Pharmacy Management Drug Policy

SUBJECT: Botulinum Toxin (Botox, Dysport, Myobloc, Xeomin) – For Medicaid Managed Care Essential Plan and Child Health Plus
POLICY NUMBER: PHARMACY-77
EFFECTIVE DATE: 12/2019
LAST REVIEW DATE: 08/24/2023

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☐ Commercial Group (e.g., EPO, HMO, POS, PPO)	☐ Medicare Advantage
	☐ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☐ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☐ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Botulinum toxin is produced by anaerobic fermentation of the bacterium Clostridium botulinum. A number of different C. botulinum strains have been identified; they produce eight immunologically distinct serotypes (type A–H) and consist of the botulinum neurotoxin complexed with a number of associated proteins. Of the seven immunologically distinct botulinum toxins, only three have been linked to cases of botulism in humans, and only serotypes A and B are available for clinical use. There are currently three neurotoxin type A (BoNT/A) products on the market, OnabotulinumtoxinA (ONA; Botox), Abobotulinum toxin A (ABO; Dysport) and Incobotulinum toxin A (INCO; Xeomin) and 1 neurotoxin type B, RimabotulinumtoxinB (Myobloc).

In nature, BoNT-A is synthesized as macromolecular protein complexes. These protein complexes are referred to as progenitor toxins and consist of nontoxic accessory proteins (NAPs) bonded to the 150-kD active neurotoxin. The BoNT-A progenitor toxins vary in molecular weight (300–900 kD) depending on the composition of NAPs and the manufacturing process. The 150-kD neurotoxin must dissociate from NAPs to exert its pharmacologic effects. Dissociation occurs in physiologic pH conditions. When administered intramuscularly, these toxins reduce muscle tone by interference with the release of acetylcholine from nerve endings.

Dosing patterns are specific to each biological product and can differ between and within serotypes. Please refer to FDA labeling for current dosing information for each individual product.

Each individual neurotoxin product should be dosed accordingly based on each individual products current FDA approved indication(s) and dosage guidelines. Recent studies have shown that the different serotypes of Botulinium Toxins **can be interchanged**, but **not at a 1:1 ratio**. Currently accepted unit conversion ratios between the various products are provided below. As a result, all Botulinium Toxins included within this policy shall be considered interchangeable for each of the indications listed within this policy, unless specifically noted otherwise.

NOTE: Dosing and conversion information is provided as **guidance only**, FDA approved labeling, compendia or primary literature should be referenced for detailed dosage information.

The following products, OnabotulinumtoxinA (Botox), AbobotulinumtoxinA (Dysport), IncobotulinumtoxinA (Xeomin), and RimabotulinumtoxinB (Myobloc), are included within this policy and coverage is provided under the medical benefit.

Refer to Corporate Medical Protocol 7.01.11 regarding Cosmetic and Reconstructive Procedures.

POLICY:

Based upon our criteria and review of the peer-reviewed literature, OnabotulinumtoxinA (ONA; Botox), Abobotulinum toxin A (ABO; Dysport), Incobotulinum toxin A (INCO; Xeomin) and RimabotulinumtoxinB (Myobloc) therapy has been medically proven effective and therefore may be considered **medically appropriate** for the following conditions when the appropriate criteria are met.

I. Cervical Dystonia
(spasmodic torticollis) to reduce the severity of abnormal head position and neck pain

A. Initial Request:
1. Diagnosis of cervical dystonia **AND**
2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist **AND**
3. 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 **AND**
4. Contractions are causing pain and functional impairment **AND**
5. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Age restriction: ≥ 16 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. 400 units is the FDA approved maximum dosing however there is evidence to support the safety and efficacy of total doses up to 600 units. Requests exceeding 400 units will be reviewed on a case-by-case basis and only authorized if there is evidence that 400 units did not provide an adequate response.
b. Dose based on the patient's head and neck position, localization of pain, muscle hypertrophy, patient response, and adverse event history; use lower initial dose in botulinum toxin naïve patients.
c. Average dose: 198 to 300 units divided among affected muscles; up to 50 units per site.
d. Average duration of effect: 4 - 6 weeks to 3 months. Retreatment no sooner than 12 weeks from last injection.

B. Recertification:
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration. **AND**
3. Requests for dose increase must not exceed 400 units per treatment session. (Requests exceeding 400 units will be reviewed on a case-by-case basis and only authorized if there is evidence that 400 units did not provide an adequate response, with a maximum allowed dose of 600 units) **AND**
4. May repeat doses when effects have lessened, but no sooner than 12 weeks after previous injection

II. Blepharospasm (a focal dystonia) or Strabismus
Associated with dystonia, including benign essential blepharospasm or VII nerve disorders

A. Initial Request:
1. Diagnosis of:
   a. Blepharospasm (i.e., abnormal contraction of eyelid muscles) **OR**
   b. Strabismus (i.e., misalignment of the eyes) **AND**
2. Prescribed by or in consultation with a neurologist or ophthalmologist **AND**
3. Member has significant disability in daily functional activities due to interference with vision **AND**
4. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Age restriction: ≥ 12 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

Blepharospasm:
a. Dose does not exceed 5 units per site per treatment session (maximum of 200 units total in a 30-day period)
b. Time to retreat: No sooner than 3 months from previous treatment

Strabismus:
a. The dose is based on prism diopter correction or previous response to treatment with Botox.
b. Dose does not exceed 25 units per treatment session
c. Average duration of effect: 6-8 weeks to 6-12 months
d. Time to retreat: No sooner than 6 weeks from previous treatment

B. Recertification:
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration. **AND**

3. Requests for dose increase must not exceed for Blepharospasm: 5 units per site per treatment session (maximum of 200 units total in a 30-day period) and for Strabismus: 25 units per muscle per treatment session

III. Upper Limb Spasticity

Patients ≥ 2 years to decrease the severity of increased muscle tone in elbow, wrist, finger and thumb flexors, that ARE NOT due to Cerebral Palsy (Please see "Spasticity Associated with Cerebral Palsy" below)

A. Initial Request:

1. Diagnosis of upper limb spasticity **AND**
2. Focal increased muscle tone causing functional impairment, **AND**
3. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist **AND**
4. Failure of an age appropriate, adequate trial of baclofen, tizanidine or dantrolene unless contraindicated, not age appropriate or not clinically appropriate for diagnosis **AND**
5. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Age restriction: ≥ 2 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

Adults: ≥18 years of age:

a. The FDA approved maximum cumulative dose of Botox for adults is 400 units every 12 weeks. However, there is evidence to support the safety and efficacy of total doses up to 600 units. Requests exceeding 400 units will be reviewed on a case-by-case basis and only authorized if there is evidence that 400 units did not provide an adequate response
b. May repeat doses when effects have lessened, but no sooner than 12 weeks after previous injection

Children: 2 - 17 years of age:

a. Dosing in initial and sequential treatment sessions should be tailored to the individual based on the size, number and location of muscles involved, severity of spasticity, the presence of local muscle weakness, the patient's response to previous treatment, or adverse event history with OnabotulinumtoxinA (Botox), AbobotulinumtoxinA (Dysport), IncobotulinumtoxinA (Xeomin), or RimabotulinumtoxinB (Myobloc).
b. The FDA approved maximum total **cumulative** dose 340 units in a 3-month interval
c. Repeat treatment may be administered when the effect of a previous injection has diminished, but no sooner than 12 weeks after the previous injection

Limitations: Safety and effectiveness of OnabotulinumtoxinA (Botox), AbobotulinumtoxinA (Dysport), IncobotulinumtoxinA (Xeomin), and RimabotulinumtoxinB (Myobloc), has not been established for the treatment of the upper limb muscle groups other than those specified in the

FDA approved labeling or for the treatment of upper limb spasticity in pediatric patients under 2 years of age.

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than:
    a. Adults ≥ 18 years of age: 400 cumulative units over the last 3 months (unless there is history of previous approval to use more than 400 units)
    b. Children 2-17 years of age: 340 cumulative units over the last 3 months **AND**
3. It has been 12 weeks (3 months) since the last injection **AND**
4. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Requests for dose increase must not exceed 400 units per treatment session for Adults ≥ 18 years of age*, and 340 units per treatment session for Children 2-17 years of age.
(*Requests exceeding 400 units in adults, will be reviewed on a case-by-case basis, and only authorized if there is evidence that 400 units did not provide an adequate response, with a maximum allowed dose of 600 units. Doses exceeding 340 units in children will not be approved as there is no data available showing doses exceeding 340 units in children is safe or effective).

IV. Lower Limb Spasticity
In patients ≥ 2 years to decrease the severity of increased muscle tone in ankle and toe flexors, that ARE NOT due to Cerebral Palsy (Please see "Spasticity Associated with Cerebral Palsy" below).

A. Initial Request:
1. Diagnosis of lower limb spasticity **AND**
2. Focal increased muscle tone causing functional impairment, **AND**
3. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist **AND**
4. Failure of an age appropriate, adequate trial of baclofen, tizanidine or dantrolene unless contraindicated, not age appropriate or not clinically appropriate for diagnosis **AND**
5. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Age restriction: ≥ 2 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

Adults: ≥18 years of age:

a. Dosing in initial and sequential treatment sessions should be tailored to the individual based on the size, number and location of muscles involved, severity of spasticity, the

presence of local muscle weakness, the patient's response to previous treatment, or adverse event history with OnabotulinumtoxinA

b. Usual Dosage:
Total dose of 300 to 400 units IM across 5 muscles. Use the lowest dose when starting treatment
c. Maximum Dose per site: 50 units.
d. The FDA approved maximum cumulative dose of Botox for adults is 400 units every 12 weeks. However, there is evidence to support the safety and efficacy of total doses up to 600 units. Requests exceeding 400 units will be reviewed on a case-by-case basis and only authorized if there is evidence that 400 units did not provide an adequate response
e. May repeat doses when effects have lessened, but no sooner than 12 weeks after previous injection

Children: 2 - 17 years of age:

a. Dosing in initial and sequential treatment sessions should be tailored to the individual based on the size, number and location of muscles involved, severity of spasticity, the presence of local muscle weakness, the patient's response to previous treatment, or adverse event history with OnabotulinumtoxinA (Botox), AbobotulinumtoxinA (Dysport), IncobotulinumtoxinA (Xeomin), or RimabotulinumtoxinB (Myobloc).
b. Usual Dosage: 4 to 8 units/kg IM divided among the affected muscles
c. Maximum dose: 8 units/kg or 300 units per treatment session, whichever is lower.
d. The FDA approved maximum total **cumulative** dose 340 units in a 3-month interval
e. Repeat treatment may be administered when the effect of a previous injection has diminished, but no sooner than 12 weeks after the previous injection

Limitations: Safety and effectiveness of OnabotulinumtoxinA (Botox), AbobotulinumtoxinA (Dysport), IncobotulinumtoxinA (Xeomin), and RimabotulinumtoxinB (Myobloc), has not been established for the treatment of the upper limb muscle groups other than those specified in the FDA approved labeling or for the treatment of upper limb spasticity in pediatric patients under 2 years of age.

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than:
a) Adults ≥ 18 years of age: 400 cumulative units over the last 3 months (unless there is history of previous approval to use more than 400 units)
b) Children 2-17 years of age: 340 cumulative units over the last 3 months **AND**
3. It has been 12 weeks (3 months) since the last injection **AND**
4. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Requests for dose increase must not exceed 400 units per treatment session for adults ≥ 18 years of age*, and 340 units per treatment session for Children 2-17 years of age. (*Requests exceeding 400 units in Adults, will be reviewed on a case-by-case basis, and only authorized if there is evidence that

400 units did not provide an adequate response, with a maximum allowed dose of 600 units. Doses exceeding 340 units in children will not be approved as there is no data available showing doses exceeding 340 units in children is safe or effective).

V. Spasticity Associated with Cerebral Palsy (CP) In Patients ≥ 2 years

A. Initial Request:

1. Diagnosis of spasticity associated with cerebral palsy (CP) **AND**
2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist **AND**
3. Indicated in patients who have increased muscle tone that interferes with function or is likely to lead to joint contracture with growth **AND**
4. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Age restriction: Age ≥ 2 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Dose does not exceed 400 units per treatment session.
b. Dosing depends on the muscles injected, body weight, muscle bulk, the number of muscles being injected simultaneously, and the patient's response to previous therapy
c. Average duration of effect / time to retreat: 12 weeks
d. The FDA approved maximum cumulative dose of Botox for adults is 400 units every 12 weeks.

However, there is evidence to support the safety and efficacy of total doses up to 600 units. Requests exceeding 400 units will be reviewed on a case-by-case basis and only authorized if there is evidence that 400 units did not provide an adequate response

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than 400 units over the past 3 months, **AND** it has been 12 weeks (3 months) since the last injection **AND**
3. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Requests for dose increase must not exceed 400 units per treatment session. (Requests exceeding 400 units will be reviewed on a case-by-case basis and only authorized if there is evidence that 400 units did not provide an adequate response, with a maximum allowed dose of 600 units)

VI. Chronic Migraine

A. Initial Request:

1. Must be used for the prevention of migraine headaches in adult patients with a diagnosis of chronic migraine headache.
2. A diagnosis of chronic migraine headache is defined as a headache occurring on 15 or more days/month for more than 3 months, which, on at least 8 days/month, has the features of migraine headache
    i. the features of migraine, include but are not limited to:
        a. Unilateral location
        b. Pulsating quality
        c. Moderate or Severe pain intensity
        d. Aggravation by or causes avoidance of routine physical activity
        e. Nausea and/or vomiting
        f. Photophobia and/or phonophobia
3. The patient must be experiencing 4 or more migraine headache days per month
4. Prescribed by or in consultation with a neurologist or pain specialist **AND**
5. The provider must attest that the patient has had serious side effects or drug failure, at an effective dose, to at least 3 months of THREE preventative oral medications from THREE different classes including, but not limited to:
        a. Anti-Depressants
        b. Serotonin-Norepinephrine Reuptake Inhibitors
        c. Beta-Blockers
        d. Anti-Convulsant
6. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

If the patient is unable to tolerate a medication, a 3-month trial of that medication is not required.

Age Restrictions: Botox for Chronic Migraine headaches will only be approved for use in those who are ≥ 18 years of age. Botox will not be approved for Chronic Migraine under any circumstances for those under 18 years of age.

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Dose does not exceed 200 units per treatment session.
b. Recommended dose is 155 units given as 5 units into each of 31 sites across 7 specific head/neck muscle areas
c. Average duration of effect: 3 – 4 months.

Initial approval of therapy for chronic migraines will consist of a maximum quantity of up to three (3) treatments in a 6-month period (one (1) treatment every 12 weeks).

Therapy with any botulinum toxin will **NOT** be approved for use in combination with large molecule Calcitonin Gene-Related Peptide (CGRP) Antagonists (including, but not limited to: Aimovig, Ajovy, Emgality) or Intravenous (IV) Calcitonin Gene-Related Peptide (CGRP) antagonists (Vyepti), which are indicated for the prevention of migraine headaches. (Small molecule CGRP antagonists [gepants]

used for the acute treatment of migraine are permissible).

Continuation of therapy will not be authorized if it has been determined that the member has had an initiation, or resumption of, a large molecule, or IV CGRP antagonist while using botulinum toxin, for any reason (migraine or other diagnosis). This will be verified via the member's prescription and medical records. The provider must attest that any existing large molecule or IV CGRP therapy will be discontinued before botulinum toxin will be approved.

B. Recertification

Previously approved by plan or has met initial approval criteria:

1. Documentation or attestation to support a significant reduction in monthly migraine headache frequency and/or intensity after at least 2 treatment sessions and that patient has been able to resume daily living activities previously unable to perform due to headache frequency and/or intensity **AND**
2. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration. **AND**
3. Request for dose increase does not exceed 200 units per treatment session **AND**
4. Continuation of therapy will not be authorized if it has been determined that the member has had an initiation, or resumption of, a large molecule, or IV CGRP antagonist while using botulinum toxin, for any reason (migraine or other diagnosis). This will be verified via the member's prescription and medical records. The provider must attest that any existing large molecule or IV CGRP therapy will be discontinued before botulinum toxin will be approved.
5. Up to a total of 5 treatment sessions will be authorized within a 12-month period, but at a dosing frequency no less than 12 weeks apart.

VII. Neurogenic detrusor overactivity

Associated with a neurologic condition in pediatric patients 5-17 years of age following inadequate response or intolerance to anticholinergic medication

A. Initial Request

1. Diagnosis of Neurogenic detrusor overactivity that is associated with a neurologic condition in pediatric patients 5 – 17 years of age who have an inadequate response to or are intolerant of anticholinergic medication **AND**
2. Prescribed by / in consultation with a neurologist or urologist that specializes in pediatrics **AND**
3. Failure of at least a 3-month trial of oxybutynin at appropriate pediatric dosing **AND**
4. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Age restriction: Children ages 5 – 17 years of age.

Dosing Guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Usual dosage (less than 34 kg): Refer to weight-based dosage
b. Usual dosage (34 kg or greater): 200 units

c. Retreatment: Consider re-injection when clinical benefit diminishes, no sooner than 12 weeks

B. Recertification

Previously approved by plan or has met initial approval criteria

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than 200 units over the past 3 months, and it has been at least 12 weeks since the last injection **AND**
3. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration

VIII. Primary Axillary Hyperhidrosis

A. Initial Request

1. Diagnosis of severe primary axillary hyperhidrosis (e.g., resulting in medical complications such as skin maceration and infection or significant disruption of professional/social life) that is inadequately managed by topical agents **AND**
2. Prescribed by / in consultation with a neurologist or dermatologist **AND**
3. Failure of a 6-month trial of topical aluminum chloride, unless contraindicated or serious side effects are experienced **AND**
4. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Age restriction: ≥ 18 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Dose does not exceed 50 units per axilla per treatment session (maximum of 100 units total).
b. Average duration of effect: 4-12 months
c. Time to retreat: 8 - 12 weeks

Limitations: The safety and effectiveness of botulinum toxin for hyperhidrosis in other body areas have not been established. Weakness of hand muscles and blepharoptosis may occur in patients who receive botulinum toxin for palmar hyperhidrosis and facial hyperhidrosis, respectively. Patients should be evaluated for potential causes of secondary hyperhidrosis (e.g., hyperthyroidism) to avoid symptomatic treatment of hyperhidrosis without the diagnosis and/or treatment of the underlying disease. Requests for hyperhidrosis for any area of the *body other than axillary hyperhidrosis*, will be denied as off-label, experimental / investigational.

B. Recertification

Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment Member has not received more than 400 units over the past 3 months **AND**

2. it has been at least 8 -12 weeks (2 - 3 months) since the last injection **AND**
3. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration **AND**
4. Requests for dose increase must not exceed 50 units per axilla per treatment session.

IX. **Overactive Bladder / Urinary Incontinence**

Overactive Bladder with symptoms of urge urinary incontinence, urgency and frequency in adults who have experienced serious side effects, drug failure or contraindications to anticholinergic medication

Urinary Incontinence due to detrusor overactivity associated with a neurologic condition [e.g., spinal cord injury (SCI), multiple sclerosis (MS)] in adults who have experienced serious side effects, drug failure or contraindications to anticholinergic medication

A. Initial request:

1. Diagnosis of:
   a. Overactive Bladder **OR**
   b. Urinary Incontinence (Detrusor Overactivity) associated with a neurologic condition (e.g., spinal cord injury, MS) **AND**
2. Prescribed by / in consultation with a neurologist or urologist **AND**
3. Failure of a trial of at least TWO anticholinergic agents (e.g., oxybutynin chloride, tolterodine tartrate), each used for at least 30 days, unless contraindicated or serious side effects are experienced **AND**
4. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Age restriction: ≥ 18 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

1. Overactive Bladder
   a. Dose does not exceed 100 units per treatment session as 0.5mL (5 Units) injections across 20 sites into the detrusor.
   b. Average duration of effect: 12 weeks
   c. Time to retreat: no sooner than 12 weeks.

2. Urinary Incontinence (Detrusor Overactivity):
   a. Dose does not exceed 200 units per treatment session as 1 mL (6.7 units) injections across 30 sites into the detrusor
   b. Average duration of effect: 8 – 12 months
   c. Time to retreat: no sooner than 12 weeks.

Limitations: botulinum toxin is contraindicated in patients with overactive bladder who have a urinary tract infection or with detrusor overactivity associated with a neurologic condition who have urinary retention.

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than 400 units over the past 3 months, **AND** it has been 12 weeks (3 months) since the last injection **AND**
3. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration **AND**
4. Requests for dose increase must not exceed for Overactive Bladder 100 units per treatment session and for Urinary Incontinence 200 units per treatment session.

OFF-LABEL INDICATIONS

Based upon our criteria and review of the peer-reviewed literature, OnabotulinumtoxinA (ONA; Botox), Abobotulinum toxin A (ABO; Dysport), Incobotulinum toxin A (INCO; Xeomin) and RimabotulinumtoxinB (Myobloc) have been medically proven effective and is considered **medically appropriate** for the following **off-label** indications when other treatments or interventions have been unsuccessful or are contraindicated.

I. Anal Fissure, Chronic: (Off-Label)

A. Initial request:
1. Diagnosis of chronic anal fissure **AND**
2. Prescribed in consultation with a gastroenterologist or colorectal surgeon **AND**
3. Must have failure of an adequate trial of nitroglycerin 0.2% to 0.4% ointment or topical calcium channel blocker (such as nifedipine or diltiazem) in addition to supportive measures (fiber, sitz bath, topical analgesic, stool softeners/laxatives) unless contraindicated or serious side effects experienced.

Age restriction: ≥ 18 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Dose does not exceed 100 units total
b. Average dose: 5 to 100 units
c. Reinjection for recurrence: at least 12 weeks

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than 100 units over the past 3 months, **AND** it has been 12 weeks (3 months) since the last injection **AND**
3. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration **AND**
4. Requests for dose increase must not exceed 100 units per treatment session.

II. Auriculotemporal syndrome / Frey's syndrome: (Off Label)
A rare neurological disorder resulting from damage to or near the parotid glands responsible for making saliva, and from damage to the auriculotemporal nerve often from surgery (i.e., parotidectomy)

A. Initial request:

1. Diagnosis of auriculotemporal syndrome / Frey's syndrome **AND**
2. Symptoms of undesirable facial flushing or profuse sweating occurring on the cheek, temple or behind the ears after eating certain foods, which are severe and accompanied by significant disruption in daily activities

Age restriction: ≥ 18 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Average dose = 15 to 75 units
b. Average duration of effect / time to retreat: 12 weeks

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than 400 units over the past 3 months, **AND** it has been 12 weeks (3 months) since the last injection **AND**
3. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration **AND**
4. Requests for dose increase must not exceed 400 units per treatment session.

III. Esophageal Achalasia (e.g., Nutcracker esophagus) (off-label)
Achalasia is characterized by a failure in relaxation of the lower esophageal sphincter with swallowing and by a lack of esophageal peristalsis in the distal esophagus.

Treatment of idiopathic, chagastic, previously untreated achalasia and pseudoachalasia. Improve symptoms of dysphagia, chest pain and regurgitation in idiopathic achalasia

A. Initial request:

1. Diagnosis of esophageal achalasia based on symptoms and diagnostic testing (upper endoscopy, esophageal manometry, barium swallow, endoscopic ultrasound):
   - Dysphagia to solids and foods
   - Heartburn unresponsive to a trial of at least 4 weeks of proton pump inhibitor therapy
   - Retained food in esophagus on upper endoscopy
   - Unusually increased resistance to passage of an endoscope through the esophagogastric junction **AND**
2. Must be prescribed by or in consultation with a gastroenterologist **AND**
3. Member is not a candidate for graded pneumatic dilation or surgical myotomy (high surgical risk due to age or comorbidities)

Age restriction: ≥ 18 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Dose does not exceed 100 units
b. Average dose of 20 to 25 units into each of four quadrants of lower esophageal sphincter
c. Time to retreat; at least 12 weeks

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than 100 units over the past 3 months, **and** it has been 12 weeks (3 months) since the last injection **AND**
3. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration **AND**
4. Requests for dose increase must not exceed 100 units per treatment session.

IV. Hirschsprung's Disease and Internal Anal Sphincter Achalasia: (off-label)

A. Initial request:
1. Must have diagnosis of either a, b, or c:
   a. Hirschsprung's Disease (a congenital motor disorder of the gut caused by failure of nerve cells to migrate during intestinal development whereby the colon is unable to relax causing functional obstruction; diagnosis occurs during neonatal period or childhood) Obstructive symptoms (including constipation) after surgery may respond to Botox when there is no mechanical obstruction and repeat biopsy is normal **OR**
   b. ultra-short segment Hirschsprung disease (USSHD) established by biopsy **OR**
   c. Internal Anal Sphincter (IAS) Achalasia
      - lack of rectoanal inhibitory reflex on anal manometry
      - rectal biopsy demonstrates the presence of ganglion cells thus excluding Hirschsprung disease
      - clinical presentation similar to functional constipation **AND**
2. Prescribed by or in consultation with a gastroenterologist **AND**
3. Must have had an adequate trial of stool softeners and laxatives that have been ineffective, or member has become medication dependent

Age restriction: ≥ 18 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Dose does not exceed 100 units
b. Time to retreat if needed: 12 weeks

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than 100 units over the past 3 months, **AND** it has been 12 weeks (3 months) since the last injection **AND**
3. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site, anticipated frequency of injection, and total dose per visit **AND**
4. Requests for dose increase must not exceed 100 units per treatment session

V. Other Dystonias: (off-label)

- Dystonia is a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both
- Dystonic movements are typically patterned, twisting, and may be tremulous
- Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation

A. Initial request:
1. Diagnosis of one of the following:
    a. Hemifacial Spasm **OR**
    b. Isolated Oromandibular Dystonia **OR**
    c. Spasm of pharyngoesophageal segment - Total laryngectomy **OR**
    d. Spastic Dysphonia **AND**
2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist **AND**
3. Documentation detailing diagnosis, symptoms, and functional impairment due to dystonia **AND**
4. For Isolated Oromandibular Dystonia and Spastic Dysphonia
   Failure of a trial of carbidopa/levodopa, trihexyphenidyl or tetrabenazine (or other anticholinergic or dopamine receptor blocker if the use of carbidopa/levodopa, trihexyphenidyl or tetrabenazine is not clinically appropriate) unless contraindicated or serious side effects are experienced **AND**
5. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration.

Age restriction: ≥ 18 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Hemifacial Spasm
   - 12 to 15 units, injected in divided doses of 2.5 or 5 units into the affected areas; total of 25 units; subsequent treatments every 3 to 4 months

b. Isolated Oromandibular Dystonia
   - Masseters 25 units, temporalis muscles 20 units. If the effect is not satisfying, in addition the internal pterygoid at a dose of 15 can be tried, subsequent treatments no sooner than every 3 months

c. Spasm of pharyngoesophageal segment – Total laryngectomy
   - 20-100 Units: 1 single injection if using unilaterally or bilaterally, 6-7 divided doses if using unilaterally, subsequent treatments no sooner than every 3 months.

d. Spastic Dysphonia
   - 5 to 20 units injected into both right and left cricothyroid muscles.

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**
2. Member has not received more than recommended dose for the condition treated over the past 3 months, **AND** it has been 12 weeks (3 months) since the last injection **AND**
3. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration **AND**
4. Requests for dose increase must not exceed off label recommended dosing per treatment session.

VI. Sialorrhea Excessive salivation associated with neurological disorders (i.e., Parkinson's disease, amyotrophic lateral sclerosis, cerebral palsy) (Off Label)

A. Initial request:
1. Diagnosis of sialorrhea, excessive salivation or excessive drooling associated with Parkinson's Disease, cerebral palsy or other neurologic disorder that has been present for at least 3 months **AND**
2. Prescribed by or in consultation with neurologist or otolaryngologist **AND**
3. Failure of an adequate trial of anticholinergic agent such as glycopyrrolate, trihexyphenidyl, scopolamine, atropine, or amitriptyline to control symptoms **AND**
4. Persistence of medically significant complications due to excessive drooling such as chronic skin maceration or bacterial / fungal skin infections despite standard topical treatments **AND**
5. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration

Age restriction: ≥ 2 years

Dosing guidelines: Please see Dosing / Conversion Guidelines section below for the appropriate serotype conversion ratios.

a. Dose does not exceed 100units
b. Dose calculated based on patient weight and rate of salivation
   Recommended dosage ranges from 1 to 5.5 units per kg distributed into 2 to 4 glands.
   Alternative dosing: 15 units/gland (body weight less than 15 kg), 20 units/gland (body weight 15 to 25 kg), or 25 units/gland (body weight greater than 25 kg)
c. Average duration of effect = 3 to 6 months; Time to retreat: 16 weeks

B. Recertification
Previously approved by plan or has met initial approval criteria:

1. Documentation to support a positive response to treatment **AND**

2. Member has not received more than 100 units over the past 3 months, **AND** it has been 16 weeks (4 months) since the last injection **AND**
3. Provider must submit the number of units to be used in each treatment session, total dose per visit and the anticipated frequency of injection administration **AND**
4. Requests for dose increase must not exceed 100 units per treatment session

All Other Non-FDA Approved Indications:
Requests for Non-FDA approved indications which are not addressed above, and are not listed as an excluded diagnosis below, must meet the Off-Label Use of FDA Approved Drugs Policy Criteria.

Excluded diagnoses/indications for which coverage will NOT be authorized:

- Episodic migraine prophylaxis:
  Safety and effectiveness of Botox have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) in seven placebo-controlled studies.

- Spasticity:
  (any upper or lower limb muscle groups other than elbow, wrist, finger, thumb, ankle, and toe flexors.) Safety and effectiveness of Botox have not been established for the treatment of other upper or lower limb muscle groups. Safety and effectiveness of Botox have not been established for the treatment of spasticity in pediatric patients under age 18 years. Botox has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture. Treatment with Botox is not intended to substitute for usual standard of care rehabilitation regimens.

- Hyperhidrosis other than axillary:
  Safety and effectiveness of Botox have not been established for the treatment of hyperhidrosis in body areas other than axillary.

- Cosmetic indications:
  Treatment of wrinkles {such as wrinkles of the upper face including glabellar frown lines, deep forehead wrinkles and periorbital wrinkles (crow's feet)} is considered a cosmetic use and is excluded from coverage due to a lack of functional deficit. (See list of included diagnoses at the end of this policy.)

- Experimental / Investigational Diagnoses:
  See list of Experimental / Investigational Diagnoses at the end of this policy.

CURRENTLY ACCEPTED CONVERSION RATIOS

Botulinum Toxin Serotype A

OnabotulinumtoxinA (ONA; Botox), Abobotulinum toxin A (ABO; Dysport) and Incobotulinum toxin A (INCO; Xeomin)

Table 1. Botulinum toxin products and protein content/100 units

Nonproprietary Name	150-kD Protein Content (ng)	Total Protein (150 kD and NAP) Content (ng)	Dose Equivalent Units
Onabotulinumtoxin A	0.73	5.00	1
Incobotulinumtoxin A	0.44	0.44	1
Abobotulinumtoxin A	0.65	0.87	2–3

NAP = nontoxic accessory proteins.

ONA (Botox) and INCO (Xeomin) have comparable efficacies with a 1:1 conversion ratio and have demonstrated therapeutic equivalence in different indications including cervical dystonia and blepharospasm. An ONA (Botox) to ABO (Dysport), a conversion ratio ≤1:3 is currently considered the most appropriate.

Botulinum Toxin Serotype B

RimabotulinumtoxinB (Myobloc)

The most recent available studies suggest that the current conversion ratio for RimabotulinumtoxinB (Myobloc): OnabotulinumtoxinA (Botox) is 50:1 (Myobloc: Botox).

POLICY GUIDELINES:

1. Prior authorization is contract dependent.
2. For treatment of diagnoses not found within this policy – Refer to the Off-label use of FDA Approved Drugs policy for the relevant line of business.
3. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
4. Supportive documentation of previous drug use must be submitted for any criterion that requires the trial of a preferred agent if the preferred drug is not found in claims history.
    a. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
    b. The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
    c. The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
    d. The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;

e. The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
f. The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
g. The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.

5. Unless otherwise stated below within the individual drug criteria, approval time periods are listed in the table below
   a. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. [Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics or other guideline-supported treatment options)] and the requested dose must continue to meet FDA approved or off-label/guideline supported dosing

Line of Business	**Medical Initial Approval**	**Medical Recertification**
Medicaid Managed Care (MMC) / Essential Plan (EP) / Child Health Plus (CHP)	Botulinium Toxins for Chronic Migraine: 6 months (12 weeks) All other indications: 12 months	12 months

Experimental / Investigational or Cosmetic Diagnoses:

The following diagnoses are considered Experimental / Investigational or Cosmetic for **ALL** Botulinum Toxin formulations and are excluded from coverage, unless provider can supply literature supporting its use that meets the plan's current Off Label Use of FDA-Approved drugs policy. (Diagnoses for these on this list are reviewed on a regular basis to ensure status as Experimental / Investigational or Cosmetic uses.)

Backache, low back pain
Cervicogenic headache
Chronic motor tic disorder (other than blepharospasm, hemifacial spasm, Meige syndrome)
Congenital esotropia
Dysphagia
Epicondylitis
Essential tremor
Excessive tear production
Fibromyalgia
Granuloma of vocal cords
Hemorrhoidectomy – postoperative pain

Injury to oculomotor nerve (acute)
Larynx closure, adjunct to surgical procedure
Migraine – first line management
Organic voice tremor
Spasm, of pharyngoesophageal segment – total laryngectomy
Stuttering
Tardive dyskinesia
Temporomandibular joint disorder
Tension-type headaches
Thoracic outlet syndrome
Trigeminal neuralgia, idiopathic, refractory
Urinary and anal sphincter dysfunction / detrusor, pelvic floor and sphincter dyssynergia
Whiplash injury to neck

UPDATES:

Date	Revision
8/24/2023	Reviewed and approved P&T Committee
8/2023	Reviewed
9/2022	P&T Committee Approval
7/2022	Revised
12/2021	Revised
9/2021	Reviewed / P&T Committee Approval
08/2021	Review / Revision
11/2020	Revision & P&T Committee Approval
3/30/2020	Revision
2/10/2020	Revision
11/15/2019	Revision
9/23/2019	Revised
09/6/2018	Created

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