

JEUVEAU- prabotulinum toxin type a powder

Evolus, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use JEUVEAU® safely and effectively. See full prescribing information for JEUVEAU.

JEUVEAU (prabotulinumtoxinA-xvfs) for injection, for intramuscular use
Initial U.S. Approval: 2019

WARNING: DISTANT SPREAD OF TOXIN EFFECT

See full prescribing information for complete boxed warning.

The effects of all botulinum toxin products, including JEUVEAU, 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. JEUVEAU is not approved for the treatment of spasticity or any conditions other than glabellar lines. (5.1)

INDICATIONS AND USAGE

JEUVEAU is an acetylcholine release inhibitor and a neuromuscular blocking agent indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients (1)

DOSAGE AND ADMINISTRATION

Glabellar Lines Administration: 0.1 mL (4 Units) by intramuscular injection into each of five sites, for a total dose of 20 Units (2.2, 2.3)

DOSAGE FORMS AND STRENGTHS

For Injection: 100 Units vacuum-dried powder in a single-dose vial (3)

CONTRAINDICATIONS

- Hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation (4.1)
- Infection at the injection site (4.2)

WARNINGS AND PRECAUTIONS

- Potency Units of JEUVEAU are not interchangeable with other preparations of botulinum toxin products (5.2, 11)
- Spread of toxin effects; swallowing and breathing difficulties can lead to death. Seek immediate medical attention if respiratory, speech, or swallowing difficulties occur (5.2, 5.7)
- Potential serious adverse reactions after JEUVEAU injections for unapproved uses (5.3)
- Adverse event reports have been received involving the cardiovascular system, some with fatal outcomes. Use caution when administering to patients with pre-existing cardiovascular disease (5.5)
- Concomitant neuromuscular disorder may exacerbate clinical effects of treatment (5.6)
- Use with caution in patients with compromised respiratory function or dysphagia (5.7)

ADVERSE REACTIONS

The most common adverse reactions are headache (12%), eyelid ptosis (2%), upper respiratory tract infection (3%), and increased white blood cell count (1%) (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Evolus at [1-877-386-5871] or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Closely observe patients receiving concomitant treatment of JEUVEAU and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like agents), or muscle relaxants because JEUVEAU's effect may be potentiated (7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 4/2021

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FULL PRESCRIBING INFORMATION

WARNING: DISTANT SPREAD OF TOXIN EFFECT

The effects of all botulinum toxin products, including JEUVEAU, 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. JEUVEAU is not approved for the treatment of spasticity or any conditions other than glabellar lines. [See *Warnings and Precautions (5.1)*]

1 INDICATIONS AND USAGE

JEUVEAU is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients.

2 DOSAGE AND ADMINISTRATION

2.1 Instructions for Safe Use

The potency Units of JEUVEAU (prabotulinumtoxinA-xvifs) for injection 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 [see *Warnings and Precautions (5.2) and Description (11)*].

Retreatment of JEUVEAU should be administered no more frequently than every three months. Consideration of the cumulative dose is necessary when treating adult patients with JEUVEAU for glabellar lines if other botulinum toxin products are or have been used to treat other indications approved for those products.

The safe and effective use of JEUVEAU depends upon proper storage of the product, selection of the correct dose, and proper reconstitution and administration techniques. Physicians administering JEUVEAU must understand the relevant neuromuscular and/or orbital anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures [see *Warnings and Precautions (5.4)*].

2.2 Preparation and Dilution Technique

JEUVEAU is supplied in a single-dose 100 Unit vial. Prior to intramuscular injection, reconstitute each vacuum-dried vial of JEUVEAU with only sterile, preservative-free 0.9% Sodium Chloride Injection, USP to obtain a reconstituted solution at a concentration of 4 Units/0.1 mL and a total treatment dose of 20 Units in 0.5 mL (see Table 1). Slowly inject the diluent into the vial. Discard the vial if a vacuum does not pull the diluent into the vial.

Dispose of any unused saline. Gently mix JEUVEAU with 0.9% Sodium Chloride Injection USP by rotating the vial. JEUVEAU should be administered within 24 hours after reconstitution. During this time period, unused reconstituted JEUVEAU should be stored in a refrigerator between 2° to 8°C (36°F to 46°F) in the original carton to protect from light for up to 24 hours until time of use. Do not freeze reconstituted JEUVEAU. JEUVEAU vials are for single-dose only. After reconstitution, JEUVEAU should be used for only one injection session and for only one patient. Discard any remaining solution after administration.

Table 1. Dilution Instructions for JEUVEAU Vials (100 Units)

Diluent* Added to 100 Unit Vial	Resulting Dose Units per 0.1 mL
2.5 mL	4 Units

* Preservative-free 0.9% Sodium Chloride Injection, USP

Reconstituted JEUVEAU should be clear, colorless, and free of particulate matter otherwise it should not be injected. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

2.3 Administration

Glabellar facial lines arise from the activity of the corrugator and orbicularis oculi muscles. These muscles move the brow medially and the procerus and depressor supercillii pull the brow inferiorly. This creates a frown or “furrowed brow”. The location, size, and use of the muscles vary markedly among individuals. Lines induced by facial expression occur perpendicular to the direction of action of contracting facial muscles. An effective dose for facial lines is determined by gross observation of the patient’s ability to activate the superficial muscles injected.

In order to reduce the complication of eyelid ptosis the following steps should be taken:

- Avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes.
- Lateral corrugator injections should be placed at least 1 cm above the bony supraorbital ridge.
- Ensure the injected volume/dose is accurate and where feasible kept to a minimum.
- Avoid injecting JEUVEAU closer than 1 centimeter above the central eyebrow.

Draw at least 0.5 mL of the properly reconstituted JEUVEAU into a sterile syringe and expel any air bubbles in the syringe barrel. Remove the needle used to reconstitute the product and attach a 30-33 gauge needle. Confirm the patency of the needle. Inject a dose of 0.1 mL (4 Units) intramuscularly into each of five sites: the inferomedial and superior middle of each corrugator, and one in the mid-line of the procerus muscle for a total dose of 20 Units (See Figure 1).

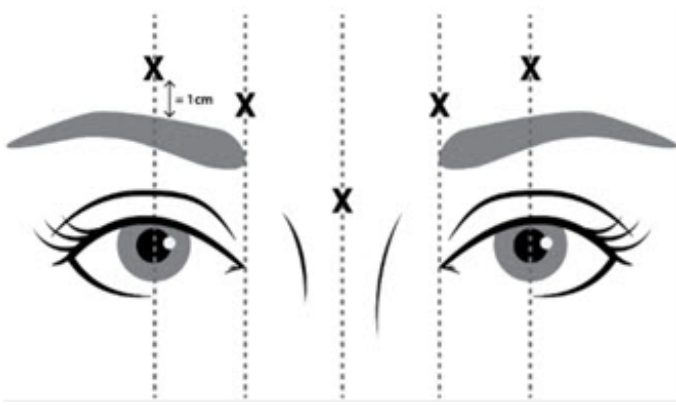


Figure 1

3 DOSAGE FORMS AND STRENGTHS

- For injection: 100 Units, vacuum-dried powder in a single-dose vial for reconstitution with preservative-free 0.9% Sodium Chloride Injection, USP.

4 CONTRAINDICATIONS

4.1 Known Hypersensitivity to Botulinum Toxin

JEUVEAU is contraindicated in individuals with known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation [See *Warnings and Precautions (5.4)*].

4.2 Infection at the Injection Site(s)

JEUVEAU is contraindicated in the presence of infection at the proposed injection site(s).

5 WARNINGS AND PRECAUTIONS

5.1 Spread of Toxin Effect

Postmarketing safety data from other approved botulinum toxins suggest that botulinum toxin effects may be observed beyond the site of local injection. The symptoms are consistent with the mechanism of action of botulinum toxin and may include asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, blurred vision, 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 related to spread of toxin effects. In unapproved uses, including upper limb spasticity in children and approved indications, symptoms consistent with spread of toxin effect have been reported at doses comparable to or lower than the maximum recommended total dose [see *Use in Specific Populations (8.4)*]. JEUVEAU is not approved for the treatment of spasticity or any conditions other than glabellar lines. Patients or caregivers should be advised to seek immediate medical care if swallowing, speech, or respiratory difficulties occur.

5.2 Lack of Interchangeability between Botulinum Toxin Products

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 [see *Description (11)*].

5.3 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 botulinum toxin 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 botulinum toxin products 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 botulinum toxin products.

5.4 Hypersensitivity Reactions

Serious and/or immediate hypersensitivity reactions have been reported for botulinum toxin products. These reactions include anaphylaxis, serum sickness, urticaria, soft tissue edema, and dyspnea. If such a reaction occurs, further injection of JEUVEAU should be discontinued and appropriate medical therapy immediately instituted. The use of JEUVEAU in patients with a known hypersensitivity to any botulinum neurotoxin or to any of the components in the formulation could lead to a life threatening allergic reaction [See *Contraindications (4.1)*].

5.5 Cardiovascular System

There have been reports following administration of botulinum toxins 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.

5.6 Increased Risk of Clinically Significant Effects with Pre-Existing Neuromuscular Disorders

Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junction disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) were excluded from the clinical studies of JEUVEAU. 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 typical doses of JEUVEAU.

5.7 Dysphagia and Breathing Difficulties

Treatment with botulinum toxin products, including JEUVEAU, 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 has been 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 *Warnings and Precautions (5.1)*].

Deaths as a complication of severe dysphagia have been reported after treatment with botulinum toxin. Dysphagia may persist for several months, and require use of a feeding tube to maintain adequate nutrition and hydration. Aspiration may result from severe dysphagia and is a particular risk when treating patients in whom swallowing or respiratory function is already compromised.

Treatment with botulinum toxins, including JEUVEAU, may weaken neck muscles that serve as accessory muscles of ventilation. This may result in a critical loss of breathing capacity in patients with respiratory disorders who may have become dependent upon these accessory muscles. There have been postmarketing reports from other botulinum toxin products of serious breathing difficulties, including respiratory failure.

Patients with smaller neck muscle mass and patients who require bilateral injections into the sternocleidomastoid muscle for the treatment of cervical dystonia have been reported to be at greater risk for dysphagia. Injections into the levator scapulae for the treatment cervical dystonia may be associated with an increased risk of upper respiratory infection and dysphagia. JEUVEAU is not approved for the treatment of cervical dystonia.

Patients treated with botulinum toxin products, including JEUVEAU, may require immediate medical attention should they develop problems with swallowing, speech, or breathing. These reactions can occur within hours to weeks after injection with botulinum toxin [see *Warnings and Precautions (5.1)*].

5.8 Pre-existing Conditions at the Injection Site

Caution should be used when JEUVEAU 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).

Caution should be used when JEUVEAU treatment is used in patients who have marked facial asymmetry, ptosis, excessive dermatochalasis, deep dermal scarring, thick sebaceous skin, or when subjects do not respond to 20 Units of botulinum toxin (e.g., the inability to substantially lessen glabellar lines even by physically spreading them apart). Do not exceed the recommended dosage and frequency of administration of JEUVEAU.

5.9 Ophthalmic Adverse Reactions in Patients Treated with Botulinum Toxin Products

Dry eye has been reported with the use of botulinum toxin products in the treatment of glabellar lines. Reduced tear production, reduced blinking, and corneal disorders may occur with use of botulinum toxins, including JEUVEAU. If symptoms of dry eye (e.g., eye irritation, photophobia, or visual changes) persist, consider referring patients to an ophthalmologist [see *Warnings and Precautions (5.1)*].

5.10 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.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Spread of Toxin Effects [see *Warnings and Precautions (5.1)*]
- Hypersensitivity [see *Contraindications (4.1)* and *Warnings and Precautions (5.4)*]
- Dysphagia and Breathing Difficulties [See *Warnings and Precautions (5.7)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

In general, most adverse reactions occur within the first week following injection of JEUVEAU and while generally transient, may have a duration of several months or longer. Localized pain, infection, inflammation, tenderness, swelling, erythema, and/or bleeding/bruising may be associated with the injection. Needle-related pain and/or anxiety may result in vasovagal responses, including syncope and hypotension, which may require appropriate medical therapy.

Local weakness of the injected muscle(s) represents the expected pharmacological action of botulinum toxin. However, weakness of nearby muscles may also occur due to spread of toxin effect [see *Warnings and Precautions (5.1)*].

Glabellar Lines

The adverse reactions below reflect exposure to JEUVEAU in the treatment of glabellar lines in placebo-controlled trials [See *Clinical Studies (14)*].

Table 2. Adverse Reactions Reported at Higher Frequency ($\geq 1\%$) in the JEUVEAU Group Compared to the Placebo Group

	JEUVEAU EV-001, EV-002 N=492 n (%)	PLACEBO EV-001, EV-002, N=162 n (%)
Headache	57 (12%)	21 (13%)
Eyelid Ptosis	8 (2%)	0 (0%)
Upper Respiratory Tract Infection	13 (3%)	1 (1%)

**White blood cell
count increase**

6 (1%)

0 (0%)

Two multi-center, open label, 1-year repeat dose safety trials, EV-004 [NCT02184988] and EV-006 [NCT02428608], were also conducted with JEUVEAU. Both trials evaluated repeat treatments of 20 units of JEUVEAU, up to a maximum total of 80 units, for the treatment of moderate to severe glabellar lines in adult subjects. Of the 922 subjects enrolled, the median number of treatments was three. The adverse events profile was similar to that reported in single dose trials.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to prabotulinumtoxinA-xvfs in the studies described below, with the incidence of antibodies in other studies, or to other products may be misleading.

Treatment with botulinum toxins may result in the formation of antibodies that may reduce the effectiveness of subsequent treatments by inactivating biological activity of the toxin. Among 1,414 subjects treated with prabotulinumtoxinA-xvfs, 2 subjects were found to have pre-existing antibodies and 2 subjects had treatment-emergent antibodies.

7 DRUG INTERACTIONS

No formal drug interaction studies have been conducted with JEUVEAU (prabotulinumtoxinA-xvfs) for injection. However, the potential for certain drugs to potentiate the effects of JEUVEAU warrant consideration given the potential risks involved and should be used with caution.

- Aminoglycosides or other agents interfering with neuromuscular transmission
- Anticholinergic drugs
- Botulinum neurotoxin products
- Muscle relaxant

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

The limited available data on JEUVEAU use in pregnant women are insufficient to inform a drug associated risk of adverse developmental outcomes. An embryofetal developmental study conducted with JEUVEAU in pregnant rats revealed no treatment-related effects to the developing fetus when JEUVEAU was administered intramuscularly during organogenesis at doses up to 12 times the maximum recommended human

dose (MRHD) (see *Data*).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In an embryofetal developmental study, intramuscular doses up to 4 Unit/kg JEUVEAU were administered to pregnant rats once daily during organogenesis (gestation days 6 to 16). No maternal or embryofetal toxicities were observed at doses up to 4 Unit/kg (12 times the MRHD of 20 Units, based on Unit/kg comparison).

8.2 Lactation

There is no information regarding the presence of prabotulinumtoxinA-xvfs in human or animal milk, its effects on the breastfed infant, or on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for JEUVEAU and any potential adverse effects on the breastfed infant from JEUVEAU or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

The two clinical trials of JEUVEAU included 68 subjects age 65 and greater. Although no differences in safety or efficacy were observed between older and younger subjects, clinical studies of JEUVEAU did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

10 OVERDOSAGE

There is no information regarding overdose from clinical studies of JEUVEAU. Excessive doses of JEUVEAU (prabotulinumtoxinA-xvfs) injection may be expected to produce neuromuscular weakness with a variety of symptoms.

Symptoms of overdose are likely not to be present immediately following injection. Should accidental injection or oral ingestion occur, or overdose be suspected, these patients should be considered for further medical evaluation and appropriate medical therapy immediately instituted, which may include hospitalization. The person should be medically supervised for several weeks for signs and symptoms of systemic muscular weakness which could be local or distant from the site of injection [*see Boxed Warning and Warnings and Precautions (5.1)*].

If the musculature of the oropharynx and esophagus are affected, aspiration may occur which may lead to development of aspiration pneumonia. If the respiratory muscles become paralyzed or sufficiently weakened, intubation and assisted respiration may be

necessary until recovery takes place. Supportive care could involve the need for a tracheostomy and/or prolonged mechanical ventilation, in addition to other general supportive care.

In the event of overdose, antitoxin raised against botulinum toxin is available from the Centers for Disease Control and Prevention (CDC) in Atlanta, GA. However, the antitoxin will not reverse any botulinum toxin-induced effects already apparent by the time of antitoxin administration. In the event of suspected or actual cases of botulinum toxin poisoning, please contact your local or state Health Department to process a request for antitoxin through the CDC. If you do not receive a response within 30 minutes, please contact the CDC directly at 1-770-488-7100. More information can be obtained at <http://www.cdc.gov/ncidod/srp/drugs/formulary.html#1a>.

11 DESCRIPTION

PrabotulinumtoxinA-xvfs is an acetylcholine release inhibitor and a neuromuscular blocking agent. PrabotulinumtoxinA-xvfs is supplied as a sterile, vacuum-dried powder in a single-dose vial intended for intramuscular use after reconstitution.

PrabotulinumtoxinA-xvfs is a 900 kDa botulinum toxin type A, produced from fermentation of *Clostridium botulinum*.

The primary release procedure for JEUVEAU uses an animal based potency assay to determine the potency relative to a reference standard. The assay is specific to Evolus' product, JEUVEAU. One Unit of JEUVEAU corresponds to the calculated median intraperitoneal lethal dose (LD₅₀) in mice. Due to specific details of this assay, Units of biological activity of JEUVEAU cannot be converted into Units of any other botulinum toxin or any toxin assessed with any other specific assay method.

Each vial of JEUVEAU (prabotulinumtoxinA-xvfs) for injection contains 100 Units of botulinum toxin type A neurotoxin complex, human serum albumin (0.5 mg), and sodium chloride (0.9 mg) in a sterile, vacuum-dried form without a preservative.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

JEUVEAU blocks neuromuscular transmission by binding to acceptor sites on motor nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. This inhibition occurs as the neurotoxin cleaves SNAP-25, a protein integral to the successful docking and release of acetylcholine from vesicles situated within nerve endings. When injected intramuscularly at therapeutic doses, JEUVEAU produces partial chemical denervation of the muscle resulting in a localized reduction in muscle activity. In addition, the muscle may atrophy, axonal sprouting may occur, and extrajunctional acetylcholine receptors may develop. There is evidence that reinnervation of the muscle may occur, thus slowly reversing muscle denervation produced by JEUVEAU.

12.2 Pharmacodynamics

No formal pharmacodynamic studies have been conducted with JEUVEAU.

12.3 Pharmacokinetics

Using currently available analytical technology, it is not possible to detect JEUVEAU in the peripheral blood following intramuscular injection at the recommended doses.

No drug interaction studies have been conducted with JEUVEAU.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to evaluate the carcinogenic, mutagenic, or impairment of fertility potential of JEUVEAU.

14 CLINICAL STUDIES

Two randomized, multi-center, double-blind, placebo-controlled trials (EV-001 [NCT02334423] and EV-002 [NCT02334436]) of identical design were conducted to evaluate JEUVEAU for use in the temporary improvement of the appearance of moderate to severe glabellar facial lines. These trials enrolled 654 subjects, randomized 3 to 1 to a single treatment with JEUVEAU (n=492) or placebo (n=162).

The trials enrolled healthy adults (ranging in age from 18 to 81) with glabellar lines of at least moderate severity at maximum frown. The trials excluded subjects who had ptosis, deep dermal scarring, or an inability to substantially lessen glabellar lines even by physically spreading the glabellar lines apart. Injection volume was 0.1 mL/injection site, for a dose/injection site in the active treatment groups of 4 Units. Subjects were injected intramuscularly at five sites, one in the procerus muscle and two in each corrugator supercilii muscle, for a total dose in the active treatment groups of 20 Units.

The primary efficacy endpoint was measured at Day 30 and was defined as the proportion of subjects achieving ≥ 2 -grade improvement from baseline at maximum frown, as assessed independently by both the investigator and the subject using the Glabellar Line Scale (GLS). The GLS is a 4-point grading scale (0=none, 1=mild, 2=moderate, 3=severe). The results of these two efficacy trials are presented below (See Table 3).

The mean age was 51 years, with 68 subjects (10%) ≥ 65 years of age. Most of the subjects were women (91%), and a majority of the subjects were white (84%).

**Table 3. Trials EV-001 and EV-002:
Composite Investigator and Subject
Assessment of Glabellar Line Severity
at Maximum Frown at Day 30 -
Responder Rates (% of Subjects
Achieving ≥ 2 -Grade Improvement
from Baseline)**

Trial	JEUVEAU	Placebo
Trial EV-001	N=246 68%	N=84 1%
Trial EV-002	N=246	N=78

70%

1%

16 HOW SUPPLIED/STORAGE AND HANDLING

JEUVEAU (prabotulinumtoxinA-xvfs) for injection is a vacuum-dried powder supplied in a single-dose vial in the following size:

100 Units (NDC 72301-595-10)

Storage

Unopened vials of JEUVEAU should be stored in a refrigerator between 2° to 8°C (36° to 46° F) in the original carton to protect from light.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Advise patients to inform their doctor if they develop any unusual symptoms (including difficulty with swallowing, speaking, or breathing), or if any known symptom persists or worsens [see *Warnings and Precautions* (5.1, 5.4)].

Inform patients that JEUVEAU injection may cause eye dryness. Advise patients to report symptoms of eye dryness (e.g., eye pain, eye irritation, photosensitivity, or changes in vision) to their doctor [see *Warnings and Precautions* (5.9)].

Inform patients that if loss of strength, muscle weakness, blurred vision, or drooping eyelids occur, they should avoid driving a car or engaging in other potentially hazardous activities.

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DWG-131 Rev. D

MEDICATION GUIDE
JEUVEAU (pronounced Jū vō)
(prabotulinumtoxinA-xvfs)
for Injection

What is the most important information I should know about JEUVEAU? JEUVEAU may cause serious side effects that can be life threatening. Call your healthcare provider or get medical help right away if you have any of these problems after treatment with JEUVEAU:

- **Problems swallowing, speaking, or breathing. These problems can happen hours, days, or weeks after an injection of JEUVEAU** if the muscles that you use to breathe and swallow become weak after the injection. Death can happen as a complication if you have severe problems with swallowing or breathing after treatment with JEUVEAU.
 - o People with certain breathing problems may need to use muscles in their neck to help them breathe. These people may be at greater risk for serious breathing problems with JEUVEAU.
 - o Swallowing problems may last for several months. People who cannot swallow well may need a feeding tube to receive food and water. If swallowing problems are severe, food or liquids may go into your lungs. People who already have swallowing or breathing problems before receiving JEUVEAU have the highest risk of getting these problems.
- **Spread of toxin effects.** In some cases, the effect of botulinum toxin may affect areas of the body away from the injection site and cause symptoms of a serious condition called botulism. The symptoms of botulism include:
 - o loss of strength and muscle weakness all over the body
 - o blurred vision and drooping eyelids
 - o trouble saying words clearly
 - o trouble breathing
 - o double vision
 - o hoarseness or change or loss of voice
 - o loss of bladder control
 - o trouble swallowing

These symptoms can happen hours, days, or weeks after you receive an injection of JEUVEAU.

These problems could make it unsafe for you to drive a car or do other dangerous activities. See **“What should I avoid while receiving JEUVEAU?”**

What is JEUVEAU?

JEUVEAU is a prescription medicine that is injected into muscles and used in adults for a short period of time (temporary) to improve the look of moderate to severe frown lines between the eyebrows (glabellar lines).

It is not known if JEUVEAU is safe and effective for use in children.

Do not receive JEUVEAU if you:

- are allergic to JEUVEAU or any of the ingredients in JEUVEAU. See the end of the

Medication Guide for a list of ingredients in JEUVEAU.

- had an allergic reaction to any other botulinum toxin product such as rimabotulinumtoxinB (MYOBLOC®), onabotulinumtoxinA (BOTOX®, BOTOX® COSMETIC), abobotulinumtoxinA (DYSPORT®), or incobotulinumtoxinA (XEOMIN®).
- have a skin infection at the planned injection site.

Before receiving JEUVEAU, tell your healthcare provider about all your medical conditions, including if you:

- have a disease that affects your muscles and nerves (such as amyotrophic lateral sclerosis [ALS or Lou Gehrig’s disease], Myasthenia gravis or Lambert-Easton syndrome). See **“What is the most important information I should know about JEUVEAU?”**
- had any side effect from any botulinum toxin product in the past.
- have or have had a breathing problem, such as asthma or emphysema.
- have or have had swallowing problems.
- have or have had bleeding problems.
- have or have had heart problems.
- have plans to have surgery.
- have weakness of your forehead muscles, such as trouble raising your eyebrows.
- have drooping eyelids.
- have had surgery on your face.
- have had dry eye with use of botulinum toxin products in the past.
- are pregnant or plan to become pregnant. It is not known if JEUVEAU can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if JEUVEAU passes into breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with JEUVEAU.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Using JEUVEAU with certain other medicines may cause serious side effects. **Do not start any new medicines until you have told your healthcare provider that you have received JEUVEAU in the past.**

Especially tell your healthcare provider if you:

- have received any other botulinum toxin product in the last 4 months.
- have received injections of botulinum toxin, such as onabotulinumtoxinA (BOTOX®, BOTOX® COSMETIC) rimabotulinumtoxinB (MYOBLOC®), abobotulinumtoxinA (DYSPORT®), or incobotulinumtoxinA (XEOMIN®). Be sure your healthcare provider knows exactly which product you received.

Know the medicines you take. Keep a list of your medicines with you to show your healthcare provider and pharmacist each time you get a new medicine.

How will I receive JEUVEAU?

- JEUVEAU is an injection that your healthcare provider will give you.
- JEUVEAU is injected into your affected muscles.
- JEUVEAU should not be received more than 1 time every 3 months.

- Your healthcare provider may change your dose of JEUVEAU, until you and your healthcare provider find the best dose for you.
- Your healthcare provider will tell you how often you will receive your dose of JEUVEAU injections.

What should I avoid while receiving JEUVEAU?

JEUVEAU may cause loss of strength or general muscle weakness, vision problems, or dizziness within hours to weeks of receiving JEUVEAU. **If this happens, do not drive a car, operate machinery, or do other dangerous activities.** See “**What is the most important information I should know about JEUVEAU?**”

What are the possible side effects of JEUVEAU?

JEUVEAU can cause serious side effects, including:

- See “**What is the most important information I should know about JEUVEAU?**”
- **Allergic reactions.** Symptoms of an allergic reaction to JEUVEAU may include: itching, rash, hives, wheezing, trouble breathing, or you may become dizzy or faint. Tell your healthcare provider or get emergency medical help right away if you develop wheezing or trouble breathing, or if you feel dizzy or faint.
- **Heart problems.** Irregular heartbeat and heart attack that have caused death have happened in some people who received botulinum toxin products.
- **Eye problems.** Dry eye, reduced blinking, and corneal problems have happened in some people who receive JEUVEAU to treat glabellar lines. Tell your healthcare provider if you develop eye pain or irritation, sensitivity to light, or changes in your vision.

The most common side effects of JEUVEAU include:

- headache
- eyelid drooping
- upper respiratory infection
- increased white blood cell count in your blood

These are not all the possible side effect of JEUVEAU.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of JEUVEAU.

Medicines are sometime prescribed for purposes other than those listed in a Medication Guide. You can ask your healthcare provider or pharmacist for information about JEUVEAU that is written for healthcare professionals.

What are the ingredients in JEUVEAU?

Active ingredient: botulinum toxin type A

Inactive ingredients: human serum albumin and sodium chloride

Manufactured by: Evolus Inc., 520 Newport Center Drive, Suite 1200, Newport Beach, CA 92660

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This Medication Guide has been approved by the U.S. Food and Drug Administration.

Issued: 04 2021

PRINCIPAL DISPLAY PANEL - Carton Label



Carton Label

Principal Panel

prabotulinumtoxinA-xvfs

Jeuveau®
for Injection

100 UNITS/VIAL

For Intramuscular Use
1 Single-Dose Vial

**ATTENTION: Dispense the enclosed
Medication Guide to each patient**

Designed by Evolus

Left Panel

WARNING: Dosing units of botulinum toxins are not interchangeable between commercial products.

Store unopened vial refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. DO NOT FREEZE.

Each vial of Jeuveau (prabotulinumtoxinA-xvfs) contains 100 Units of botulinum toxin type A neurotoxin complex, human serum albumin (0.5 mg), and sodium chloride (0.9 mg).

No U.S. standard of potency.

Vacuum-dried.

Contains no preservative.

Rx only

Manufactured by: Evolus, Inc.
Newport Beach, CA
US License No. 2070

at: Daewoong Pharmaceuticals
Seoul, Korea

www.jeuveau.com
NDC 72301-595-10

Made in Korea

Right Panel

Single-Dose Vial. Discard unused portion.

Only reconstitute each vial with sterile, preservative-free 0.9% Sodium Chloride Injection, USP by slowly injecting diluent and gently rotating the vial. Store unused reconstituted JEUVEAU refrigerated between 2° to 8°C (36°F to 46°F) in the original carton to protect from light for up to 24 hours until time of use. Do not

freeze reconstituted JEUVEAU.
Discard 24 hours after reconstitution.

Dosage and Dilution: See Prescribing Information.

JEUVEAU				
prabotulinum toxin type a powder				
Product Information				
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:72301-595	
Route of Administration	INTRAMUSCULAR			
Active Ingredient/Active Moiety				
Ingredient Name		Basis of Strength	Strength	
BOTULINUM TOXIN TYPE A (UNII: E211KPY694) (BOTULINUM TOXIN TYPE A - UNII:E211KPY694)		BOTULINUM TOXIN TYPE A	100 [USP'U]	
Inactive Ingredients				
Ingredient Name			Strength	
ALBUMIN HUMAN (UNII: ZIF514RVZR)				
SODIUM CHLORIDE (UNII: 451W47IQ8X)				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:72301-595-10	1 in 1 CARTON	02/13/2019	
1		1 in 1 VIAL; Type 0: Not a Combination Product		
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
BLA	BLA761085	02/13/2019		

Labeler - Evolus, Inc. (842821881)