BOTOX® (onabotulinumtoxinA) is a prescription medicine that contains tiny amounts of a highly purified botulinum toxin protein refined from the bacterium, *Clostridium botulinum*.

BOTOX® decreases muscle activity by blocking the overactive nerve impulses that trigger excessive muscle contractions or glandular activities.

When injected at doses approved by the U.S. Food and Drug Administration (FDA) into a specific muscle or gland, BOTOX® neurotoxin is expected to produce a safe and effective result, usually lasting between three to ten months depending on the approved indication and on the individual patient.

FACTS YOU SHOULD KNOW

- BOTOX® was first approved by the FDA 25 years ago for the treatment of two eye muscle disorders – strabismus (a disorder where the eyes do not line up in the same direction) and blepharospasm (involuntary spasm of the eyelids) – making it the first botulinum toxin type A product to be approved in the world.
- Since its first approval in 1989, BOTOX® has been recognized by regulatory authorities worldwide as an effective treatment for 27 different indications in approximately 88 countries,¹ benefiting millions of patients worldwide.
- In addition, the safety and efficacy of BOTOX® has been well-established in approximately 78 randomized, placebo-controlled clinical trials and in approximately

Please see additional Important Information on the following pages.
17,000 patients treated with BOTOX® (onabotulinumtoxinA) and BOTOX® Cosmetic in Allergan’s clinical trials.²

- Worldwide, approximately 47 million vials of BOTOX® and BOTOX® Cosmetic have been distributed over the past 23 years (1990-2013).³
- With approximately 2,800 articles on BOTOX® and BOTOX® Cosmetic published in scientific and medical journals, BOTOX® neurotoxin is one of the most widely researched medicines in the world.

**U.S. FOOD AND DRUG ADMINISTRATION APPROVED INDICATIONS**

In the United States, BOTOX® neurotoxin is approved to treat eight medical conditions, including the following:

- treatment of strabismus (disorder where the eyes do not line up in the same direction) in people 12 years and older;
- treatment of abnormal spasms of the eyelids (blepharospasm) in people 12 years and older;
- treatment of increased muscle stiffness in elbow, wrist, and finger muscles in people 18 years and older with upper limb spasticity;
- prevention of headaches in adults with chronic migraine who have 15 or more days each month with headache lasting 4 or more hours each day in people 18 years or older;
- treatment of overactive bladder symptoms such as a strong need to urinate with leaking or wetting accidents (urge urinary incontinence), a strong need to urinate right away (urgency), and urinating often (frequency) in adults 18 years and older when another type of medicine (anticholinergic) does not work well enough or cannot be taken.
- to treat leakage of urine (incontinence) in adults 18 years and older with overactive bladder due to neurologic disease who still have leakage or cannot tolerate the side effects after trying an anticholinergic medication.
- to prevent headaches in adults with chronic migraine who have 15 or more days each month with headache lasting 4 or more hours each day in people 18 years or older.
- to treat increased muscle stiffness in elbow, wrist, and finger muscles in people 18 years and older with upper limb spasticity.
- to treat the abnormal head position and neck pain that happens with cervical dystonia (CD) in people 16 years and older.
- to treat certain types of eye muscle problems (strabismus) or abnormal spasm of the eyelids (blepharospasm) in people 12 years and older.

BOTOX® is also injected into the skin to treat the symptoms of severe underarm sweating (severe primary axillary hyperhidrosis) when medicines used on the skin (topical) do not work well enough in people 18 years and older.

BOTOX® Cosmetic is a prescription medicine that is injected into muscles and used to improve the look of moderate to severe frown lines between the eyebrows (glabellar lines) in adults younger than 65 years of age for a short period of time (temporary).

BOTOX® Cosmetic is a prescription medicine that is injected into the area around the side of the eyes to improve the look of moderate to severe crow’s feet lines in adults for a short period of time (temporary).

It is not known whether BOTOX® and BOTOX® Cosmetic are safe or effective to prevent headaches in patients with migraine who have 14 or fewer headache days each month (episodic migraine).

Please see additional Important Safety Information on the following pages.
It is not known whether BOTOX® is safe or effective to treat increased stiffness in upper-limb muscles other than those in the elbow, wrist, and fingers, or to treat increased stiffness in lower-limb muscles. BOTOX® has not been shown to help people perform task-specific functions with their upper limbs or increase movement in joints that are permanently fixed in position by stiff muscles. Treatment with BOTOX® is not meant to replace your existing physical therapy or other rehabilitation that your doctor may have prescribed.

Do not take BOTOX® or BOTOX® Cosmetic if you: are allergic to any of the ingredients in BOTOX® (see Medication Guide for ingredients); had an allergic reaction to any other botulinum toxin product such as Myobloc® (rimabotulinumtoxinB), Dysport® (abobotulinumtoxinA), or Xeomin® (incobotulinumtoxinA); have a skin infection at the planned injection site.

Do not take BOTOX® for the treatment of urinary incontinence if you: have a urinary tract infection (UTI) or cannot empty your bladder on your own and are not routinely catheterizing.

Due to the risk of urinary retention (not being able to empty the bladder), only patients who are willing and able to initiate catheterization post-treatment, if required, should be considered for treatment.

In addition to its therapeutic uses, the same formulation of BOTOX® (onabotulinumtoxinA) with dosing specific for aesthetic patients has been approved by the FDA under the trade name BOTOX® Cosmetic (onabotulinumtoxinA). BOTOX® Cosmetic is injected into muscles and used to temporarily improve the appearance of moderate to severe frown lines between the eyebrows (glabellar lines) and moderate to severe crow’s feet lines (lateral canthal lines) in adults.

Today, Allergan is working in collaboration with many academic institutions, researchers, scientists and physicians to continue exploring the full therapeutic potential of this versatile medicine and to develop new medical uses for BOTOX® in other areas where there is a need for new treatment options.

TREATMENT ADMINISTRATION
BOTOX® is administered in small therapeutic doses by intramuscular or intradermal injections directly into the affected area, depending on the indication, producing a decrease in muscle or gland activity.

The therapeutic effect of BOTOX® is temporary and usually lasts between three to ten months depending on the indication, producing a temporary decrease in muscle or gland activity. Over time the nerve inhibition produced by BOTOX® neurotoxin is reversed as nerve endings recover and begin to release acetylcholine again, at which time another injection of BOTOX® may be needed to maintain therapeutic effect.
Patients treated for 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 these 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.

Patients treated for overactive bladder due to neurologic disease
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 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.

The dose of BOTOX® and BOTOX® Cosmetic is not the same as, or comparable to, any other botulinum toxin product.

Serious and/or immediate allergic reactions have been reported. These reactions include itching, rash, red itchy welts, wheezing, asthma symptoms, or dizziness or feeling faint. Tell your doctor or get medical help right away if you experience any such symptoms; further injection of BOTOX® or BOTOX® Cosmetic should be discontinued.

Tell your doctor about all your muscle or nerve conditions such as amyotrophic lateral sclerosis (ALS or Lou Gehrig’s disease), myasthenia gravis, or Lambert-Eaton syndrome, as you may be at increased risk of serious side effects including severe dysphagia (difficulty swallowing) and respiratory compromise (difficulty breathing) from typical doses of BOTOX® or BOTOX® Cosmetic.

Tell your doctor if you have any breathing-related problems. Your doctor will want to monitor you for any breathing problems during your treatment with BOTOX® for upper limb spasticity or for detrusor overactivity associated with a neurologic condition. The risk of pulmonary effects in patients with compromised respiratory status is increased in patients receiving BOTOX®.

Cornea problems have been reported. Cornea (surface of the eye) problems have been reported in some people receiving BOTOX® for their blepharospasm, especially in people with certain nerve disorders. BOTOX® may cause the eyelids to blink less, which could lead to the surface of the eye being exposed to air more than is usual. Tell your doctor if you experience any problems with your eyes while receiving BOTOX®. Your doctor may treat your eyes with drops, ointments, contact lenses, or with an eye patch.

Bleeding behind the eye has been reported. Bleeding behind the eyeball has been reported in some people receiving BOTOX® for their strabismus. Tell your doctor if you notice any new visual problems while receiving BOTOX®.

Bronchitis and upper respiratory tract infections (common colds) have been reported. Bronchitis was reported more frequently in people receiving BOTOX® for their upper limb spasticity. Upper respiratory infections (common colds) were also reported more frequently in people with prior breathing-related problems.

Please see additional Important Safety Information on the following page.
REFERENCES:

1. Allergan data on file
2. Allergan data on file; Global Medical Affairs
3. Allergan data on file; Global Safety and Epidemiology
4. Allergan data on file; Global Literature & Information Services and Global Regulatory Affairs

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