BOTOX® onabotulinumtoxinA injection

Elements of Provider Documentation Consistent with Medicare Guidelines

1 Document medical necessity

Include a statement that BOTOX® (onabotulinumtoxinA) treatment is reasonable and necessary and that the patient will benefit from the treatment. In order to be considered reasonable and necessary, services must be documented as:

- Consistent with symptoms or diagnosis of the illness or injury under treatment
- Necessary and consistent with generally accepted professional standards
- Provided safely and effectively at the appropriate level

Note: Complete an examination of the patient and document symptoms and test results, such as limitations in functions and prior treatment administered.

2 Document covered diagnoses

Medicare Part B policies list the *ICD-10-CM* diagnosis codes for those conditions covered by Medicare. These are conditions for which BOTOX® has been proven efficacious and/or is the standard of care in the local community.

Note: Review the Medicare Part B policy for BOTOX® for your area if the contractor has published an LCD. Ensure that the patient's diagnosis is included in the list of covered diagnoses, documented in the medical record, recorded in Block 21 of the CMS-1500 form, and linked to the appropriate procedure code via notation in Block 24E.

IMPORTANT SAFETY INFORMATION, INCLUDING BOXED WARNING

WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of BOTOX® and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening, and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity, but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have an underlying condition that would predispose them to these symptoms. In unapproved uses, including spasticity in children, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and spasticity and at lower doses.

Please see Indications and additional Important Safety Information about BOTOX® on following pages.

BOTOX® Practice Solutions

3 Document that traditional therapies have been tried and failed

The medical policy for BOTOX® (onabotulinumtoxinA) requires documentation that the patient has been unresponsive to conventional medical treatments such as medication, physical therapy, and other appropriate methods used to control or treat the condition.

Note: Be certain to record the treatments that have been tried before and failed to demonstrate adequate efficacy.

4 Document the services provided and dates of service

Most payers will reimburse for the portion of BOTOX® that cannot be used and must be discarded. It is important, however, to follow specific guidelines (eg, Medicare Part B policies for BOTOX®) on how to document and record this wastage. These guidelines can vary considerably from payer to payer, so it is important to follow each payer's specific guidelines. Documentation in the patient's medical record should always reflect the exact amount of BOTOX® injected, any unavoidable wastage, and the exact amount discarded. Review your local carrier's policies on billing for waste.

5 Document supporting medical necessity for the use of electromyography (EMG), if applicable

The EMG procedure codes specified in the Medicare policy may be covered if the physician has difficulty in determining the proper injection site(s). The difficulty in locating the injection site(s) must be documented. If providers submit claims electronically, medical justification must be noted on the patient's medical record in the event that an explanation is later required. Insurers limit EMG service to 1 Unit per treatment session. Ensure that providers use an appropriate EMG code and that the code selected is included in the insurer's coverage policy for BOTOX®.

Note: The statement in the chart should indicate that EMG was necessary to properly isolate the muscle.

Indications

Bladder Dysfunction:

Overactive Bladder

BOTOX® for injection is indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication.

Detrusor Overactivity Associated With a Neurologic Condition

BOTOX® is indicated for the treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (eg, SCI, MS) in adults who have an inadequate response to or are intolerant of an anticholinergic medication.

Chronic Migraine

BOTOX® is indicated for the prophylaxis of headaches in adult patients with chronic migraine (≥ 15 days per month with headache lasting 4 hours a day or longer).

Important Limitations

Safety and effectiveness have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) in 7 placebo-controlled studies.

Please see additional Indications and Important Safety Information about BOTOX® on following pages.

6 Document clinical effectiveness of BOTOX® (onabotulinumtoxinA)

Successful outcomes of the treatment must be documented in the medical record to support requests for coverage for subsequent treatments. Medicare carriers often give 2 successive chances for BOTOX® to work. If the injection to the same site has failed twice, providers may refuse to cover future injections. Certain carriers may allow patients to re-try BOTOX® 1 year after the second injection. Consult your local carrier for specific limitations in this regard.

Note: Record the patient's condition after the injection and response to treatment in the medical record.

7 Document specific injection site(s) and amount of toxin injected at each site

Medicare requires that the specific muscles injected are documented in the medical record, along with the amount of toxin used at each site.

Note: You must document the number of BOTOX® injections given per site and the amount of BOTOX® used for each injection. Consider the use of an anatomical chart or depiction to record injections.

Many Medicare policies also require that you document unused portions of BOTOX® in the medical record. Please refer to your local Medicare policy for information about documenting discarded BOTOX® wastage.

The information contained herein is gathered from third-party sources and is subject to change. This information is intended for reference only. Nothing in this document is intended to serve as reimbursement or legal advice, a guarantee of coverage, or a guarantee of payment for BOTOX®. Actual benefits are determined by Medicare plan administrators. Medicare plans, coverage criteria, and formularies are subject to change without notice. Check each patient's coverage with applicable insurer. Allergan does not endorse any individual plans. Decisions regarding medical necessity and documentation to support coverage of BOTOX® must be made by the provider/physician considering the clinical facts, circumstances, and applicable coverage rules. Coverage does not imply efficacy or safety.

Indications (continued)

Spasticity:

Upper Limb Spasticity

BOTOX® is indicated for the treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), finger flexors (flexor digitorum profundus and flexor digitorum sublimis) and thumb flexors (adductor pollicis and flexor pollicis longus).

Lower Limb Spasticity

BOTOX® is indicated for the treatment of lower limb spasticity in adult patients to decrease the severity of increased muscle tone in ankle and toe flexors (gastrocnemius, soleus, tibialis posterior, flexor hallucis longus, and flexor digitorum longus).

Important Limitations

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.

Cervical Dystonia

BOTOX® is indicated for the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.

Please see additional Important Safety Information about BOTOX® on following pages.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

BOTOX® (onabotulinumtoxinA) is contraindicated in the presence of infection at the proposed injection site(s) and in individuals with known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation.

Intradetrusor injection of BOTOX® is contraindicated in patients with overactive bladder or detrusor overactivity associated with a neurologic condition who have a urinary tract infection (UTI). Intradetrusor injection of BOTOX® is also contraindicated in patients with urinary retention and in patients with post-void residual (PVR) urine volume > 200 mL, who are not routinely performing clean intermittent self-catheterization (CIC).

WARNINGS AND PRECAUTIONS

Lack of Interchangeability Between Botulinum Toxin Products
The potency Units of BOTOX® are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of BOTOX® cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method.

Spread of Toxin Effect
See Boxed Warning.

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX® for Chronic Migraine at the labeled doses have been reported.

Serious Adverse Reactions with Unapproved Use
Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received BOTOX® injections for unapproved uses. In these cases, the adverse reactions were not necessarily related to distant spread of toxin, but may have resulted from the administration of BOTOX® to the site of injection and/or adjacent structures. In several of the cases, patients had pre-existing dysphagia or other significant disabilities. There is insufficient information to identify factors associated with an increased risk for adverse reactions associated with the unapproved uses of BOTOX®. The safety and effectiveness of BOTOX® for unapproved uses have not been established.

Hypersensitivity Reactions
Serious and/or immediate hypersensitivity reactions have been reported. These reactions include anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea. If such a reaction occurs, further injection of BOTOX® should be discontinued and appropriate medical therapy immediately instituted. One fatal case of anaphylaxis has been reported in which lidocaine was used as the diluent, and consequently the causal agent cannot be reliably determined.

Increased Risk of Clinically Significant Effects with Pre-Existing Neuromuscular Disorders
Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis or neuromuscular junction disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should be monitored when given botulinum toxin. Patients with neuromuscular disorders may be at increased risk of clinically significant effects including generalized muscle weakness, diplopia, ptosis, dysphonia, dysarthria, severe dysphagia and respiratory compromise from therapeutic doses of BOTOX® (see *Warnings and Precautions*).

Dysphagia and Breathing Difficulties
Treatment with BOTOX® and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with pre-existing swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or oropharyngeal muscles that control swallowing or breathing (*see Boxed Warning*).

Pulmonary Effects of BOTOX® in Patients With Compromised Respiratory Status Treated for Spasticity or for Detrusor Overactivity Associated With a Neurologic Condition
Patients with compromised respiratory status treated with BOTOX® (onabotulinumtoxinA) for spasticity or detrusor overactivity associated with a neurologic condition should be monitored closely.

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity
Bronchitis was reported more frequently as an adverse reaction in patients treated for upper limb spasticity with BOTOX® (3% at 251-360 Units total dose) compared to placebo (1%). In patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with BOTOX® (11% at 360 Units total dose; 8% at 240 Units total dose) compared to placebo (6%). In adult patients treated for lower limb spasticity, upper respiratory tract infections were reported more frequently as an adverse event in patients treated with BOTOX® (2% at 300 Units to 400 Units total dose), compared to placebo (1%).

Autonomic Dysreflexia in Patients Treated for Detrusor Overactivity Associated With a Neurologic Condition
Autonomic dysreflexia associated with intradetrusor injections of BOTOX® could occur in patients treated for detrusor overactivity associated with a neurologic condition and may require prompt medical therapy. In clinical trials, the incidence of autonomic dysreflexia was greater in patients treated with BOTOX® 200 Units compared with placebo (1.5% versus 0.4%, respectively).

Urinary Tract Infections in Patients With Overactive Bladder
BOTOX® increases the incidence of urinary tract infection. Clinical trials for overactive bladder excluded patients with more than 2 UTIs in the past 6 months and those taking antibiotics chronically due to recurrent UTIs. Use of BOTOX® for the treatment of overactive bladder in such patients and in patients with multiple recurrent UTIs during treatment should only be considered when the benefit is likely to outweigh the potential risk.

Urinary Retention in Patients Treated for Bladder Dysfunction
Due to the risk of urinary retention, treat only patients who are willing and able to initiate catheterization post-treatment, if required, for urinary retention.

In patients who are not catheterizing, post-void residual (PVR) urine volume should be assessed within 2 weeks post-treatment and periodically as medically appropriate up to 12 weeks, particularly in patients with multiple sclerosis or diabetes mellitus. Depending on patient symptoms, institute catheterization if PVR urine volume exceeds 200 mL and continue until PVR falls below 200 mL. Instruct patients to contact their physician if they experience difficulty in voiding as catheterization may be required.

Overactive Bladder
In clinical trials, 6.5% of patients (36/552) initiated clean intermittent catheterization for urinary retention following treatment with BOTOX® 100 Units as compared to 0.4% of patients (2/542) treated with placebo. The median duration of catheterization for patients treated with BOTOX® 100 Units was 63 days (minimum 1 day to maximum 214 days) as compared to a median duration 11 days (minimum 3 days to maximum 18 days) for patients receiving placebo.

Patients with diabetes mellitus treated with BOTOX® were more likely to develop urinary retention than non-diabetics. In clinical trials, 12.3% of patients (10/81) with diabetes developed urinary retention following treatment with BOTOX® 100 Units vs 0% patients (0/69) treated with placebo. In patients without diabetes, 6.3% of patients (33/526) developed urinary retention following treatment with BOTOX® 100 Units vs 0.6% of patients (3/516) treated with placebo.

Please see additional Important Safety Information about BOTOX® on following page.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Urinary Retention in Patients Treated for Bladder Dysfunction (continued)

Detrusor Overactivity Associated With a Neurologic Condition

In clinical trials, 30.6% of patients (33/108) who were not using clean intermittent catheterization (CIC) prior to injection, required catheterization for urinary retention following treatment with BOTOX® (onabotulinumtoxinA) 200 Units as compared to 6.7% of patients (7/104) treated with placebo. The median duration of post-injection catheterization for these patients treated with BOTOX® 200 Units (n = 33) was 289 days (minimum 1 day to maximum 530 days) as compared to a median duration 358 days (minimum 2 days to maximum 379 days) for patients receiving placebo (n = 7).

Among patients not using CIC at baseline, those with MS were more likely to require CIC post-injection than those with SCI.

Human Albumin and Transmission of Viral Diseases

This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is also considered extremely remote. No cases of transmission of viral diseases or CJD have ever been reported for albumin.

ADVERSE REACTIONS

The following adverse reactions to BOTOX® for injection are discussed in greater detail in the following sections: Spread of Toxin Effect (see *Boxed Warning*); Serious Adverse Reactions with Unapproved Use (see *Warnings and Precautions*); Hypersensitivity Reactions (see *Contraindications* and *Warnings and Precautions*); Increased Risk of Clinically Significant Effects with Pre-Existing Neuromuscular Disorders (see *Warnings and Precautions*); Dysphagia and Breathing Difficulties (see *Warnings and Precautions*); Pulmonary Effects of BOTOX® in Patients with Compromised Respiratory Status Treated for Spasticity or for Detrusor Overactivity associated with a Neurologic Condition (see *Warnings and Precautions*); Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity (see *Warnings and Precautions*); Autonomic Dysreflexia in Patients Treated for Detrusor Overactivity associated with a Neurologic Condition (see *Warnings and Precautions*); Urinary Tract Infections in Patients with Overactive Bladder (see *Warnings and Precautions*); and Urinary Retention in Patients Treated for Bladder Dysfunction (see *Warnings and Precautions*).

Overactive Bladder

The most frequently reported adverse reactions for overactive bladder occurring within 12 weeks of injection include urinary tract infection (BOTOX® 18%, placebo 6%), dysuria (BOTOX® 9%, placebo 7%), urinary retention (BOTOX® 6%, placebo 0%), bacteriuria (BOTOX® 4%, placebo 2%), and residual urine volume (BOTOX® 3%, placebo 0%).

A higher incidence of urinary tract infection was observed in patients with diabetes mellitus treated with BOTOX® 100 Units and placebo than non-diabetics.

The incidence of UTI increased in patients who experienced a maximum post-void residual (PVR) urine volume ≥ 200 mL following BOTOX® injection compared to those with a maximum PVR < 200 mL following BOTOX® injection, 44% versus 23%, respectively.

Detrusor Overactivity Associated With a Neurologic Condition

The most frequently reported adverse reactions within 12 weeks of BOTOX® injection for detrusor overactivity associated with a neurologic condition include urinary tract infection (BOTOX® 24%, placebo 17%), urinary retention (BOTOX® 17%, placebo 3%), and hematuria (BOTOX® 4%, placebo 3%).

The following adverse event rates were reported at any time following initial injection and prior to reinjection or study exit (median duration of 44 weeks of exposure): urinary tract infections (49%), urinary retention (17%), constipation (4%), muscular weakness (4%), dysuria (4%), fall (3%), gait disturbance (3%), and muscle spasm (2%).

Chronic Migraine

The most frequently reported adverse reactions following injection of BOTOX® (onabotulinumtoxinA) for chronic migraine include neck pain (9%), headache (5%), eyelid ptosis (4%), migraine (4%), muscular weakness (4%), musculoskeletal stiffness (4%), bronchitis (3%), injection-site pain (3%), musculoskeletal pain (3%), myalgia (3%), facial paresis (2%), hypertension (2%), and muscle spasms (2%).

Severe worsening of migraine requiring hospitalization occurred in approximately 1% of BOTOX® treated patients in study 1 and study 2, usually within the first week after treatment, compared with 0.3% of placebo-treated patients.

Upper Limb Spasticity

The most frequently reported adverse reactions following injection of BOTOX® for upper limb spasticity include pain in extremity, muscle weakness, fatigue, nausea, and bronchitis.

Lower Limb Spasticity

The most frequently reported adverse reactions following injection of BOTOX® for lower limb spasticity include arthralgia, back pain, myalgia, upper respiratory tract infection, and injection site pain.

Cervical Dystonia

The most frequently reported adverse reactions following injection of BOTOX® for cervical dystonia include dysphagia (19%), upper respiratory infection (12%), neck pain (11%), and headache (11%).

Post Marketing Experience

There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have also been reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including cardiovascular disease. The exact relationship of these events to the botulinum toxin injection has not been established.

DRUG INTERACTIONS

Co-administration of BOTOX® and aminoglycosides or other agents interfering with neuromuscular transmission (eg, curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated. Use of anticholinergic drugs after administration of BOTOX® may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxin products at the same time or within several months of each other is unknown. Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin. Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of BOTOX®.

For more information on BOTOX®, please see the accompanying full Prescribing Information, including Boxed Warning and Medication Guide.

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