Pr NUCEIVA™
prabotulinumtoxinA
injection

Please consult the Product Monograph available at
https://pdf.hres.ca/dpd_pm/00046932.PDF
or upon request by calling 800-668-5236.

Introducing

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Introducing Nuceiva™

Indications

Nuceiva™ is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines in adult patients < 65 years of age.[1]

Proprietary Manufacturing Process

Manufactured in a modern, state-of-the-art facility using a proprietary process.[2]

Clinical Trials

Studied in >1100 subjects[3-5] in the global clinical trials program including 2 Phase 3 US trials.[3,4]

What's in the vial

900 kDa

MOLECULAR MASS

A botulinumtoxin type A that is purified from clostridium botlulinum.[1]

*clinical significance has not been established

100U vial

VIAL

100 Units of botulinum toxin type A neurotoxin complex, 0.5 mg human serum albumin (HSA), and 0.9 mg sodium chloride (NaCl). Sterile, vacuum-dried without a preservative and stored at 2–8°C.[1]

2.5mL diluent

RECONSTITUTION

Reconstitute the 100 Unit Vial with 2.5 mL preservative-free 0.9% sodium chloride injection (not included) to obtain a concentration of 4 Units/0.1 mL.[1]

Trusted

Dosing & Administration

Total dose of 20U

DOSING CONSIDERATIONS

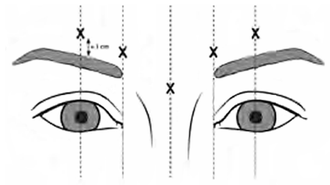
- For Intramuscular Use Only.[1]
- The potency Units of Nuceiva™ are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, Units of biological activity of Nuceiva™ cannot be compared to or converted into Units of any other botulinum toxin products assessed with any other specific assay method.[1]
- Nuceiva™ should be administered no more than every 3 months.[1]
- Treatment should be administered at no more than the recommended dose and interval.[1]

5 injection sites

5 INJECTION SITES

Glabellar lines:
Four (4) Units should be injected intramuscularly at each of five injection sites, 2 in each corrugator muscle and 1 in the procerus muscle for a total dose of 20 Units.[1]

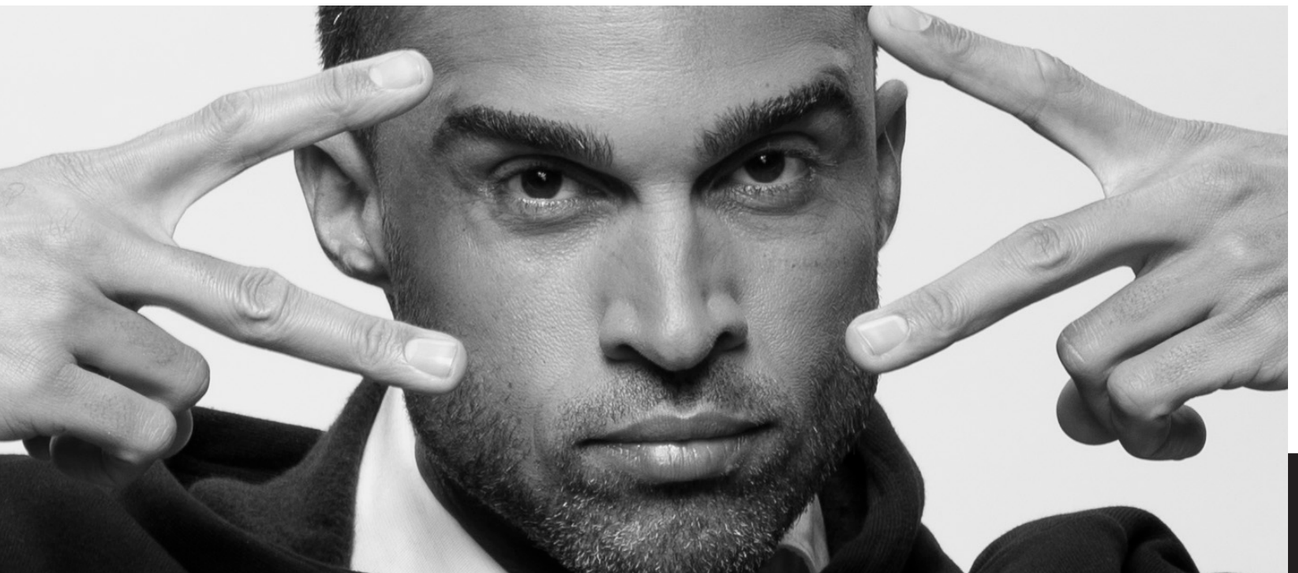
For complete dosing and administration information, please refer to the Product Monograph.



ADMINISTRATION

Physicians administering Nuceiva™ must understand the relevant neuromuscular and/or orbital anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures.

Please refer to the Product Monograph for Administration Instructions.



Studied In Clinical Trials

Tested

Nuceiva™ vs Placebo

EV-001 AND EV-002
Phase III randomized, multi-center, double-blind, placebo-controlled US trials

Glabellar Line Scale
At Maximum Frown

STUDY OVERVIEW[1]

- Two identical Phase III studies (EV-001 and EV-002)
  EV-001 (N=330) | EV-002 (N=324)
- Patient population: Adults with moderate to severe glabellar lines at maximum frown.
- Subjects randomized 3:1 to receive a single dose of 20U Nuceiva™ or placebo[6]
- Primary endpoint was proportion of responders on day 30 where investigator and subject independently agreed that a ≥ 2 point improvement had occurred on the Glabellar Line Scale (GLS) at maximum frown.[6]

Nuceiva™ vs Placebo

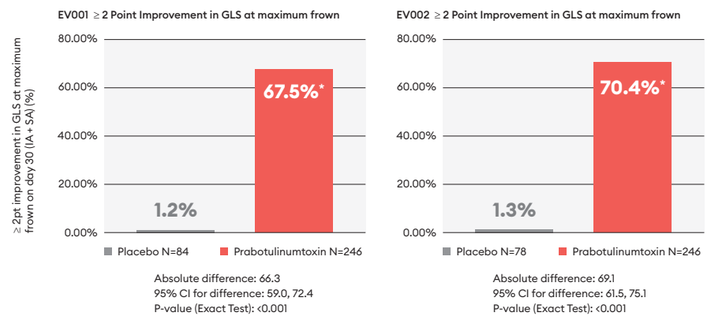
EV-001 AND EV-002
Phase III randomized, multi-center, double-blind trials (EV-001, EV-002)

EV001 ≥ 2 Point Improvement in GLS at maximum frown

INVESTIGATOR ASSESSED		COMPOSITE (IA+SA)		SUBJECT ASSESSED	
Placebo	Nuceiva™	Placebo	Nuceiva™	Placebo	Nuceiva™
1.2%	77.5%	1.2%	67.5%	3.6%	76.7%

EV002 ≥ 2 Point Improvement in GLS at maximum frown

INVESTIGATOR ASSESSED		COMPOSITE (IA+SA)		SUBJECT ASSESSED	
Placebo	Nuceiva™	Placebo	Nuceiva™	Placebo	Nuceiva™
2.7%	82.5%	1.3%	70.4%	4.0%	76.3%



COMPOSITE PRIMARY ENDPOINT [6]

Proportion of responders on day 30 where investigator and subject independently agreed that a ≥ 2 point improvement had occurred on the GLS at maximum frown (0=none, 1=mild, 2=moderate, 3=severe)

Nuceiva™ demonstrated a statistically significant improvement in the composite primary endpoint vs. placebo.[6]

Nuceiva™ vs Placebo

ADVERSE EVENTS (AEs) OBSERVED IN EV-001, EV-002 & EVB-003
Phase III randomized, multi-center, double-blind trials
(Observed in EV-001, EV-002 and EVB-003)

	Pooled Single Dose Nuceiva™ N=737 (%)	Pooled Placebo N=211 (%)
All AEs in ≥1% of Subjects	22.7%	21.8%
Headache	12.3%	13.3%
Gastroenteritis Viral	0.4%	1.4%
Influenza	0.7%	0.9%
Nasopharyngitis	3.5%	1.4%
Sinusitis	0.9%	2.4%
Upper Respiratory Tract Infection	1.8%	1.4%
Eyelid Ptosis	1.6%	0.0%
Hypertension	0.5%	0.9%

Table shows treatment-emergent adverse events with ≥ 1% incidence following a single dose of 20 Units in the glabellar region[1]

Most adverse events were mild to moderate in severity and none considered study drug related were serious.[1]

Before & After

BASELINE (DAY 0)	DAY 30

Nuceiva™ patient at maximum frown.
Unaltered results with no complementary products.Depicts typical results-Individual results may vary.

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INDICATIONS AND CLINICAL USE:

- **NUCEIVA** is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines in adult patients < 65 years of age.
- **Pediatrics (< 18 years of age): NUCEIVA** is not recommended for use in children.
- **Geriatrics (≥ 65 years of age):** The clinical data for subjects ≥ 65 years of age are limited. No specific dose adjustment is required for use in the elderly.

CONTRAINDICATIONS:

NUCEIVA is contraindicated in patients:

- who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see Dosage Forms, Strengths, Composition and Packaging;
- with infection or inflammation at the proposed injection sites.

MOST SERIOUS WARNINGS AND PRECAUTIONS:

Distant Spread of Toxin Effect: The effects of **NUCEIVA** and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. 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 occur in adults, particularly in those patients who have underlying conditions that would predispose them to these symptoms. Nuceiva is not indicated for the treatment of spasticity in children.

Dosing Units: The term "Unit" upon which dosing is based, is a specific measurement of toxin activity that is unique to this formulation of Botulinum toxin Type A. Therefore, the Units used to describe NUCEIVA activity are different from those used to describe that of other botulinum toxin preparations and the Units representing NUCEIVA activity are not interchangeable with other products.

Administration: NUCEIVA should only be administered by physicians with the appropriate qualifications and experience in the use of botulinum toxins.

Dosing and Administration: Follow the recommended dosage and frequency of administration for **NUCEIVA** (See **WARNINGS AND PRECAUTIONS, General and DOSAGE AND ADMINISTRATION**).

OTHER RELEVANT WARNINGS AND PRECAUTIONS:

- Indication-specific dosage and administration recommendations should be followed.
- Caution should be exercised when administering **NUCEIVA** to patients with neuromuscular junction disorders or when excessive weakness or atrophy is present in the target muscle, and in patients with prolonged bleeding times, surgical alterations to the facial anatomy, marked facial asymmetry, inflammation at the injection site(s), ptosis, excessive dermatochalasis, deep dermal scarring, or thick sebaceous skin.
- Progressive signs or symptoms of muscular weakness remote to the site of injection may include ptosis and diplopia, as well as other serious adverse effects including swallowing and speech disorders. Patients with a history of underlying neurologic disorders, dysphagia and/or aspiration are at a greater risk of these effects and should be treated with extreme caution.
- This product contains human serum 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. The theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) also is considered extremely remote.
- Use caution when administering to patients with pre-existing cardiovascular disease.
- Serious and/or immediate hypersensitivity reactions such as anaphylaxis and serum sickness have been rarely reported, as well as other manifestations of hypersensitivity including urticaria, soft tissue edema, and dyspnea.
- Caution should be exercised when administering **NUCEIVA** to individuals with peripheral motor neuropathy (e.g., amyotrophic lateral sclerosis or other motor neuropathy), facial palsy or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome). Patients with neuromuscular disorders may be at an increased risk of clinically significant systemic effects such as severe dysphagia and respiratory compromise.
- Caution should be exercised when administering **NUCEIVA** to individuals with eye disorders, including dry eye and eyelid oedema.
- Caution should be exercised when administering **NUCEIVA** to patients with inflammation at the injection site(s), deep dermal scarring, or thick sebaceous skin.
- **NUCEIVA** should not be used during pregnancy.
- The use of **NUCEIVA** during lactation is not recommended.

FOR MORE INFORMATION:

Please consult the Product Monograph available at https://pdf.hres.ca/dpd_pm/00046932.PDF for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.

The product monograph is also available by calling us at 800-668-5236.

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REFERENCES

1. Product Monograph Nuceiva (April 15, 2020)
2. Kim CS, Song KY, Min KM, An YD, inventors; Daewoong Co, Ltd, assignee. Method for production of botulinum toxin. US patent 9,512,418 B2. December 6, 2016.
3. Data on file; CSR EV-001, BLA761085. Evolus, Inc., Santa Barbara, CA.
4. Data on file; CSR EV-002, BLA761085. Evolus, Inc., Santa Barbara, CA.
5. Data on File; CSR EVB-003, BLA761085, Evolus, Inc., Santa Barbara, CA.
6. Beer K. Efficacy and Safety of PrabotulinumtoxinA for the Treatment of Glabellar Lines in Adult Subjects: Results From 2 Identical Phase III Studies. Dermatol Surg 2019;00:1–13.

Manufactured by:
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NU-PHYBRO-01

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