BOTOX®
COSMETIC
onabotulinumtoxinA injection

JUST LIKE NO TWO FINGERPRINTS ARE THE SAME

# No two neurotoxins are the same

Differences in biological assays and subsequent variations in biological activity are well recognized by the FDA.[1]

**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
- Moderate to severe platysma bands associated with platysma muscle 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 the following page.**

BOTOX® COSMETIC onabotulinumtoxinA injection

# Botulinum toxins are not equivalent[2-7]

Unique manufacturing and formulations result in lack of equivalency.[2-7]

| | | Bacterial strain | Molecular size | Potency assay | Units per vial |
|---|---|---|---|---|---|
| **OnabotulinumtoxinA** |  | Hall[2] | ~ 900 kDa[8] | Cell based[1,2] | 50 BOTOX® Cosmetic Units[2]<br>100 BOTOX® Cosmetic Units[2] |
| **AbobotulinumtoxinA** |  | Hall[3] | ≤ 500 kDa[1] | Cell based[3] | 300 Dysport Units[3] |
| **IncobotulinumtoxinA** |  | Hall[4] | ~ 150 kDa[1] | Cell based[4] | 50 Xeomin Units[4]<br>100 Xeomin Units[4] |
| **PrabotulinumtoxinA-xvfs** |  | Hall[9] | 900 kDa[5] | Animal based[5] | 100 Jeuveau Units[5] |
| **DaxibotulinumtoxinA-lanm** |  | Hall[10] | ~ 150 kDa[6] | Cell based[11] | 50 Daxxify Units[6]<br>100 Daxxify Units[6] |
| **LetibotulinumtoxinA-wlbg** |  | CBFC26[12] | 900 kDa[7] | Animal based[12] | 50 Letybo Units[7]<br>100 Letybo Units[7] |

- The BOTOX® Cosmetic (onabotulinumtoxinA) molecule consists of the core neurotoxin (150 kDa) and associated proteins (~ 750 kDa)[8]
- The exact biochemical composition of Dysport (abobotulinumtoxinA) is unknown.[1] Exact proportion of associated proteins to the core neurotoxin is unknown
- Both the Xeomin (incobotulinumtoxinA) and Daxxify (daxibotulinumtoxinA-lanm) molecules consist of only the core neurotoxin (150 kDa)[4,6]

**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 Equivalency Between Botulinum Toxin Products**
**The potency Units of BOTOX® Cosmetic are specific to the preparation and assay method utilized. BOTOX® Cosmetic is not equivalent to 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.**

**Please see additional Important Safety Information on following page.**

BOTOX® COSMETIC onabotulinumtoxinA injection

## Even elements that may be similarly characterized are unique in the details, creating the complex "fingerprint" of the final product.[1,13,14]

| | Excipients |
|---|---|
| **OnabotulinumtoxinA**  | Human albumin: 0.25 mg per 50-Unit vial; 0.5 mg per 100-Unit vial[2]<br>Sodium chloride: 0.45 mg per 50-Unit vial; 0.9 mg per 100-Unit vial[2] |
| **AbobotulinumtoxinA**  | Human albumin: 0.125 mg per 300-Unit vial[3]<br>Lactose: 2.5 mg per 300-Unit vial[3] |
| **IncobotulinumtoxinA**  | Human albumin: 1.0 mg per 50-Unit or 100-Unit vial[4]<br>Sucrose: 4.7 mg per 50-Unit or 100-Unit vial[4] |
| **PrabotulinumtoxinA-xvfs**  | Human albumin: 0.5 mg per 100-Unit vial[5]<br>Sodium chloride: 0.9 mg per 100-Unit vial[5] |
| **DaxibotulinumtoxinA-lanm**  | RTP004 peptide: 11.7 µg; polysorbate 20: 0.1 mg; L-histidine: 0.14 mg; L-histidine-HCl monohydrate: 0.65 mg; trehalose dihydrate: 36 mg per 50-Unit or 100-Unit vial[6] |
| **LetibotulinumtoxinA-wlbg**  | Human albumin: 0.25 mg per 50-Unit vial; 0.5 mg per 100-Unit vial[7]<br>Sodium chloride: 0.45 mg per 50-Unit vial; 0.9 mg per 100-Unit vial[7] |

**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 preexisting 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 page.**

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| | | Stabilization | Number of FDA-approved aesthetic indications |
|---|---|---|---|
| **OnabotulinumtoxinA** |  | Vacuum drying[2] | 4 indications[2] |
| **AbobotulinumtoxinA** |  | Lyophilization[3] | 1 indication[3] |
| **IncobotulinumtoxinA** |  | Lyophilization[4] | 3 indications[4] |
| **PrabotulinumtoxinA-xvfs** |  | Vacuum drying[5] | 1 indication[5] |
| **DaxibotulinumtoxinA-lanm** |  | Lyophilization[6] | 1 indication[6] |
| **LetibotulinumtoxinA-wlbg** |  | Lyophilization[7] | 1 indication[7] |

## Product attributes of Botulinum Toxin A products differ due to many factors[1,13]

BACTERIAL STRAIN MANUFACTURING PROCESS UNIT POTENCY ASSAY METHOD

**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, discontinue further injection of BOTOX® Cosmetic and immediately institute appropriate medical therapy. 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.

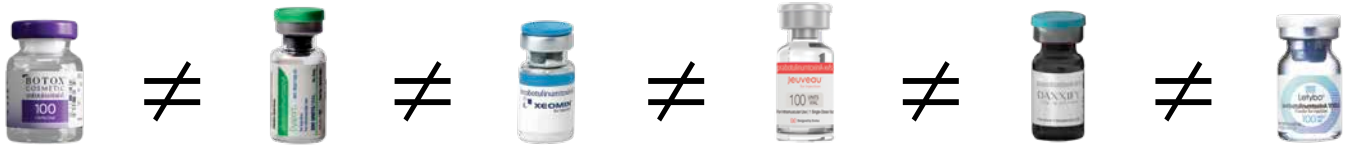
**Cardiovascular System**
There have been reports following administration of BOTOX® of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors, including preexisting cardiovascular disease.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

**Please see additional Important Safety Information on following page.**

BOTOX® COSMETIC onabotulinumtoxinA injection

# Botulinum toxin potency units are not universal measurements[2-7]

They are unique to each product and its manufacturing process.[2-7]



| 100 Units | 300 Units | 100 Units | 100 Units | 100 Units | 100 Units |
|---|---|---|---|---|---|
| BOTOX® COSMETIC onabotulinumtoxinA injection | Dysport (abobotulinumtoxinA) | XEOMIN® IncobotulinumtoxinA | Jeuveau prabotulinumtoxinA-xvfs injection | DAXXIFY daxibotulinumtoxinA-lanm injection | Letybo® letibotulinumtoxinA 100U Powder for Injection |

- "The potency Units of **BOTOX® Cosmetic** are specific to the preparation and assay method utilized. BOTOX® Cosmetic is not equivalent to 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"[2]
- "The potency units of **Dysport** 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 **Dysport cannot be compared to or converted into** units of any other botulinum toxin products assessed with any other specific assay method"[3]
- "The potency units of **Xeomin** are specific to the preparation and assay method utilized. Units of biological activity of **Xeomin cannot be compared to or converted into** units of any other botulinum toxin products assessed with any other specific assay method"[4]
- "The potency units of **Jeuveau** 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 **Jeuveau cannot be compared to nor converted into** units of any other botulinum toxin products assessed with any other specific assay method"[5]
- "The potency units of **Daxxify** are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products; therefore, units of biological activity of **Daxxify cannot be compared to or converted to** units of any other botulinum toxin products assessed with any other specific assay method"[6]
- "The potency units of **Letybo** 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 **Letybo cannot be compared to or converted into** units of any other botulinum toxin products assessed with any other specific assay method"[7]

## There is no dose ratio between botulinum toxin products.

**IMPORTANT SAFETY INFORMATION (continued)**
**WARNINGS AND PRECAUTIONS (continued)**
**Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders**
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*). Monitor individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis or neuromuscular junction disorders (eg, myasthenia gravis or Lambert-Eaton syndrome) when given botulinum toxin.

**Dysphagia and Breathing Difficulties**
Treatment with BOTOX® and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with preexisting 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 page.**

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**IMPORTANT SAFETY INFORMATION (continued)**
**WARNINGS AND PRECAUTIONS (continued)**
**Preexisting Conditions at the Injection Site**
Use caution 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).

**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 a 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), which would also be considered 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%).

The safety profile of BOTOX® Cosmetic treatment of platysma bands is consistent with the known safety profile of BOTOX® Cosmetic for other indications.

**DRUG INTERACTIONS**
Coadministration 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 BOTOX® Cosmetic full Prescribing Information, including Boxed Warning and Medication Guide.**

References: 1. Brin MF, James C, Maltman J. Botulinum toxin type A products are not interchangeable: a review of the evidence. *Biologics*. 2014;8:227-241. 2. BOTOX® Cosmetic Prescribing Information, October 2024. 3. Dysport Prescribing Information, September 2023. 4. Xeomin Prescribing Information, July 2024. 5. Jeuveau Prescribing Information, April 2023. 6. Daxxify Prescribing Information, November 2023. 7. Letybo Prescribing Information, February 2024. 8. Lietzow MA, Gielow ET, Le D, Zhang J, Verhagen MF. Subunit stoichiometry of the *Clostridium botulinum* type A neurotoxin complex determined using denaturing capillary electrophoresis. *Protein J*. 2008;27(7-8):420-425. 9. Kim CS, Jang WS, Son IP, et al. Electrophysiological study for comparing the effect of biological activity between type A botulinum toxins in rat gastrocnemius muscle. *Hum Exp Toxicol*. 2013;32(9):914-920. 10. Solish N, Carruthers J, Kaufman J, Rubio RG, Gross TM, Gallagher CJ. Overview of daxibotulinumtoxinA for injection: a novel formulation of botulinum toxin type A. *Drugs*. 2021;81(18):2091-2118. 11. US Food and Drug Administration. BLA approval: Daxxify (daxibotulinumtoxinA-lanm) for injection. US FDA. September 7, 2022. Accessed May 14, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/761127Orig1s000ltr.pdf. 12. Kim BJ, Kwon HH, Park SY, et al. Double-blind, randomized non-inferiority trial of a novel botulinum toxin A processed from the strain CBFC26, compared with onabotulinumtoxinA in the treatment of glabellar lines. *JEADV*. 2014;28:1761-1767. 13. Samizadeh S, De Boulle K. Botulinum neurotoxin formulations: overcoming the confusion. *Clin Cosmet Investig Dermatol*. 2018;11:273-287. 14. Pickett A. Botulinum toxin as a clinical product: manufacture and pharmacology. In: Foster KA, ed. *Clinical Applications of Botulinum Neurotoxin*. Springer+BusinessMedia; 2014:7-49. *Current Topics in Neurotoxicity*; vol 5.

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