.

O. Chronic idiopathic constipation (CIC)[96]
P. Plantar fasciitis[100]
Q. Depression
R. Postnatal brachial plexus injury[101]
S. Refractory interstitial cystitis[99]
T. Carpal tunnel syndrome[97]
U. Tremor, including benign essential tremor of the hands, head and vocal tremors
V. Tardive dyskinesia
W. Thoracic outlet syndrome
X. Upper esophageal sphincter dysfunction[98]
Y. Painful bruxism[102]
Z. Acute and chronic shoulder pain
AA. First-bite syndrome, with or without pain that has failed traditional analgesics
BB. Palatal myoclonus
CC. Post-radiation myokymia, including facial myokymia and trismus

IncobotulinumtoxinA (Xeomin) (J0588)

The use of IncobotulinumtoxinA (Xeomin) for any other indication not listed above is *not covered* by Oscar, as it is considered experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

A. Hyperhidrosis, including axillary, palmar, and craniofacial
    a. *Rationale for non-coverage:* Xeomin and Botox were compared in a double-blind trial in treating palmar hyperhidrosis. There were no significant differences in short- or long-term efficacy outcomes, however only 25 patients were included in the study. Given the small sample size and lack of confirmatory studies, further evidence is required. Similar limitations are present in comparable studies on axillary hyperhidrosis. Further evidence is needed to determine a potential benefit of Xeomin for this indication.[1-3]
B. Migraine prophylaxis
    a. *Rationale for non-coverage:* The evidence for Xeomin in migraine prophylaxis comes from small, retrospective case series and poster presentations, indicating further prospective, randomized evidence is required to guide any potential clinical application.[4-5]
C. Detrusor hyperactivity (e.g. bladder overactivity)
    a. *Rationale for non-coverage:* There is limited evidence on Xeomin in patients with overactive bladder. Preliminary results on 95 patients from a double-blinded study on Xeomin and Botox in bladder overactivity were presented at the 27th Annual Congress of the European Association of Urology. However, further peer-reviewed randomized evidence is currently lacking, limiting guidance for clinical application.[6-7]

D. Post-stroke lower limb spasticity
    a. *Rationale for non-coverage:* A prospective, open label study on 71 patients demonstrated safety and efficacy of Xeomin in post-stroke lower limb spasticity, however further randomized studies are required to establish clinical use. Furthermore, the 2016 American Academy of Neurology Guidelines state that there "is insufficient evidence to support or refute the use of incoBoNT-A for the treatment of lower limb spasticity." [8, 22]
E. Sialorrhea
    a. *Rationale for non-coverage:* A recent meta-analysis and randomized double-blind placebo-controlled cross-over study on sialorrhea in Parkinson's disease patients revealed minimal efficacy, and the authors concluded that further studies should be conducted. The clinical evidence for Xeomin in sialorrhea is insufficient to determine any potential clinical benefit.[9]
F. Atrial fibrillation[10]
G. Spasticity in children with cerebral palsy
    a. *Rationale for non-coverage:* A single randomized, double-blind trial assessing safety of Xeomin in 35 children with spasticity due to cerebral palsy demonstrated a similar safety profile to Botox, however further studies with greater patient populations are indicated to determine potential clinical benefit.[11]

RimabotulinumtoxinB (Myobloc) (J0587)

The use of RimabotulinumtoxinB (Myobloc) for any other indication not listed above is *not covered* by Oscar, as it is considered experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

A. Bladder dysfunction (e.g. overactive bladder, detrusor hyperreflexia)
    a. *Rationale for non-coverage:* The evidence has been contradictory or inconclusive, with some studies showing RimabotulinumtoxinB efficacy while others have demonstrated a lack of benefit. A 2011 Cochrane review (updating the previous 2007 review) identified 19 studies meeting inclusion criteria, and found that the efficacy of RimabotulinumtoxinB was inferior to that of type A toxins with a substantially shorter duration of benefit across randomized trials for bladder dysfunction.[1-4]
B. Hyperhidrosis;
    a. *Rationale for non-coverage:* The clinical evidence for RimabotulinumtoxinB (type B agent) is substantially limited compared to type A agents. The literature consists primarily of one randomized trial comparing RimabotulinumtoxinB and OnabotulinumtoxinA in 24 patients with axillary hyperhidrosis that shows comparable anhidrotic effect. Other studies are similarly limited in sample size and the general

consensus indicates that long-term, larger studies are needed to determine potential clinical benefit.[5-9]

C. Spasticity in adults, including post-stroke spasticity and spasticity of the upper and/or lower extremities associated with other neurological disorders
    a. *Rationale for non-coverage:* The clinical evidence for RimabotulinumtoxinB (type b agent) is substantially limited compared to type A agents. A single randomized trial on 24 patients showed possible improvements with RimabotulinumtoxinB but concluded that larger studies with long-term follow up were needed for further evidence. The US Pharmacopeial Convention has stated that off-label use of RimabotulinumtoxinB for spasticity secondary to stroke or brain injury may be indicated, however updated data has failed to demonstrated the statistically significant benefit seen in earlier studies. The American Academy of Neurology currently states (per 2016 guidelines), that the data is insufficient to determine the efficacy of Myobloc in lower limb spasticity, and the evidence is limited to a single Class I study for upper limb spasticity. [10-13]
D. Spasticity in children with cerebral palsy (CP)
    a. *Rationale for non-coverage:* A review by the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society concluded that the evidence was limited in children with CP, and that the existing evidence on RimabotulinumtoxinB showed inferior efficacy compared to type A toxins.[14]
E. Upper esophageal dysfunction or achalasia
    a. *Rationale for non-coverage:* A 2014 Cochrane review revealed no randomized clinical trials on RimabotulinumtoxinB for upper esophageal dysfunction.[15]
F. Migraine prophylaxis
G. Incontinence after spinal cord injury
H. Blepharospasm[33]
I. Hemifacial spasm[32]
J. Spasmodic dysphonia

Applicable Billing Codes (CPT/HCPCS/ICD-10 Codes)

Codes covered if clinical criteria are met:

CPT/HCPCS Codes covered if criteria are met:	
Code	*Description*
J0585	Injection, onabotulinumtoxinA, 1 unit (Botox®)

J0586	Injection, abobotulinumtoxinA, 5 units (Dysport®)
J0587	Injection, rimabotulinumtoxinB, 100 units (Myobloc®)
J0588	Injection, incobotulinumtoxinA, 1 unit (Xeomin®)
ICD-10 codes covered if criteria are met for onabotulinumtoxinA (J0585) :	
F95.0	Transient tic disorder
F95.1	Chronic motor or vocal tic disorder
F95.8	Other tic disorders
F95.9	Tic disorder, unspecified
G04.1	Tropical spastic paraplegia
G11.4	Hereditary spastic paraplegia
G12.21	Amyotrophic lateral sclerosis
G20	Parkinson's disease
G24.3	Spasmodic torticollis
G24.5	Blepharospasm
G24.8	Other dystonia
G35	Multiple sclerosis
G43.001	Migraine without aura, not intractable, with status migrainosus
G43.009	Migraine without aura, not intractable, without status migrainosus
G43.011	Migraine without aura, intractable, with status migrainosus
G43.019	Migraine without aura, intractable, without status migrainosus
G43.101	Migraine with aura, not intractable, with status migrainosus
G43.109	Migraine with aura, not intractable, without status migrainosus
G43.111	Migraine with aura, intractable, with status migrainosus
G43.119	Migraine with aura, intractable, without status migrainosus
G43.401	Hemiplegic migraine, not intractable, with status migrainosus
G43.409	Hemiplegic migraine, not intractable, without status migrainosus
G43.411	Hemiplegic migraine, intractable, with status migrainosus
G43.419	Hemiplegic migraine, intractable, without status migrainosus

G43.501	Persistent migraine aura without cerebral infarction, not intractable, with status migrainosus
G43.509	Persistent migraine aura without cerebral infarction, not intractable, without status migrainosus
G43.511	Persistent migraine aura without cerebral infarction, intractable, with status migrainosus
G43.519	Persistent migraine aura without cerebral infarction, intractable, without status migrainosus
G43.601	Persistent migraine aura with cerebral infarction, not intractable, with status migrainosus
G43.609	Persistent migraine aura with cerebral infarction, not intractable, without status migrainosus
G43.611	Persistent migraine aura with cerebral infarction, intractable, with status migrainosus
G43.619	Persistent migraine aura with cerebral infarction, intractable, without status migrainosus
G43.701	Chronic migraine without aura, not intractable, with status migrainosus
G43.709	Chronic migraine without aura, not intractable, without status migrainosus
G43.711	Chronic migraine without aura, intractable, with status migrainosus
G43.719	Chronic migraine without aura, intractable, without status migrainosus
G43.801	Other migraine, not intractable, with status migrainosus
G43.809	Other migraine, not intractable, without status migrainosus
G43.811	Other migraine, intractable, with status migrainosus
G43.819	Other migraine, intractable, without status migrainosus
G43.901	Migraine, unspecified, not intractable, with status migrainosus
G43.909	Migraine, unspecified, not intractable, without status migrainosus
G43.911	Migraine, unspecified, intractable, with status migrainosus
G43.919	Migraine, unspecified, intractable, without status migrainosus
G43.D0	Abdominal migraine, not intractable
G43.D1	Menstrual migraine, not intractable, with status migrainosus

G43.829	Menstrual migraine, not intractable, without status migrainosus
G43.831	Menstrual migraine, intractable, with status migrainosus
G43.839	Menstrual migraine, intractable, without status migrainosus
G43.B0	Ophthalmoplegic migraine, not intractable
G43.B1	Ophthalmoplegic migraine, intractable
G51.0	Bell's palsy
G51.3	Clonic hemifacial spasm
G51.8	Other disorders of facial nerve
G51.9	Disorder of facial nerve, unspecified
G80.0	Spastic quadriplegic cerebral palsy
G80.1	Spastic diplegic cerebral palsy
G80.2	Spastic hemiplegic cerebral palsy
G80.3	Athetoid cerebral palsy
G80.4	Ataxic cerebral palsy
G80.8	Other cerebral palsy
G80.9	Cerebral palsy, unspecified
G81.10	Spastic hemiplegia affecting unspecified side
G81.11	Spastic hemiplegia affecting right dominant side
G81.12	Spastic hemiplegia affecting left dominant side
G81.13	Spastic hemiplegia affecting right nondominant side
G81.14	Spastic hemiplegia affecting left nondominant side
H49.9	Unspecified paralytic strabismus
H49.881	Other paralytic strabismus, right eye
H49.882	Other paralytic strabismus, left eye
H49.883	Other paralytic strabismus, bilateral
H49.889	Other paralytic strabismus, unspecified eye
H50.9	Unspecified strabismus
H50.21	Vertical strabismus, right eye
H50.22	Vertical strabismus, left eye

I73.00 - I37.01	Raynaud's syndrome
J38.5	Laryngeal spasm
K11.7	Disturbances of salivary secretion
K22.0	Achalasia of cardia
K60.1	Chronic anal fissure
L74.510	Primary focal hyperhidrosis, axilla
M62.40	Contracture of muscle, unspecified site
M62.411	Contracture of muscle, right shoulder
M62.412	Contracture of muscle, left shoulder
M62.419	Contracture of muscle, unspecified shoulder
M62.421	Contracture of muscle, right upper arm
M62.422	Contracture of muscle, left upper arm
M62.429	Contracture of muscle, unspecified upper arm
M62.431	Contracture of muscle, right forearm
M62.432	Contracture of muscle, left forearm
M62.439	Contracture of muscle, unspecified forearm
M62.441	Contracture of muscle, right hand
M62.442	Contracture of muscle, left hand
M62.449	Contracture of muscle, unspecified hand
M62.451	Contracture of muscle, right thigh
M62.452	Contracture of muscle, left thigh
M62.459	Contracture of muscle, unspecified thigh
M62.461	Contracture of muscle, right lower leg
M62.462	Contracture of muscle, left lower leg
M62.469	Contracture of muscle, unspecified lower leg
M62.471	Contracture of muscle, right ankle and foot
M62.472	Contracture of muscle, left ankle and foot
M62.479	Contracture of muscle, unspecified ankle and foot
M62.48	Contracture of muscle, other site

M62.49	Contracture of muscle, multiple sites
M62.830	Muscle spasm of back
M62.831	Muscle spasm of calf
M62.838	Other muscle spasm
N31.0	Uninhibited neuropathic bladder, not elsewhere classified
N31.1	Reflex neuropathic bladder, not elsewhere classified
N31.2	Flaccid neuropathic bladder, not elsewhere classified
N31.8	Other neuromuscular dysfunction of bladder
N31.9	Neuromuscular dysfunction of bladder, unspecified
N39.41	Urge incontinence
R13.10	Dysphagia, unspecified
R13.11	Dysphagia, oral phase
R13.12	Dysphagia, oropharyngeal phase
R13.13	Dysphagia, pharyngeal phase
R13.14	Dysphagia, pharyngoesophageal phase
R13.19	Other dysphagia
R25.2	Cramp and spasm
R49.0	Dysphonia
ICD-10 codes covered if criteria are met for abobotulinumtoxinA (J0586) :	
G80.3	Athetoid cerebral palsy
G80.4	Ataxic cerebral palsy
G80.8	Other cerebral palsy
G80.9	Cerebral palsy, unspecified
G24.5	Blepharospasm
G24.8	Other dystonia
G80.0	Spastic quadriplegic cerebral palsy
G80.1	Spastic diplegic cerebral palsy
G80.2	Spastic hemiplegic cerebral palsy
G24.3	Spasmodic torticollis

G51.3	Clonic hemifacial spasm
G51.8	Other disorders of facial nerve
G51.9	Disorder of facial nerve, unspecified
G81.10	Spastic hemiplegia affecting unspecified side
G81.11	Spastic hemiplegia affecting right dominant side
G81.12	Spastic hemiplegia affecting left dominant side
G81.13	Spastic hemiplegia affecting right nondominant side
G81.14	Spastic hemiplegia affecting left nondominant side
H49.9	Unspecified paralytic strabismus
K11.7	Disturbances of salivary secretion
L74.510	Primary focal hyperhidrosis, axilla
M62.40	Contracture of muscle, unspecified site
M62.411	Contracture of muscle, right shoulder
M62.412	Contracture of muscle, left shoulder
M62.419	Contracture of muscle, unspecified shoulder
M62.421	Contracture of muscle, right upper arm
M62.422	Contracture of muscle, left upper arm
M62.429	Contracture of muscle, unspecified upper arm
M62.431	Contracture of muscle, right forearm
M62.432	Contracture of muscle, left forearm
M62.439	Contracture of muscle, unspecified forearm
M62.441	Contracture of muscle, right hand
M62.442	Contracture of muscle, left hand
M62.449	Contracture of muscle, unspecified hand
M62.451	Contracture of muscle, right thigh
M62.452	Contracture of muscle, left thigh
M62.459	Contracture of muscle, unspecified thigh
M62.461	Contracture of muscle, right lower leg
M62.462	Contracture of muscle, left lower leg

M62.469	Contracture of muscle, unspecified lower leg
M62.471	Contracture of muscle, right ankle and foot
M62.472	Contracture of muscle, left ankle and foot
M62.479	Contracture of muscle, unspecified ankle and foot
M62.48	Contracture of muscle, other site
M62.49	Contracture of muscle, multiple sites
ICD-10 codes covered if criteria are met for rimabotulinumtoxinB (J0587):	
G12.21	Amyotrophic lateral sclerosis
G20	Parkinson's disease
G24.3	Spasmodic torticollis
G80.0	Spastic quadriplegic cerebral palsy
G80.1	Spastic diplegic cerebral palsy
G80.2	Spastic hemiplegic cerebral palsy
G80.3	Athetoid cerebral palsy
G80.4	Ataxic cerebral palsy
G80.8	Other cerebral palsy
G80.9	Cerebral palsy, unspecified
K11.7	Disturbances of salivary secretion
ICD-10 codes covered if criteria are met for incobotulinumtoxinA (J0588) :	
G24.3	Spasmodic torticollis
G24.4	Idiopathic orofacial dystonia
G24.5	Blepharospasm
G51.3	Clonic hemifacial spasm
G51.8	Other disorders of facial nerve
G51.9	Disorder of facial nerve, unspecified
M62.40	Contracture of muscle, unspecified site
M62.411	Contracture of muscle, right shoulder
M62.412	Contracture of muscle, left shoulder
M62.419	Contracture of muscle, unspecified shoulder

M62.421	Contracture of muscle, right upper arm
M62.422	Contracture of muscle, left upper arm
M62.429	Contracture of muscle, unspecified upper arm
M62.431	Contracture of muscle, right forearm
M62.432	Contracture of muscle, left forearm
M62.439	Contracture of muscle, unspecified forearm
M62.441	Contracture of muscle, right hand
M62.442	Contracture of muscle, left hand
M62.449	Contracture of muscle, unspecified hand
M62.451	Contracture of muscle, right thigh
M62.452	Contracture of muscle, left thigh
M62.459	Contracture of muscle, unspecified thigh
M62.461	Contracture of muscle, right lower leg
M62.462	Contracture of muscle, left lower leg
M62.469	Contracture of muscle, unspecified lower leg
M62.471	Contracture of muscle, right ankle and foot
M62.472	Contracture of muscle, left ankle and foot
M62.479	Contracture of muscle, unspecified ankle and foot
M62.48	Contracture of muscle, other site
M62.49	Contracture of muscle, multiple sites

CPT/HCPCS Codes covered but may be subject to medical necessity review:	
Code	*Description*
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
46505	Chemodenervation of internal anal sphincter [covered for anal fissure only]
52287	Cystourethroscopy, with injection(s) for chemodenervation of the bladder
64611	Chemodenervation of parotid and submandibular salivary glands, bilateral

64612	Chemodenervation of muscles(s); muscles(s) innervated by facial nerve, unilateral (eg, for blepharospasm, hemifacial spasm)
64615	Chemodenervation of muscle(s); muscle(s) innervated by facial, trigeminal, cervical spinal and accessory nerves, bilateral (eg, for chronic migraine)
64616	Chemodenervation of muscle(s); neck muscle(s), excluding muscles of the larynx, unilateral (eg, for cervical dystonia, spasmodic torticollis)
64617	Chemodenervation of muscle(s); larynx, unilateral, percutaneous (eg, for spasmodic dysphonia), includes guidance by needle electromyography, when performed
64642 - 64645	Chemodenervation of one extremity
64646 - 64647	Chemodenervation of trunk muscle(s)
64650	Chemodenervation of eccrine glands; both axillae
67345	Chemodenervation of extraocular muscle
S2340	Chemodenervation of abductor muscle(s) of vocal cord
S2341	Chemodenervation of adductor muscle(s) of vocal cord
31513	Laryngoscopy, indirect; with vocal cord injection
31570	Laryngoscopy, direct, with injection into vocal cord(s), therapeutic;
31571	Laryngoscopy, direct, with injection into vocal cord(s), therapeutic; with operating microscope or telescope

CPT/HCPCS codes *not* covered:	
Code	*Description*
64653	Chemodenervation of eccrine glands; other area(s) (e.g., scalp, face, neck), per day
86609	Antibody; bacterium, not elsewhere specified [neutralizing antibodies to botulinum toxin]

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AbobotulinumtoxinA (Dysport)

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RimabotulinumtoxinB (Myobloc)

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Clinical Guideline Revision / History Information

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