BOTOX® COSMETIC onabotulinumtoxinA injection

A QUICK GUIDE TO BOTOX® COSMETIC RECONSTITUTION

BOTOX® Cosmetic (onabotulinumtoxinA) Important Information

Indications

BOTOX® Cosmetic (onabotulinumtoxinA) is indicated in adult patients for the temporary improvement in the appearance of:
- Moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity
- Moderate to severe lateral canthal lines associated with orbicularis oculi activity
- Moderate to severe forehead lines associated with frontalis activity

IMPORTANT SAFETY INFORMATION, INCLUDING BOXED WARNING

WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of BOTOX® Cosmetic 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 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.

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WHY RECONSTITUTION IS IMPORTANT

RECONSTITUTION IMPACTS SAFE AND EFFECTIVE USE OF THE PRODUCT[1]

The reconstituted formulation of BOTOX® Cosmetic was studied in clinical trials and is critical to achieve the correct dose. Results seen in clinical trials were achieved using this FDA-approved reconstitution process.[1]

Reconstitution, dosage, and injection techniques all play an important part in delivering desired results to patients.[1]

WHAT YOU WILL NEED[1]

PRODUCT:
Unreconstituted 50-Unit or 100-Unit vials should be refrigerated at 36 °F to 46 °F (2 °C to 8 °C)

DILUENT:
Sterile, preservative-free 0.9% sodium chloride injection USP

TOOLS:
Appropriately sized syringes and needles, alcohol swabs, gloves

ON-LABEL RECONSTITUTION PROVIDES PREDICTABLE OUTCOMES AND REPEATABLE RESULTS[1]

Any change to reconstitution may lead to a underdiluted OR overdiluted formulation:

UNDERDILUTING

Underdilution, or using less than 2.5 mL of diluent, has not been studied in clinical trials.

ON-LABEL
BOTOX® COSMETIC RECONSTITUTION[1]

OVERDILUTING

Overdilution, or using more than 2.5 mL of diluent, has not been studied in clinical trials.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

BOTOX® Cosmetic 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.

WARNINGS AND PRECAUTIONS

Lack of Interchangeability Between Botulinum Toxin Products

The potency units of BOTOX® Cosmetic 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® Cosmetic cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method.

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4 STEPS TO RECONSTITUTION

1 INSPECT THE VIAL AND PACKAGING

Ensure you have authentic BOTOX® Cosmetic. Look for the tamper-evident seal and the US license number 1145 on the box and a rainbow holographic film with the name Allergan and a vacuum seal on the vial.[1]

2 PREPARE THE SALINE

Draw up 2.5 mL of saline if you are reconstituting a 100-Unit vial—or 1.25 mL if you are reconstituting a 50-Unit vial. The reconstituted concentration should be 4 Units/0.1 mL.[1]

SALINE DILUTION REMINDERS[1]:

100-UNIT VIAL
2.5 mL of saline

50-UNIT VIAL
1.25 mL of saline

Reconstituted concentration: **4 Units = 0.1 mL**

3 MIX THE SOLUTION

Slowly insert the saline syringe into the top of the vial. Let the vacuum pull the saline inside. Disconnect the syringe from the needle, then gently mix BOTOX® Cosmetic with the saline by swirling the vial.[1]

4 STORE RECONSTITUTED PRODUCT UNTIL INJECTION

Record the date and time of reconstitution in the space on the label. If not using immediately, refrigerate reconstituted BOTOX® Cosmetic vials at 36 °F to 46 °F (2 °C to 8 °C). Use within 24 hours because product and diluent do not contain a preservative.[1]

Contact Allergan Aesthetics at 1-800-890-4345 with any questions or concerns about your BOTOX® Cosmetic product.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Spread of Toxin Effect
Please refer to Boxed Warning for Distant Spread of Toxin Effect.

No definitive serious adverse event reports of distant spread of toxin effect associated with dermatologic use of BOTOX® Cosmetic at the labeled dose of 20 Units (for glabellar lines), 24 Units (for lateral canthal lines), 40 Units (for forehead lines with glabellar lines), 44 Units (for simultaneous treatment of lateral canthal lines and glabellar lines), and 64 Units (for simultaneous treatment of lateral canthal lines, glabellar lines, and forehead lines) have been reported. Patients or caregivers should be advised to seek immediate medical care if swallowing, speech, or respiratory disorders occur.

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.

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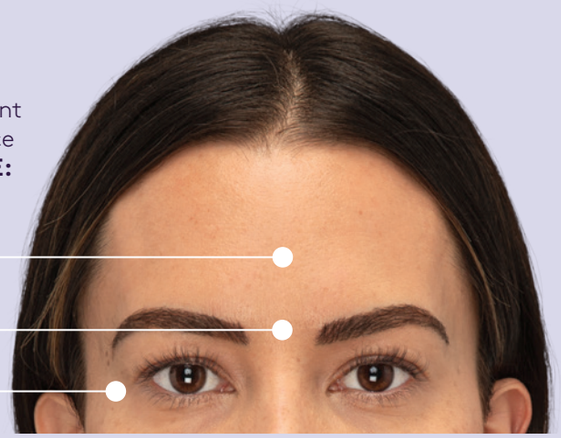
PREPARE FOR INJECTION AFTER RECONSTITUTION

USE FULL DOSE **FOR FULL RESULTS**[1]

64 Units **TOTAL FOR 3 AREAS**[1]

For temporary improvement in adults in the appearance of **MODERATE TO SEVERE:**



- **20 Units** FOREHEAD LINES (FHL)
- **20 Units** GLABELLAR LINES (GL)
- **24 Units** LATERAL CANTHAL LINES (LCL)

Real patient treated for the appearance of moderate to severe forehead lines, lateral canthal lines, and glabellar lines. ***Results may vary.***

- Attach a new sterile syringe and draw the required amount of reconstituted BOTOX® Cosmetic solution into the syringe (see right)
- Consider using a separate syringe for each area treated
- Angle the needle into the bottom corner of the vial for full extraction
- Do not completely invert the vial
- Expel any air bubbles in the syringe barrel

See **The Look of 3**℠ Dosing and Injection Guide for more on proper dosing and injection techniques.

THE REQUIRED AMOUNT OF RECONSTITUTED **BOTOX® COSMETIC SOLUTION IS**[1]**:**

20 Units 0.5 mL for moderate to severe forehead lines

20 Units 0.5 mL for moderate to severe glabellar lines

24 Units 0.6 mL for moderate to severe lateral canthal lines

Visuals are of 1-mL syringes and are not to scale.

Reconstituted concentration: **4 Units = 0.1 mL**

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 reactions occur, further injection of BOTOX® Cosmetic 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.

Cardiovascular System
There have been reports following administration of BOTOX® of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including pre-existing cardiovascular disease. Use caution when administering to patients with pre-existing cardiovascular disease.

Increased Risk of Clinically Significant Effects With Pre-existing Neuromuscular Disorders
Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junction disorders (eg, 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 onabotulinumtoxinA (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*).

Pre-existing Conditions at the Injection Site
Caution should be used when BOTOX® Cosmetic treatment is used in the presence of inflammation at the proposed injection site(s) or when excessive weakness or atrophy is present in the target muscle(s).

Please see additional Important Safety Information on back page.

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WATCH A STEP-BY-STEP RECONSTITUTION VIDEO ON **HCP.BOTOXCOSMETIC.COM**

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Dry Eye in Patients Treated With BOTOX® Cosmetic
There have been reports of dry eye associated with BOTOX® Cosmetic injection in or near the orbicularis oculi muscle. If symptoms of dry eye (eg, eye irritation, photophobia, or visual changes) persist, consider referring patients to an ophthalmologist.

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
The most frequently reported adverse reactions following injection of BOTOX® Cosmetic for glabellar lines were eyelid ptosis (3%), facial pain (1%), facial paresis (1%), and muscular weakness (1%).

The most frequently reported adverse reaction following injection of BOTOX® Cosmetic for lateral canthal lines was eyelid edema (1%).

The most frequently reported adverse reactions following injection of BOTOX® Cosmetic for forehead lines with glabellar lines were headache (9%), brow ptosis (2%), and eyelid ptosis (2%).

DRUG INTERACTIONS
Co-administration of BOTOX® Cosmetic 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® Cosmetic 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® Cosmetic.

USE IN SPECIFIC POPULATIONS
There are no studies or adequate data from postmarketing surveillance on the developmental risk associated with use of BOTOX® Cosmetic in pregnant women. There are no data on the presence of BOTOX® Cosmetic in human or animal milk, the effects on the breastfed child, or the effects on milk production.

Please see accompanying BOTOX® Cosmetic full Prescribing Information, including Boxed Warning, or visit https://www.rxabbvie.com/pdf/botox-cosmetic_pi.pdf

REFERENCE: 1. BOTOX® Cosmetic Prescribing Information, July 2020.

Allergan Aesthetics
an AbbVie company