Rx ONLY

Jeuveau®
prabotulinumtoxinA-xvfs
injection

Sponsored by evolus™

Supplement to

Modern Aesthetics®

SEPTEMBER/OCTOBER 2020

JEUVEAU®:

A PANEL DISCUSSION ABOUT A MODERN-MADE TOXIN

Jeuveau® is a prescription medicine indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adults.

Please see Important Safety Information, including Boxed Warning on pages S6-S8.

Rx ONLY

Jeuveau®

prabotulinumtoxinA-xvfs injection

JEUVEAU®: A PANEL DISCUSSION ABOUT A MODERN-MADE TOXIN

Jeuveau® is a prescription medicine indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in cadult patients.[1]

To gain a better understanding of the initial healthcare professional (HCP) and patient experience with Jeuveau® at launch, the manufacturer of Jeuveau®, Evolus, designed the Jeuveau® Experience Treatment (J.E.T.) program. Launched in May 2019, one of the most important features of the J.E.T. program was a survey of HCPs and patients.

Modern Aesthetics® assembled three of the J.E.T. program's most influential participants to learn about their experiences with the Jeuveau® launch and glean some takeaways for their peers.

All of our panelists agree that prior to the launch of Jeuveau® the market was ripe for a competitor in the neurotoxin market. They feel that Jeuveau® is a unique 900-kD neurotoxin product and a well-studied, cost-effective alternative to the market leader.

LORRIE KLEIN, MD

Medical Director, OC Dermatology in Laguna Niguel, CA. Dr. Klein is on the scientific advisory board for Senté and the medical advisory boards for RealSelf, Cearna Aesthetics, the Aesthetic Guide, Medesthetics Magazine, and Zalea.

KAREN HARKAWAY, MD

Medical Director, Harkaway Center for Dermatology and Aesthetics in New Jersey. Dr. Harkaway is Chief of Dermatology at Lourdes Medical Center of Burlington. She is affiliated with Our Lady of Lourdes Medical Center and is on the Clinical Advisory Council of ThermiAesthetics.

JUSTIN HARPER, MD

Founder & Medical Director, Juvly Aesthetics, with offices in Columbus, OH, and Dallas. Dr. Harper is also Founder and CEO of Aesthetic Record, an end-to-end EMR and Practice Management software.

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.

Please see Important Safety Information, including Boxed Warning on pages S6-S8.

PHASE 3 CLINICAL TRIAL RESULTS

Phase 3 clinical trials with Jeuveau® consisted of two identical multi-center, double blind, randomized, placebo-controlled studies (EV-001 = 330 subjects; EV-002 = 324 subjects) and showed a statistically significant 2-point composite response rate in glabellar lines.[2]

As Dr. Harper puts it, the clinical study data is "solid."

In US pivotal clinical studies, 68% and 70% of Jeuveau® patients had a 2-grade or better composite improvement in frown lines at Day 30, compared to 1% of placebo ($p<0.001$ in both studies).[1] At Day 150, 5% and 5% had a 2-grade or better composite improvement in frown lines compared to 0% of placebo ($p<0.05$ in both studies).[2] There were no serious adverse events assessed as drug related across these studies.

"They held themselves to a rigorous standard," says Harper. "A two-point composite primary endpoint with a large sample size. The rigor of the studies, the rigor of the data are there, and the endpoints were appropriately tested."

Dr. Harkaway says her patients' results mirrored the trial results.

"I would say that my patients have experienced similar, very high responses to Jeuveau® in the glabella which is always the major application we anchor to," she says.

Panelists also discussed a study that was conducted in Europe and Canada and is one of the largest Phase 3 head-to-head studies vs. Botox® Cosmetic in glabellar lines.[3]

The study, which involved 540 subjects, demonstrated non-inferiority vs. Botox® Cosmetic with 87.2% of patients demonstrating a response at Day 30 compared to 82.8% of Botox® Cosmetic patients vs. 4.2% for placebo (primary endpoint, $p<0.001$ vs. placebo for both active arms).[3]

"Impressive results," Dr. Klein says. "Peers should be advised to review the head-to-head study for themselves. They will see the clinical performance of Jeuveau® vs. Botox® Cosmetic when they look at the graphs."

Dr. Harkaway echoes this sentiment. "The fact that they actually did compare themselves to Botox® Cosmetic in a Phase 3 study was significant," she says. "None of the other neurotoxins had the gall to do that. Even in the pharmaceutical world, most drugs that are being launched, they don't compare themselves in a study to the market leader."

Further, the Phase 3 study assessed more than 30 head-to-head endpoints vs. Botox® Cosmetic. Of note, 54% of patients had visible results as early as 2 days after treatment, 38% at 5 months after treatment, both as defined by a ≥1-grade physician-rated improvement in frown lines.*[3]

When we asked our panelists to comment on their and their patients' experience with Jeuveau®, all three independently brought up the perception of early effect.

Dr. Harkaway feels onset may prove to be important once aesthetic practices begin opening up post COVID-19, as people will be missing the effects of their neurotoxins.

JEUVEAU® TRANSPARENCY CLINICAL PROGRAM[4-8]

5	>2,100
Clinical studies	Subjects

*In a study conducted in Europe and Canada, 54% of patients had a ≥1-grade improvement in frown lines at Day 2 based on physician assessment compared to 12% for placebo ($p<0.001$, secondary endpoint). In US studies, 46% and 56% had a ≥1-grade improvement in frown lines at Day 2 based on physician-assessment compared to 8% and 17% for placebo (exploratory endpoint). *In a study conducted in Europe and Canada, 38% of patients had a ≥1-grade improvement in frown lines at 5 months based on physician assessment compared to 8% for placebo ($p<0.001$, secondary endpoint). In US studies, almost 5% of patients had a ≥2-grade improvement in frown lines at 5 months based on both patient and physician assessments compared to 0% for placebo (secondary endpoint). Results based on a 1-point improvement or comparisons against placebo at Day 2 or Day 150 may not be clinically meaningful. 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.

Jeuveau® is a prescription medicine indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adults.

JEUVEAU is contraindicated in individuals with known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation.

Please see Important Safety Information, including Boxed Warning on pages S6-S8.

Rx ONLY

Jeuveau®

prabotulinumtoxinA-xvfs injection

REAL-WORLD EXPERIENCE[9]

The J.E.T. (Jeuveau® Experience Treatment) program was the largest known neurotoxin experience program conducted in the United States and included healthcare practitioner (HCP) and consumer surveys deployed at baseline and on days 7, 30, 60, 90, 120 and 150 to collect demographic data as well as document patient experience. Survey results among almost 30,000 participants treated with Jeuveau® showed considerable interest among patients of various ages, with a sizeable uptake among patients under 40 years old (38%). 26% of patients surveyed were naïve to neurotoxins, demonstrating an opportunity for Jeuveau® to attract new patients. The results also demonstrated a willingness to switch from other neurotoxins to Jeuveau®, with more than half (51%) switching from Botox® Cosmetic.

THE MARKET TAKE

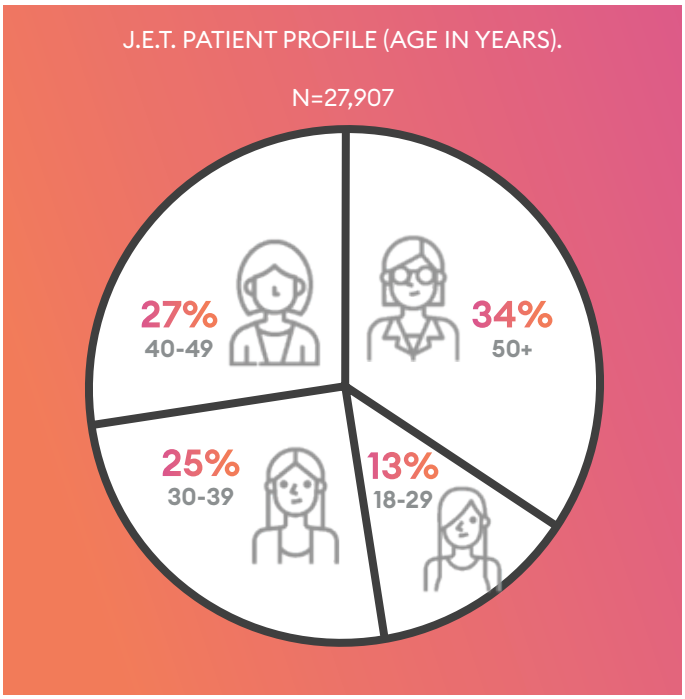
The J.E.T. program also surveyed HCPs, with surveys deployed in June, July, and October of 2019. The results revealed that physicians believe there is room for change in the neurotoxin market. Notable findings include*:

- 88% of providers surveyed agree it is time for more competition in the neurotoxin space
- 93% of providers surveyed would like to bring in more 25-39 year-old patients

These findings align with the panelists' opinion.

Dr. Harkaway believes that prior to the launch of Jeuveau®, other neurotoxins hadn't particularly made a dent in the Botox® Cosmetic market. "There was only Dysport® and Xeomin®, and neither of those had had a very significant impact," she says.

"I do think that the market was ready for another option and it's definitely an important change for us in aesthetics."



PATIENT SATISFACTION

Results from the J.E.T. survey demonstrated high levels of patient satisfaction. In a survey of >9,000 patients, 94% were satisfied with their overall Jeuveau® treatment (Day 30).** Further, at Day 150, 76% of patients surveyed expressed satisfaction with treatment.*** There were no meaningful differences observed in satisfaction rates based on age or prior experience with other neurotoxins.

Aligned with the personal observations of the panel, patients are likely to stick with Jeuveau®. In the J.E.T. survey, 88% of patients surveyed at Day 30 were likely to continue with Jeuveau®.****[9]

Dr. Harkaway surveyed her own patients receiving Jeuveau® asking about their experience. Tellingly, 88% of Dr. Harkaway's new patients have decided to stick with

* J.E.T. HCP Survey data, June 2020 report (n=811); Slightly to extremely agree on a 5-point rating scale.
** J.E.T. Survey data collected 30 days after treatment, June 2020 report (n=9,151); Slightly to extremely satisfied on a 5-point rating scale.
***J.E.T. Survey data collected 150 days after treatment, June 2020 report (n=2,782); Slightly to strongly agree on a 5-point rating scale.
****J.E.T. Survey data collected 30 days after treatment, June 2020 report (n=9,151); slightly to extremely likely on a 5-point rating scale.

Jeuveau® is a prescription medicine indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adults.

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

Please see Important Safety Information, including Boxed Warning on pages S6-S8.

Jeuveau®. She says these are people who come in without a preference and are often willing to go with what she recommends. When she mentions that she even uses it on herself and her staff, they tend to follow her lead. "They don't have a history with Botox® [Cosmetic] so they're even more open to Jeuveau®," she says.

But patients who have tried other neurotoxins have also tended to stick with Jeuveau®, she says. "Nearly everybody has stayed with it...there were only 16 out of 200 or so that switched back."

Dr. Klein's experience has been similar. "About two-thirds of my Botox® patients have tried Jeuveau®. Of these patients, 80% have stayed with Jeuveau®; 20% switched back to Botox®. My patients have been happy with their results."

Dr. Harper concurs. "I didn't specifically measure this yet, but a lot of patients actually really did like it and wanted to continue with it. And the reason why that was interesting is that in some cases that actually went against even what the provider preferred."

What could explain the receptivity to Jeuveau®? In the J.E.T. survey, 95% of patients believed results with Jeuveau® were natural-looking.[9]

Dr. Klein agrees. "Many patients liked the outcome with Jeuveau® because of the natural-looking results," she says. "This presents an opportunity with younger, millennial patients who don't want to look frozen."

ATTRACTIVE PRICING

At the outset, Evolus stated that Jeuveau® pricing was designed to maximize profit for neurotoxins, the most common aesthetic injectable procedure.

"Pricing is definitely more attractive for Jeuveau® as compared to Botox® [Cosmetic] without compromising on product performance," says Dr. Klein.

Dr. Harkaway expands on this sentiment, saying that while the competitive brand has increased its price year after year, practitioners have been unable to increase their prices to the consumer, who now has so many more options of places to go to receive treatments.

The tragic arrival of COVID-19 also plays a role in aesthetic medicine. "If price becomes more of a concern, I can price Jeuveau® lower because my price is lower, which will attract patients looking to spend less," says Dr. Klein.

In light of COVID-19, Evolus recently launched a stimulus package for healthcare professionals, offering Jeuveau® at $350/vial* to maximize profitability for practices during these uncertain times. For patients, Evolus is providing $40 off every treatment with Jeuveau®** through their new loyalty program, Evolus Rewards.

KEY TAKEAWAYS

In the end, based on feedback from our panel, there are several reasons a practice should consider moving toward Jeuveau®.

Dr. Harper says, "the clinical profile of Jeuveau®, coupled with the increased profit margin is a welcomed treatment option in my practice."

Dr. Klein adds, "Evolus as a company has been a pleasure to deal with," she says. "They make things very easy for both the practice and the patient to utilize their product."

*$350/vial if ordered in the Evolus Practice App. $375/vial if ordered through sales representative. Stimulus pricing valid through 12/31/2020.
**Patients eligible once every 90 days.

Jeuveau® is a prescription medicine indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adults.

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.

Please see Important Safety Information, including Boxed Warning on pages S6-S8.

IMPORTANT SAFETY INFORMATION FOR JEUVEAU® (prabotulinumtoxinA-xvfs)

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.

CONTRAINDICATIONS

JEUVEAU is contraindicated in individuals with known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation, and in the presence of infection at the proposed injection site(s).

WARNINGS AND PRECAUTIONS

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. 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.

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.

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.

Hypersensitivity Reactions

Serious and/or immediate hypersensitivity reactions have been reported for botulinum toxin products, including anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea. If such reactions occur with JEUVEAU, discontinue use of JEUVEAU and immediately institute appropriate medical therapy.

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.

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 JEUVEAU clinical studies. 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.

Dysphagia and Breathing Difficulties

Treatment with botulinum toxin products, including JEUVEAU, 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.

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.

Patients treated with botulinum toxin products, including JEUVEAU, may require immediate medical attention should they develop problems with swallowing, speech or breathing.

Pre-existing Conditions at the Injection Site

Caution should be used when JEUVEAU 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.

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 patient to an ophthalmologist.

Human Albumin and Transmission of Viral Diseases

JEUVEAU 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. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is also considered extremely remote. No cases of transmission of viral diseases or CJD have ever been reported for albumin.

ADVERSE REACTIONS

The most frequently reported adverse reactions (≥ 1% and placebo) following injection of JEUVEAU were headache (12%), eyelid ptosis (2%), upper respiratory tract infection (3%), and white blood cell count increase (1%).

DRUG INTERACTIONS

No formal drug interaction studies have been conducted with JEUVEAU. The potential for certain drugs to potentiate the effects of JEUVEAU warrant consideration given the potential risks involved and should be used with caution, including: aminoglycosides or other agents interfering with neuromuscular transmission, anticholinergic drugs, botulinum neurotoxin products, and muscle relaxants.

USE IN SPECIFIC POPULATIONS

The limited available data on JEUVEAU use in pregnant women are insufficient to inform a drug associated risk of adverse developmental outcomes.

There are no data on the presence of JEUVEAU in human or animal milk, its effects on the breastfed infant, or its effects on milk production.

Safety and effectiveness in pediatric patients have not been established.

INDICATION

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.

Please note that this information is not comprehensive. For more information about JEUVEAU, see the full Prescribing Information including BOXED WARNING, and Medication Guide, visit evolus.com.

To report side effects associated with use of JEUVEAU, please call 1-877-EVOLUS1 / 1-877-386-5871. You are encouraged to report side effects of prescription drugs to FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Exclusively licensed and manufactured for: Evolus, Inc., 520 Newport Center Drive, Suite 1200, Newport Beach, CA 92660

References:

1. Jeuveau® [package insert]. Newport Beach, CA: Evolus, Inc; 2019; 2. Beer K. et. al. *Dermatol Surg* 2019;00:1–13.; 3. Rzany B. et. al, *Aesthet Surg J.* 2019 Apr 5. pii: sjz110.; 4. Data on file; CSR EV-001, BLA761085. Evolus, Inc., Santa Barbara, CA.; Data on file; CSR EV-002, BLA761085. Evolus, Inc., Santa Barbara, CA; 6. Data on File; CSR EVB-003, BLA761085, Evolus, Inc., Santa Barbara, CA.; 7. Data on file; CSR EV-004, BLA761085. Evolus, Inc., Santa Barbara, CA.; 8. Data on file; CSR EV-006, BLA761085. Evolus, Inc., Santa Barbara, CA.; 9. Jeuveau® Experience Treatment (J.E.T.) program survey data, June, 2020 Report.

See Jeuveau® Brief Summary on pages S7-S8

JEUVEAU® (prabotulinumtoxinA-xvfs) for injection, for intramuscular use

Rx only

Brief Summary: This information is not comprehensive. Visit evolus.com to obtain the FDA-approved product labeling or call 1-877-EVOLUS1/1-877-386-5871.

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.

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 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.

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.

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.

4.2 Infection at the Injection Site(s)

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

5 WARNINGS

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.

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.

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.

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.

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 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.

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 subjects who may 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 patient to an ophthalmologist.

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. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is also considered extremely remote. No cases of transmission of viral diseases or CJD have ever been reported for albumin.

Jeuveau® Brief Summary continued on page S8

6 ADVERSE REACTIONS

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

- Spread of Toxin Effects
- Hypersensitivity
- Dysphagia and Breathing Difficulties

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.

Glabellar Lines

The adverse reactions below reflect exposure to JEUVEAU with glabellar lines in placebo-controlled studies.

Adverse Reactions Reported at Higher Frequency (≥1%) in the JEUVEAU Group Compared to the Placebo Group

	JEUVEAU N=492 n (%)	**PLACEBO** 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 doses 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 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 relaxants

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).

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.

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 JEUVEAU 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 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.

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.

17 PATIENT COUNSELING INFORMATION

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

Advise patients to inform their doctor or pharmacist if they develop any unusual symptoms (including difficulty with swallowing, speaking or breathing), or if any known symptom persists or worsens.

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.

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.

For more information about JEUVEAU, see the full Prescribing Information including BOXED WARNING, and Medication Guide visit evolus.com.

CAUTION: Federal law prohibits dispensing without prescription.

Exclusively licensed and manufactured for:
Evolus Inc., 520 Newport Center Drive, Suite 1200, Newport Beach, CA 92660