**Indication**

**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.

**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 additional Important Safety Information on following pages.
Retention was NOT defined as the complete inability to go\(^1\)

- In clinical studies, retention was defined as having associated symptoms (eg, voiding difficulties or sensation of bladder fullness) with 6% of BOTOX® patients experiencing it\(^1,2\)

PVR thresholds can be subjective unless when to initiate CIC is clearly defined

- Real-world clinical practice varies, but in BOTOX® clinical studies, patients had to initiate CIC if\(^2\):
  - Asymptomatic: PVR ≥ 350 mL
  - Symptomatic: PVR ≥ 200 mL to < 350 mL

6.5% of BOTOX® patients needed to use CIC in pivotal trials\(^2\)

Do you share your own personal experience with your patients? Look inside for a simple approach to consider when discussing CIC

IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS (continued)
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®.

Please see accompanying full Prescribing Information, including Boxed Warning and Medication Guide.

Share these 3 key points with your patients:

1. The majority of patients who receive BOTOX® for OAB do not need to self-catheterize
   - “About 94 out of every 100 patients in clinical studies of BOTOX® for OAB did not need to self-catheterize”
   - “If it didn’t happen, we will help you through it”

2. Demystify the word “retention” and explain that CIC is temporary, if needed
   - “Sometimes it can become temporarily difficult to empty your bladder. But remember, difficulty emptying does not mean you can’t urinate at all, it just means you have difficulty fully emptying the bladder”
   - “It is much smaller, easy to use, and you use it by yourself”
   - “Fit in your purse or pocket”
   - “Ready to use when it’s needed”

3. A self-catheter is NOT like the kind you see in a hospital
   - “It fits in your purse or pocket”

Consider using the new, animated BOTOX® patient education video at botoxoabvideo.com

Put CIC in the right perspective to help achieve BOTOX® treatment acceptance

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

BOTOX® is contraindicated in the presence of infection at the proposed injection site(s) and to any of the components in the formulation. Intradermal injection of BOTOX® is contraindicated in patients with overactive bladder who have a urinary tract infection (UTI), 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.

Serious Adverse Reactions With Unapproved Use

Safety of 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.

Hyper sensivity 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).

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).

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 using 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.

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. Patients who are not catheterized, 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, 6.3% of patients (6/99) 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 these 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 0.6% of patients (5/819) treated with placebo. In patients without diabetes, 6.3% of patients (53/856) developed urinary retention following treatment with BOTOX® 100 units vs 0.0% of patients (0/156) treated with placebo.

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.

ADVERSE REACTIONS

Adverse reactions to BOTOX® 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® 16%, 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. In clinical trials, 12.3% of patients (10/81) with diabetes developed urinary retention following treatment with BOTOX® 100 units vs 0.6% of patients (5/819) treated with placebo. In patients without diabetes, 6.3% of patients (53/856) developed urinary retention following treatment with BOTOX® 100 units vs 0.0% of patients (0/156) treated with placebo.

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.

DIAGNOSTIC USES

Co-administration of BOTOX® or 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.

Please see additional Important Safety Information on back.