BOTOX® onabotulinumtoxinA injection

Clinic Day Scheduling

BOTOX® for appropriate patients

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).

Limitations of Use

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.

Adult Spasticity:

Adult 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, wrist, finger, and thumb flexors (biceps, flexor carpi radialis, flexor carpi ulnaris, flexor digitorum profundus, flexor digitorum sublimis, adductor pollicis, and flexor pollicis longus).

Adult 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).

Limitations of Use

Safety and effectiveness of BOTOX® have not been established for the treatment of other upper or lower limb muscle groups. BOTOX® has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture.

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 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 additional Indications and Important Safety Information on following pages.

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Clinic day scheduling

Having a structured approach to scheduling BOTOX® patients may help additional BOTOX® patients gain access to treatment. One such approach to consider is clinic day scheduling, which refers to the grouping of a specific type of patients, such as BOTOX® patients for therapeutic indications Chronic Migraine, Adult Upper Limb Spasticity (stiffness of the elbow, wrist, fingers, and thumb), and Cervical Dystonia, who are seen during one block of time.

The rationale behind this methodology is that it may be more efficient to group patients who are likely to require similar evaluation and treatment, allowing the physician and the entire team to have the same "mindset" when treating these patients, helping to deliver consistent patient education, streamlining processes, and helping to provide an enhanced patient experience. The practice needs to consider the most effective method of patient scheduling that will work best in the office. The following are considerations for dedicated BOTOX® clinic scheduling:

1. Evaluate the current volume of patients to determine the viability of grouping similar patients together during a clinic session.
2. Assess the average time required per injection visit to determine how many patients can be scheduled during a given block of time. Remember to include time for the assessment, patient education, and any other tasks that must be completed as part of the visit.
3. Identify appropriate blocks of time on the physician's schedule for clinic days. Consider what days and times work best for the provider as well as the staff. The frequency of the injection clinic days should be determined based upon practice needs and the number of patients being treated. For example, some practices may choose to have weekly injection clinics, while others will have sessions on a monthly basis.

Indications (continued)
Pediatric Spasticity:
Pediatric Upper Limb Spasticity
BOTOX® is indicated for the treatment of upper limb spasticity in pediatric patients 2 to 17 years of age.

Pediatric Lower Limb Spasticity, Excluding Spasticity Caused by Cerebral Palsy
BOTOX® is indicated for the treatment of lower limb spasticity in pediatric patients 2 to 17 years of age, excluding spasticity caused by cerebral palsy.

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.

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4. Establish BOTOX® clinic day processes, including staff roles and responsibilities for:

Patient Check-In	• Verify demographics and insurance information • Collect patient out-of-pocket responsibilities
Patient Intake	• Review and verify patient information • Complete patient history and physical examination
Informed Consent Protocols	• Provide treatment risk/benefits • Complete informed consent forms
BOTOX® Reconstitution	• Responsible party to oversee • Consider when to reconstitute and the amount of time required
Room Preparation, Set-Up, and Turnover	• Ensure appropriate equipment and supplies are available • Responsibility for restocking supplies
Patient Check-Out	• Schedule next injection appointment • Review charge sheet for accuracy

5. Per the physician's direction, utilize practice staff (physician assistants, nurse practitioners, medical assistants, etc) to assist with the BOTOX® treatment process. Consider how staff should assist with clinic day processes to help enhance the patient experience by promoting a quality provider-patient interaction.

6. Conduct regular training to ensure all staff members are educated on BOTOX® clinic day processes as well as roles and responsibilities.

7. Assess and modify the clinic day schedules on a regular basis to promote BOTOX® patient access to care and a positive BOTOX® patient experience.

Indications (continued)

Blepharospasm and Strabismus

BOTOX® is indicated for the treatment of Strabismus and Blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and older.

Primary Axillary Hyperhidrosis

BOTOX® is indicated for the treatment of severe primary axillary hyperhidrosis that is inadequately managed with topical agents.

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

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Clinic day scheduling implementation plan

This template is designed to guide the implementation of considerations for clinic day scheduling of BOTOX® as a treatment option for appropriate patients within the practice. This implementation plan is intended to be modified and customized as needed, per provider direction.

CONSIDERATIONS	METHOD	RESPONSIBLE PARTY	COMPLETION DATE
1. Evaluate current volume of BOTOX® patients to determine viability of clinic day scheduling.			
2. Determine how many BOTOX® patients can be scheduled during a given block of time by assessing the average time per treatment session/visit. Consider allocation time for new patients (first injection) vs repeat injections.			
3. Identify appropriate time blocks on the schedule for clinic days.			
4. Establish clinic day protocols including staff roles and responsibilities.			
5. Utilize practice staff, as appropriate, to assist with patient flow.			
6. Establish a timeline to conduct regular staff training.			
7. Assess the clinic day schedules on a regular basis, and modify as needed.			

Indications (continued)
Limitations of Use

The safety and effectiveness of BOTOX® for hyperhidrosis in other body areas have not been established. Weakness of hand muscles and blepharoptosis may occur in patients who receive BOTOX® for palmar hyperhidrosis and facial hyperhidrosis, respectively. Patients should be evaluated for potential causes of secondary hyperhidrosis (eg, hyperthyroidism) to avoid symptomatic treatment of hyperhidrosis without the diagnosis and/or treatment of the underlying disease.

Safety and effectiveness of BOTOX® have not been established for the treatment of axillary hyperhidrosis in pediatric patients under age 18.

Please see additional Important Safety Information on following pages.

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Alternative BOTOX® scheduling implementation plan

CONSIDERATIONS	METHOD	RESPONSIBLE PARTY	COMPLETION DATE

IMPORTANT SAFETY INFORMATION (continued)
CONTRAINDICATIONS

BOTOX® is contraindicated in the presence of infection at the proposed injection site(s) and in patients who are hypersensitive to any botulinum toxin product or to any of the components in the formulation.

BOTOX® is contraindicated for intradetrusor injection in patients with a urinary tract infection; or in patients with urinary retention or post-void residual (PVR) urine volume > 200 mL who are not routinely performing clean intermittent self-catheterization (CIC).

Please see additional Important Safety Information on following pages.

BOTOX® onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS

Spread of Toxin Effect
See Boxed Warning.

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX® for Blepharospasm at the recommended dose (30 Units and below), severe primary axillary hyperhidrosis at the recommended dose (100 Units), Strabismus, or for Chronic Migraine at the labeled doses have been reported.

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.

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.

Please see additional Important Safety Information on following pages.

BOTOX® onabotulinumtoxinA injection

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IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

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 (ALS), or neuromuscular junction disorders (eg, myasthenia gravis or Lambert-Eaton syndrome) should be monitored when given botulinum toxin. Patients with known or unrecognized neuromuscular disorders or neuromuscular junction 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*).

Please see additional Important Safety Information on following pages.

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Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

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*).

Please see additional Important Safety Information on following pages.

BOTOX® onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

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® for adult spasticity or detrusor overactivity associated with a neurologic condition should be monitored closely.

Corneal Exposure and Ulceration in Patients Treated With BOTOX® for Blepharospasm
Reduced blinking from BOTOX® injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect, and corneal ulceration, especially in patients with VII nerve disorders.

Retrobulbar Hemorrhages in Patients Treated With BOTOX® for Strabismus
During the administration of BOTOX® for the treatment of Strabismus, retrobulbar hemorrhages sufficient to compromise retinal circulation have occurred. It is recommended that appropriate instruments to decompress the orbit be accessible.

Please see additional Important Safety Information on following pages.

BOTOX® onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

Bronchitis was reported more frequently as an adverse reaction in adult patients treated for upper limb spasticity with BOTOX® (3% at 251 Units to 360 Units total dose) compared to placebo (1%). In adult 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 reaction in patients treated with BOTOX® (2% at 300 Units to 400 Units total dose) compared to placebo (1%). In pediatric patients treated for upper limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX® (17% at 6 Units/kg and 10% at 3 Units/kg) compared to placebo (9%). In pediatric patients treated for lower limb spasticity, upper respiratory tract infection was not reported with an incidence greater than placebo.

Please see additional Important Safety Information on following pages.

BOTOX® onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

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.

Please see additional Important Safety Information on following pages.

BOTOX® onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

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 of 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 nondiabetics. In clinical trials, 12.3% of patients (10/81) with diabetes developed urinary retention following treatment with BOTOX® 100 Units vs 0% of 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 on following pages.

BOTOX® onabotulinumtoxinA injection

Notes

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® 200 Units as compared to 6.7% of patients (7/104) treated with placebo. The median duration of postinjection 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 of 358 days (minimum 2 days to maximum 379 days) for patients receiving placebo (n = 7).

Among patients not using CIC at baseline, those with multiple sclerosis were more likely to require CIC post injection than those with spinal cord injury.

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 and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would also be considered extremely remote. No cases of transmission of viral diseases, CJD, or vCJD have ever been identified for licensed albumin or albumin contained in other licensed products.

Please see additional Important Safety Information on following pages.

BOTOX® onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS

Adverse reactions to BOTOX® for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *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 nondiabetics.

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% vs 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%).

Please see additional Important Safety Information on following pages.

BOTOX® onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Chronic Migraine
The most frequently reported adverse reactions following injection of BOTOX® 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%).

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

Adult 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.

Pediatric Upper Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX® in pediatric upper limb spasticity include upper respiratory tract infection (includes upper respiratory tract infection and viral upper respiratory tract infection), injection-site pain, nausea, constipation, rhinorrhea, nasal congestion, and seizure (includes seizure and partial seizure).

Please see additional Important Safety Information on following page.

BOTOX® onabotulinumtoxinA injection

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Pediatric Lower Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX® in pediatric lower limb spasticity include injection-site erythema, injection-site pain, oropharyngeal pain, ligament sprain, skin abrasion, and decreased appetite.

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%).

Blepharospasm
The most frequently reported adverse reactions following injection of BOTOX® for Blepharospasm include ptosis (21%), superficial punctate keratitis (6%), and eye dryness (6%).

Strabismus
The most frequently reported adverse events following injection of BOTOX® for Strabismus include ptosis (15.7%) and vertical deviation (16.9%).

Primary Axillary Hyperhidrosis
The most frequently reported adverse events (3%-10% of adult patients) following injection of BOTOX® for severe primary axillary hyperhidrosis in double-blind studies include injection-site pain and hemorrhage, nonaxillary sweating, infection, pharyngitis, flu syndrome, headache, fever, neck or back pain, pruritus, and anxiety.

Postmarketing Experience
Adverse reactions that have been identified during postapproval use of BOTOX® are discussed in greater detail in Postmarketing Experience (Section 6.3 of the Prescribing Information).

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 other agents interfering with neuromuscular transmission (eg, aminoglycosides, 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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