JUVÉDERM®
VOLBELLA® XC

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed physician or properly licensed practitioner.

BEFORE USING PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.

1. DEVICE DESCRIPTION

JUVÉDERM® VOLBELLA® XC injectable gel is a sterile, biodegradable, non-pyrogenic, viscoelastic, clear, colorless, homogeneous gel implant. It consists of cross-linked hyaluronic acid (HA) produced by *Streptococcus* species of bacteria, formulated to a concentration of 15 mg/mL with 0.3% w/w lidocaine in a physiologic buffer.

2. INTENDED USE/INDICATIONS

JUVÉDERM® VOLBELLA® XC injectable gel is indicated for injection into the lips for lip augmentation and for correction of perioral rhytids in adults over the age of 21.

JUVÉDERM® VOLBELLA® XC is indicated for the improvement of infraorbital hollowing in adults over the age of 21.

3. CONTRAINDICATIONS

- JUVÉDERM® VOLBELLA® XC is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.
- JUVÉDERM® VOLBELLA® XC contains trace amounts of Gram-positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.
- JUVÉDERM® VOLBELLA® XC contains lidocaine and is contraindicated for patients with a history of allergies to such material.

4. WARNINGS

- The product must not be injected into blood vessels. Introduction of JUVÉDERM® VOLBELLA® XC injectable gel into the vasculature may lead to embolization, occlusion of the vessels, ischemia, or infarction. Take extra care when injecting soft-tissue fillers; for example, after insertion of the needle, and just before injection, the plunger rod can be withdrawn slightly to aspirate and verify the needle is not intravascular, inject the product slowly, and apply the least amount of pressure necessary. Rare, but serious, adverse events associated with the intravascular injection of soft-tissue fillers in the face have been reported and include temporary or permanent vision impairment, blindness, cerebral ischemia or cerebral hemorrhage leading to stroke, skin necrosis, and damage to underlying facial structures. Immediately stop the injection if a patient exhibits any of the following symptoms, including changes in vision, signs of a stroke, blanching of the skin, or unusual pain during or shortly after the procedure. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care professional specialist should an intravascular injection occur (see Health Care Professional Instructions #19).
- Product use at specific sites in which an active inflammatory process (skin eruptions such as cysts, pimples, rashes, or hives) or infection is present should be deferred until the underlying process has been controlled.
- Injection-site responses consist mainly of short-term inflammatory symptoms starting early after treatment and lasting ≤ 30 days. Refer to the ADVERSE EVENTS section for details.

5. PRECAUTIONS

- JUVÉDERM® VOLBELLA® XC injectable gel is packaged for single-patient use. Do not resterilize. Do not use if package is opened or damaged.
- In order to minimize the risks of potential complications, this product should only be used by health care professionals who have been trained in facial anatomy and vasculature, safe injection techniques, and identification and management of potential adverse events, including intravascular complications.
- Health care professionals are encouraged to discuss all potential risks of soft-tissue injection with their patients prior to treatment and ensure that patients are aware of signs and symptoms of potential complications.
- Based on preclinical studies, patients should be limited to 20 mL of any JUVÉDERM® injectable gel per 60 kg (130 lbs) body mass per year. The safety of injecting greater amounts has not been established.
- The safety and effectiveness for the treatment of anatomic regions other than the lips, perioral area, and infraorbital hollows have not been established in controlled clinical studies.
- Injection of more than 6.0 mL of JUVÉDERM® VOLBELLA® XC injectable gel for lip augmentation and correction of perioral rhytids, and more than 2.2 mL per infraorbital hollow, has not been studied.
- As with all transcutaneous procedures, dermal filler implantation carries a risk of infection. Standard precautions associated with injectable materials should be followed.
- JUVÉDERM® VOLBELLA® XC injectable gel is to be used as supplied. Modification or use of the product outside the Directions for Use may adversely impact the sterility, homogeneity, and performance of the product.
- The safety for use during pregnancy, in breastfeeding females, or in patients under 22 years has not been established.
- The safety in patients with known susceptibility to keloid formation, hypertrophic scarring, and pigmentation disorders has not been studied.
- JUVÉDERM® VOLBELLA® XC injectable gel should be used with caution in patients on immunosuppressive therapy.
- Patients who are using substances that can prolong bleeding (such as aspirin, nonsteroidal anti-inflammatory drugs, and warfarin) may, as with any injection, experience increased bruising or bleeding at injection sites.
- Patients may experience late-onset adverse events with use of dermal fillers, including JUVÉDERM® VOLBELLA® XC. Refer to ADVERSE EVENTS section for details.
- After use, treatment syringes and needles are biohazards. Handle and dispose of these items in accordance with accepted medical practice and applicable local, state, and federal requirements.
- JUVÉDERM® VOLBELLA® XC injectable gel is a clear, colorless gel without visible particulates. In the event that the content of a syringe shows signs of separation and/or appears cloudy, do not use the syringe; notify Allergan Product Support at 1-877-345-5372.
- JUVÉDERM® VOLBELLA® XC should only be used by health care professionals who have appropriate experience and who are knowledgeable about the anatomy and the product for use in the lips, perioral area, and infraorbital hollows.
- If laser treatment, chemical peeling, or any other procedure based on active dermal response is considered after treatment with JUVÉDERM® VOLBELLA® XC, there is a possible risk of eliciting an inflammatory reaction at the implant site. An inflammatory reaction is also possible if the product is administered before the skin has healed completely after such a procedure.
- Failure to comply with the needle attachment instructions could result in needle disengagement and/or product leakage at the LUER-LOK® and needle hub connection.

6. ADVERSE EVENTS

A. US Pivotal Study of JUVÉDERM® VOLBELLA® XC for Lip Augmentation and Perioral Rhytids

In the multicenter, double-blind, randomized, controlled clinical trial to evaluate the safety and effectiveness of JUVÉDERM® VOLBELLA® XC versus *Restylane-L*® (control) for lip augmentation and correction of perioral rhytids, subjects were randomized and treated in a 3:1 ratio with either JUVÉDERM® VOLBELLA® XC (n = 168) or control (n = 56).

Subjects used preprinted diary forms to record specific signs and symptoms of injection-site responses (ISRs) experienced during the 30 days after initial treatment, touch-up treatment (if performed), and repeat treatment. Subjects were instructed to rate each ISR listed on the diary as Mild, Moderate, Severe, or None.

- Mild ISRs were defined as awareness of sign or symptom but easily tolerated.
- Moderate ISRs were defined as discomfort enough to cause interference with usual activity.
- Severe ISRs were defined as incapacitating with inability to work or do usual activity.

The severity and duration of all ISRs reported by > 5% of subjects who completed posttreatment diary forms after initial treatment are summarized in Table 1 and Table 2, respectively. Table 3 shows the severity and duration of all ISRs after repeat treatment reported by > 5% of subjects. The majority of ISRs were mild or moderate in intensity, and their duration was short lasting (30 days or less). There were no significant differences in ISRs reported between JUVÉDERM® VOLBELLA® XC and control. The incidence, severity, and duration of ISRs reported after the touch-up and repeat treatments were generally lower than those reported after initial treatment.

Table 1. Injection-Site Responses by Severity After Initial Treatment Occurring in > 5% of Treated Subjects

Injection-Site Response	JUVÉDERM® VOLBELLA® XC				Control			
	Total % (n/N[a])	Mild[b] %	Moderate[b] %	Severe[b] %	Total % (n/N[a])	Mild[b] %	Moderate[b] %	Severe[b] %
Any ISR	97.4% (150/154)	14.7%	45.3%	40.0%	98.0% (50/51)	8.0%	44.0%	48.0%
Swelling	92.9% (143/154)	23.1%	49.7%	27.3%	98.0% (50/51)	16.0%	46.0%	38.0%
Tenderness	89.6% (138/154)	53.6%	32.6%	13.8%	92.2% (47/51)	23.4%	66.0%	10.6%
Firmness	89.0% (137/154)	32.8%	48.2%	19.0%	92.2% (47/51)	25.5%	59.6%	14.9%
Bruising	89.0% (137/154)	35.0%	40.9%	24.1%	90.2% (46/51)	30.4%	47.8%	21.7%
Lumps/ Bumps	87.7% (135/154)	43.0%	42.2%	14.8%	90.2% (46/51)	30.4%	52.2%	17.4%
Redness	83.1% (128/154)	47.7%	39.1%	13.3%	88.2% (45/51)	40.0%	44.4%	15.6%
Pain	80.5% (124/154)	58.9%	30.6%	10.5%	92.2% (47/51)	42.6%	46.8%	10.6%
Discoloration	41.6% (64/154)	54.7%	34.4%	10.9%	49.0% (25/51)	40.0%	36.0%	24.0%
Itching	30.5% (47/154)	76.6%	17.0%	6.4%	37.3% (19/51)	63.2%	36.8%	0%
Dryness	5.2% (8/154)	37.5%	0%	62.5%	3.9% (2/51)	0%	50.0%	50.0%

[a]N denotes the number of subjects who recorded responses in the diaries after initial treatment.
[b]Maximum duration reported in the diary. The percentages by duration are based on the number of subjects with the corresponding injection-site response.

Table 2. Injection-Site Responses by Duration After Initial Treatment Occurring in > 5% of Treated Subjects

Injection-Site Response	JUVÉDERM® VOLBELLA® XC					Control				
	Total % (n/N[a])	1-3 Days[b] %	4-7 Days[b] %	8-14 Days[b] %	15-30 Days[b] %	Total % (n/N[a])	1-3 Days[b] %	4-7 Days[b] %	8-14 Days[b] %	15-30 Days[b] %
Any ISR	97.4% (150/154)	9.3%	30.0%	20.0%	40.7%	98.0% (50/51)	6.0%	44.0%	8.0%	42.0%
Swelling	92.9% (143/154)	46.9%	34.3%	13.3%	5.6%	98.0% (50/51)	42.0%	36.0%	12.0%	10.0%
Tenderness	89.6% (138/154)	47.8%	29.0%	15.2%	8.0%	92.2% (47/51)	31.9%	36.2%	25.5%	6.4%
Firmness	89.0% (137/154)	39.4%	27.0%	18.2%	15.3%	92.2% (47/51)	29.8%	40.4%	10.6%	19.1%
Bruising	89.0% (137/154)	32.8%	49.6%	13.9%	3.6%	90.2% (46/51)	26.1%	65.2%	8.7%	0%
Lumps/ Bumps	87.7% (135/154)	24.4%	25.2%	17.0%	33.3%	90.2% (46/51)	32.6%	23.9%	4.3%	39.1%
Redness	83.1% (128/154)	65.6%	28.1%	5.5%	0.8%	88.2% (45/51)	57.8%	35.6%	6.7%	0%
Pain	80.5% (124/154)	75.8%	18.5%	4.8%	0.8%	92.2% (47/51)	61.7%	31.9%	6.4%	0%
Discoloration	41.6% (64/154)	64.1%	26.6%	6.3%	3.1%	49.0% (25/51)	68.0%	20.0%	4.0%	8.0%
Itching	30.5% (47/154)	72.3%	17.0%	8.5%	2.1%	37.3% (19/51)	78.9%	21.1%	0%	0%
Dryness	5.2% (8/154)	37.5%	0%	37.5%	25.0%	3.9% (2/51)	0%	50.0%	0%	50.0%

[a]N denotes the number of subjects who recorded responses in the diaries after initial treatment.
[b]Maximum duration reported in the diary. The percentages by duration are based on the number of subjects with the corresponding injection-site response.

Table 3. Injection-Site Responses by Severity and Duration After Repeat Treatment with JUVÉDERM® VOLBELLA® XC Occurring in > 5% of Treated Subjects

Injection-Site Response	Total % (n/N[a])	Severity[b]			Duration[c]			
		Mild %	Moderate %	Severe %	1-3 Days %	4-7 Days %	8-14 Days %	15-30 Days %
Any ISR	90.2% (111/123)	18.9%	44.1%	36.9%	18.0%	30.6%	25.2%	26.1%
Swelling	87.8% (108/123)	36.1%	41.7%	22.2%	50.9%	33.3%	13.9%	1.9%
Tenderness	83.7% (103/123)	47.6%	35.9%	16.5%	52.4%	27.2%	16.5%	3.9%
Firmness	80.5% (99/123)	39.4%	39.4%	21.2%	39.4%	22.2%	25.3%	13.1%
Lumps/ Bumps	79.7% (98/123)	41.8%	39.8%	18.4%	39.8%	22.4%	15.3%	22.4%
Bruising	77.2% (95/123)	36.8%	43.2%	20.0%	40.0%	43.2%	16.8%	0%
Pain	72.4% (89/123)	44.9%	47.2%	7.9%	68.5%	15.7%	12.4%	3.4%
Redness	69.9% (86/123)	48.8%	37.2%	14.0%	62.8%	29.1%	7.0%	1.2%
Discoloration	30.9% (38/123)	60.5%	31.6%	7.9%	76.3%	21.1%	2.6%	0%
Itching	26.0%	50.0%	46.9%	3.1%	71.9%	18.8%	6.3%	3.1%

Most subjects treated with JUVÉDERM® experienced mild (42.3%, 71/168) or mo treatment-related AEs. Similar results we treatment with control (41.1% [23/56] an experienced mild and moderate AEs, res treatment group, the treatment-related A action to be taken and resolved without

Table 4. Treatment-Related Adverse Initial Treatment Occurring in > 5

Adverse Event	JUVÉDERM® VOLBELLA® XC (n = 168)			
	Subjects[a]	Mild[a]	Moderate[a]	Severe[a]
Injection-Site Mass	32.1%	26.8%	4.2%	1.2%
Injection-Site Bruising	17.9%	10.7%	7.1%	0%
Injection-Site Pain	11.9%	7.7%	4.2%	0%
Injection-Site Induration	8.9%	7.7%	0.6%	0.6%
Injection-Site Swelling	8.3%	4.8%	3.6%	0%
Injection-Site Dryness	4.2%	3.0%	1.2%	0%

[a]The percentages are based on the number of subjects who r corresponding product.

Table 5. Treatment-Related Adverse Initial Treatment Occurring in > 5

Adverse Event	JUVÉDERM® VOLBELLA® XC					
	Events % (n/N)	≤ 7 Days[a] %	8-14 Days[a] %	15-30 Days[a] %	> 30 Days[a] %	Not yet Resolved[a] %
Injection-Site Mass	29.0% (100/345)	5.0%	1.0%	15.0%	76.0%	3.0%
Injection-Site Bruising	15.9% (55/345)	52.7%	2.9%	14.5%	3.6%	0%
Injection-Site Pain	12.2% (42/345)	50.0%	9.5%	4.8%	35.7%	0%
Injection-Site Induration	12.5% (43/345)	0%	4.7%	0%	95.3%	0%
Injection-Site Swelling	9.3% (32/345)	43.8%	18.8%	6.3%	31.3%	0%
Injection-Site Dryness	3.8% (13/345)	0%	46.2%	0%	53.8%	0%

[a]The percentages by duration are based on the number of ev adverse event.

Treatment-related AEs after initial treatm occurring in ≤ 5% of subjects included c lips, general physical condition abnorma (lumps), lip injury, oral herpes, presyncop site discoloration, discomfort, edema, er hyperaesthesia, hypoaesthesia, laceratio paraesthesia, pruritus, and reaction.

In the clinical study, 7 subjects had lump occurred weeks to months after treatme mild or moderate. Swelling was treated w doxycycline, and no treatment was given these events resolved without sequelae.

3 reports of injection-site mass and 1 report of oral herpes. None required treatment. Of the 4 AEs, 2 were mild (1 injection-site mass [lumps/bumps] and 1 oral herpes), which resolved without sequelae, and 2 were reported with a maximum severity of severe (both events were injection-site mass [lumps/bumps] in 1 subject) and then mild at the completion of the study.

C. US Pivotal Study of JUVÉDERM® VOLBELLA® XC for the Improvement of Infraorbital Hollowing

In the randomized, controlled clinical trial to evaluate the safety and effectiveness of JUVÉDERM® VOLBELLA® XC, there were 105 subjects treated in the infraorbital hollows during the primary phase of the study. Touch-up treatments occurred approximately 30 days after initial injection. After the 3-month, no-treatment control period, control subjects were allowed to receive treatment; 29 control subjects were treated in the study.

Subjects used an electronic diary to record specific signs and symptoms of ISRs experienced during the 30 days after initial treatment, touch-up treatment (if performed), and repeat treatment. Subjects were instructed to rate each ISR listed on the diary as Mild, Moderate, Severe, or None.

The severity and duration of ISRs reported by treatment-group subjects who completed posttreatment diary forms after initial treatment are summarized in Table 7. Table 8 shows the severity and duration of ISRs after repeat treatment. The majority of ISRs were mild, and their duration was short lasting (7 days or less). The incidence, severity, and duration of ISRs reported after the touch-up and repeat treatments were generally lower than those reported after initial treatment.

Table 7. ISRs by Severity and Duration After Initial Treatment Occurring in > 5% of Treated Subjects

Injection-Site Response	Total % (n/N[a])	Severity[b]			Duration[c]			
		Mild %	Moderate %	Severe %	1-3 Days %	4-7 Days %	8-14 Days %	15-30 Days %
Tenderness to Touch	47.7% (63/132)	88.9% (56/63)	9.5% (6/63)	1.6% (1/63)	57.1% (36/63)	22.2% (14/63)	15.9% (10/63)	4.8% (3/63)
Bruising	40.2% (53/132)	77.4% (41/53)	18.9% (10/53)	3.8% (2/53)	43.4% (23/53)	20.8% (11/53)	22.6% (12/53)	13.2% (7/53)
Swelling	41.7% (55/132)	80.0% (44/55)	18.2% (10/55)	1.8% (1/55)	49.1% (27/55)	20.0% (11/55)	23.6% (13/55)	7.3% (4/55)
Lumps/ Bumps	38.6% (51/132)	82.4% (42/51)	17.6% (9/51)	0% (0/51)	49.0% (25/51)	15.7% (8/51)	13.7% (7/51)	21.6% (11/51)
Redness	34.8% (46/132)	87.0% (40/46)	13.0% (6/46)	0% (0/46)	67.4% (31/46)	17.4% (8/46)	6.5% (3/46)	8.7% (4/46)
Pain after Injection	33.3% (44/132)	81.8% (36/44)	18.2% (8/44)	0% (0/44)	79.5% (35/44)	11.4% (5/44)	6.8% (3/44)	2.3% (1/44)
Firmness	33.3% (44/132)	86.4% (38/44)	13.6% (6/44)	0% (0/44)	50.0% (22/44)	25.0% (11/44)	13.6% (6/44)	11.4% (5/44)
Discoloration	18.9% (25/132)	88.0% (22/25)	12.0% (3/25)	0% (0/25)	52.0% (13/25)	16.0% (4/25)	20.0% (5/25)	12.0% (3/25)
Itching	11.4% (15/132)	80.0% (12/15)	20.0% (3/15)	0% (0/15)	53.3% (8/15)	20.0% (3/15)	13.3% (2/15)	13.3% (2/15)

[a]N denotes the number of subjects who recorded responses in the diaries after initial treatment.

[b]Maximum reported severity in the diary. The percentages by severity are based on the number of subjects with the corresponding ISR.

[c]Maximum duration reported in the diary. The percentages by duration are based on the number of subjects with the corresponding ISR.

Table 8. ISRs Responses by Severity and Duration After Repeat Treatment with JUVÉDERM® VOLBELLA® XC Occurring in > 5% of Treated Subjects

Injection-Site Response	Total % (n/N[a])	Severity[b]			Duration[c]			
		Mild %	Moderate %	Severe %	1-3 Days %	4-7 Days %	8-14 Days %	15-30 Days %
Tenderness to Touch	34.3% (12/35)	83.3% (10/12)	8.3% (1/12)	8.3% (1/12)	41.7% (5/12)	25.0% (3/12)	8.3% (1/12)	25.0% (3/12)
Pain after Injection	28.6% (10/35)	90.0% (9/10)	0% (0/10)	10% (1/10)	60.0% (6/10)	10.0% (1/10)	10.0% (1/10)	20.0% (2/10)
Firmness	28.6% (10/35)	90.0% (9/10)	10% (1/10)	0% (0/10)	60.0% (6/10)	20.0% (2/10)	10.0% (1/10)	10.0% (1/10)
Swelling	28.6% (10/35)	70.0% (7/10)	20.0% (2/10)	10.0% (1/10)	40.0% (4/10)	20.0% (2/10)	20.0% (2/10)	20.0% (2/10)
Lumps/ Bumps	25.7% (9/35)	77.8% (7/9)	11.1% (1/9)	11.1% (1/9)	44.4% (4/9)	11.1% (1/9)	22.2% (2/9)	22.2% (2/9)
Redness	25.7% (9/35)	77.8% (7/9)	11.1% (1/9)	11.1% (1/9)	55.6% (5/9)	44.4% (4/9)	0% (0/9)	0% (0/9)
Bruising	20.0% (7/35)	85.7% (6/7)	14.3% (1/7)	0% (0/7)	28.6% (2/7)	28.6% (2/7)	42.9% (3/7)	0% (0/7)
Discoloration	8.6% (3/35)	100% (3/3)	0% (0/3)	0% (0/3)	66.7% (2/3)	0% (0/3)	33.3% (1/3)	0% (0/3)
Itching	5.7% (2/35)	50.0% (1/2)	50.0% (1/2)	0% (0/2)	100% (2/2)	0% (0/2)	0% (0/2)	0% (0/2)

[a]N denotes the number of subjects who recorded responses in the diaries after repeat treatment.

[b]Maximum severity reported in the diary. The percentages by severity are based on the number of subjects with the corresponding ISR.

[c]Maximum duration reported in the diary. The percentages by duration are based on the number of subjects with the corresponding ISR.

AEs were reported by the Treating Investigator at follow-up visits. After initial treatment (or touch-up treatment, if performed), treatment-related AEs were reported in 9.5% (10/105) of subjects in the treatment group. The most common treatment-related AEs were injection-site bruising (3.8%) and injection-site swelling (3.8%). Other treatment-related AEs included dizziness, injection-site pain, injection-site edema, and syncope. All treatment-related AEs were mild, generally required no action to be taken, and resolved without sequelae.

In the clinical study, 3 subjects had mild swelling that occurred greater than 30 days after treatment. The swelling was treated with antibiotics for 1 subject; the other subjects did not require treatment. All of these events resolved within 45 days without sequelae.

There were no treatment-related AEs after repeat treatment with JUVÉDERM® VOLBELLA® XC.

There were no treatment-related serious AEs reported in the study.

Safety assessments such as Tyndall effect, visual acuity, confrontational visual fields, and ocular motility were evaluated at the screening visit and throughout the study. None of the safety assessments were remarkable or presented safety concerns after treatment with JUVÉDERM® VOLBELLA® XC.

Safety Subgroup Analyses

Subgroup analyses for ISRs and AEs were performed based on baseline Allergan Infraorbital Hollows Scale (AIHS), injection volume, primary injection instrument (cannula or needle), gender, Fitzpatrick Skin Phototype, age, and investigational site. Swelling (as an ISR) by

journals and voluntary reports. All AEs o
surveillance are listed in order of numbe
inflammatory reaction, loss/lack of corre
allergic reaction, hematoma, infection, n
as increase or decrease of sensation, va
abscess, anxiety, varied injuries, flu-like
herpes, headache, angioedema, bleedin
malaise, scarring, necrosis, cyst, dyspne
exacerbation, calcification, depression, v

In many cases the symptoms resolved v
Reported treatments included the use o
analgesics, antibiotics, antifungals, antil
drainage, eye drops, hyaluronidase, ice,
NSAIDs, petroleum jelly, steroids, ultras
and warm compress. Outcomes for thes
from resolved to ongoing at the time of

Vision abnormalities have been reporte
JUVÉDERM® VOLBELLA® XC into the gl
periorbital area, with a time to onset ran
to 2 months following injection. Reporte
antibiotics, anti-inflammatories, hyaluro
steroids. Outcomes ranged from resolv
of last contact (see WARNINGS section

Adverse reactions should be reported t
Surveillance Department at 1-877-345-5

7. CLINICAL STUDIES

A. Pivotal Study of JUVÉDERM® VOL Augmentation and Perioral Rhytids

Pivotal Study Design

A prospective, double-blind, randomized clinical study was conducted to evaluate of JUVÉDERM® VOLBELLA® XC versus the lips and perioral area (vermilion, verm columns, Cupid's bow, perioral lines, an lip augmentation and the correction of p 224 subjects were randomized and unde JUVÉDERM® VOLBELLA® XC (n = 168) o outset of the study. An optional touch-up approximately 1 month after the initial tr necessary, to achieve optimal correction

The follow-up period consisted of safety up visits at 1, 3, 6, 9, and 12 months afte Subjects were then eligible for a repeat t VOLBELLA® XC, with posttreatment follo repeat treatment, at which time all subje

Study Endpoints

The primary effectiveness measure for th non-inferiority of JUVÉDERM® VOLBELL terms of change from baseline to month on Evaluating Investigator assessments Allergan Lip Fullness Scale (LFS).

Secondary measures included Evaluatin of subjects' perioral lines using the valid Scale (POLSS) and subjects' satisfactio validated *Satisfaction With Lips* module

Table 10. Effectiveness Results Through 1 Year

	JUVÉDERM® VOLBELLA® XC
	% (n/N)
1 Month	86.2% (131/152)
3 Months	80.3% (122/152)
6 Months	71.1% (106/149)
9 Months	65.1% (95/146)
1 Year	61.8% (76/123)

At 3 months, improvements in perioral lines severity at rest were observed in 65.4% (53/81) of subjects treated with JUVÉDERM® VOLBELLA® XC. At 1 year, 66.2% (45/68) of subjects treated with JUVÉDERM® VOLBELLA® XC maintained improvement in perioral lines severity at rest.

At 3 months, 96.1% (147/153) of subjects treated with JUVÉDERM® VOLBELLA® XC reported improvement in satisfaction with their lips, based on the *Satisfaction With Lips* module of the FACE-Q®, with the mean score increasing from 38.5 at baseline to 76.5. At 1 year, 79.7% (98/123) of subjects reported improved satisfaction with their lips over baseline, with a mean score of 59.6.

Through 1 year in the JUVÉDERM® VOLBELLA® XC group, improvements in upper- and lower-lip fullness were similar to the improvements seen in overall lip fullness. Subjects treated with JUVÉDERM® VOLBELLA® XC in the perioral lines and oral commissures also saw improvement in perioral lines severity at maximal contraction and oral commissures severity through 1 year.

On the GAIS at 3 months, 92.9% (143/154) of subjects in the JUVÉDERM® VOLBELLA® XC group were scored as improved or much improved in appearance. At 1 year, the percentage of subjects scored as improved or much improved was 58.5% (72/123) in the JUVÉDERM® VOLBELLA® XC group.

At 1 year, 74.8% (92/123) of subjects treated with JUVÉDERM® VOLBELLA® XC reported improvement in satisfaction with their lip lines based on the *Satisfaction With Lip Lines* module of the FACE-Q®, with the mean score increasing from 37.5 at baseline to 56.3.

Follow-up After Repeat Treatment

Repeat treatment with JUVÉDERM® VOLBELLA® XC was administered to 124 subjects in the JUVÉDERM® VOLBELLA® XC randomization group. The effectiveness profile after repeat treatment was similar to that after initial treatment. At 1 month after repeat treatment, the responder rate was similar to that after initial treatment, with 94.3% (115/122) of subjects showing at least a 1-point improvement in lip fullness, based on the Evaluating Investigator assessment.

B. Pivotal Study of JUVÉDERM® VOLBELLA® XC for the Improvement of Infraorbital Hollowing

Pivotal Study Design

A prospective, multicenter, single-blind, randomized, controlled clinical study was conducted to evaluate the safety and effectiveness of JUVÉDERM® VOLBELLA® XC for the treatment of infraorbital hollowing. Across 15 investigational sites, a total of 140 subjects were randomized and underwent treatment with JUVÉDERM® VOLBELLA® XC (n = 105) or delayed-treatment control (n = 35) at the outset of the study. Investigators were given the option

The follow-up period consisted of safety and effectiveness follow-up visits at 1, 3, 6, 9, and 12 months after the last treatment. Treatment-group subjects were then eligible for a repeat treatment with JUVÉDERM® VOLBELLA® XC, with posttreatment follow-up for 1 month after repeat treatment, at which time all subjects completed the study.

Study Endpoints

The primary effectiveness measure for the study was the blinded Evaluating Investigator's live assessment of infraorbital hollowing using the validated 5-point photonumeric AIHS, which was performed separately for each infraorbital area. The primary endpoint would be met if the responder rate for the treatment group was statistically significantly greater than that for the control group at month 3. The responder rate is the percentage of subjects who showed at least a 1-point improvement in both infraorbital areas from baseline on the AIHS.

Secondary measures included independent assessments by the Evaluating Investigator and the subject for global aesthetic improvement using the GAIS and the *Appraisal of Lower Eyelids* module of the FACE-Q®.

Additional effectiveness measures included volume change of each infraorbital area as assessed by 3D facial digital imaging. Subjects performed self-assessments of natural look and feel of the eyes, as well as dark circles. The Treating Investigators also assessed injection ease and product moldability.

Safety measures included incidence, severity, and duration of ISRs and AEs; subjects' assessments of procedural pain; Evaluating Investigators' assessments of Tyndall effect; and vision assessments including Snellen visual acuity, confrontational visual fields, and ocular motility.

Subject Demographics

Subject demographics and pretreatment characteristics of the JUVÉDERM® VOLBELLA® XC treatment group and no-treatment control group are presented in Table 11.

Table 11. Subject Demographics and Pretreatment Characteristics (N = 135)

	JUVÉDERM® VOLBELLA® XC	Control	Total
	(n = 103) % (n/N)	(n = 32) % (n/N)	(N = 135) % (n/N)
Gender			
Female	90.3% (93/103)	96.9% (31/32)	91.9% (124/135)
Male	9.7% (10/103)	3.1% (1/32)	8.1% (11/135)
Age			
Median	47	40	47
Range	23-68	23-59	23-68
Race			
Caucasian	78.6% (81/103)	84.4% (27/32)	80.0% (108/135)
African American	15.5% (16/103)	6.3% (2/32)	13.3% (18/135)
Asian	1.0% (1/103)	6.3% (2/32)	2.2% (3/135)
American Indian or Alaska Native	2.9% (3/103)	3.1% (1/32)	3.0% (4/135)
Other	1.9% (2/103)	0% (0/32)	1.5% (2/135)
Fitzpatrick Skin Type			
I/II	34.0% (35/103)	34.4% (11/32)	34.1% (46/135)
III/IV	49.5% (51/103)	56.3% (18/32)	59.1% (69/135)
V/VI	16.5% (17/103)	9.4% (3/32)	14.8% (20/135)
Baseline AIHS Score			
0 (None)	0% (0/103)	0% (0/32)	0% (0/135)
1 (Minimal)	0% (0/103)	0% (0/32)	0% (0/135)

Effectiveness Results

JUVÉDERM® VOLBELLA® XC provided a significant improvement in the appearan compared to the no-treatment control gr primary effectiveness criteria were met i group's responder rate of 83.1% was sta greater ($P < 0.0001$) than the responder control group (15.6%) based on the mIT imputation. The mean improvement was (≥ 1 point), with the majority of subjects through 1 year (Table 12).

Table 12. Effectiveness Results on AIHS Responder Rates Us

	JUVÉDE
1 Month	8
3 Months	8
6 Months	7
9 Months	7
1 Year	7

At month 3, the GAIS responder rate wa on the Evaluating Investigators' assessm based on the subjects' assessments, wh the percent of subjects with a score of i compared to baseline. At 1 year, the GA Evaluating Investigators was 75.3%, and subjects was 78.5%.

Per the *Lower Eyelid* module of the FAC (89.5%, 94/105) were satisfied with their month 12 following treatment with JUVÉ At month 3, the majority of subjects repo little, bothered by how tired (80.2%, 81/1 the undereye area made them look com 29.8% (31/104) at baseline, respectively.

Effectiveness Subgroup Analyses

Subgroup analyses were performed bas injection volume, primary injection instru gender, Fitzpatrick Skin Phototype, age, Treatment-group subjects showed consi across different subgroups with the exce instrument and investigational site. The A subjects treated using cannula was 92.9 in subjects treated using needle at mont sites, AIHS responder rates were consis at 2 sites, which had 0% (0/7) and 57.1% However, regardless of injection instrum the majority of subjects were satisfied ac effectiveness measures.

8. INSTRUCTIONS FOR USE

A. To Attach Needle to Syringe or Ca

To ensure proper attachment to the syrin needle provided or the TSK *STERiGLIDE*

8. For lip augmentation and treatment of perioral lines, the patient's treatment goals should be characterized with regard to proper proportion of upper and lower lip; vertical height; horizontal length; vermilion fullness; contouring of the vermilion border, Cupid's bow, and philtral columns; as well as perioral lip rhytids and oral commissures. Pretreatment photographs are recommended. For treatment of infraorbital hollowing, the patient's treatment goals should be characterized by improving the infraorbital hollows for a natural-looking contour.
9. Supplementary anesthesia may be used for additional pain management during and after injection.
10. After ensuring that the patient has thoroughly washed the treatment area with soap and water, the area should be swabbed with alcohol or other antiseptic. Prior to injecting, depress the plunger rod until the product flows out of the needle.
11. After insertion of the needle, and just before injection, retract the plunger rod to slightly aspirate and verify the needle is not intravascular. If blood is withdrawn, this could indicate intravascular placement; therefore, stop immediately, reposition the needle/cannula and repeat the retraction step again. The absence of blood does not necessarily exclude intravascular placement; therefore, it is important to inject the product slowly and apply the least amount of pressure necessary.
12. After the first small amount of material has been injected into the patient, wait a full 3 seconds to allow the lidocaine to take effect before proceeding with the rest of the injection.
13. The injection technique may vary with regard to angle and orientation of the needle bevel, injection depth, and the quantity administered. Tunneling, serial puncture, fanning, or a combination of these techniques may be used for lip augmentation or treatment of infraorbital hollowing to achieve optimal results. Crosshatching and bolus injection techniques have also been used to achieve optimal results for the treatment of infraorbital hollows. Injecting the product too superficially may result in visible lumps and/or discoloration.
14. Inject JUVÉDERM® VOLBELLA® XC by applying slow and even pressure on the plunger rod. It is important that the injection be stopped before the needle is pulled out of the skin to prevent material from leaking out or being placed too superficially in the skin.
15. If the needle or cannula is blocked, do not increase the pressure on the plunger rod. Instead, stop the injection and replace the needle or cannula.
16. The typical volume injected into the lips and perioral area to achieve optimal correction was approximately 2.6 mL, which may vary depending on the goals the patient wishes to achieve. Injection volumes into the lips and perioral area after repeat treatment tended to be lower, with the typical total injection volume to achieve optimal correction being approximately 1.6 mL.
17. The typical volume injected in the infraorbital hollows to achieve optimal improvement was approximately 1.0 mL in each infraorbital area, which may vary depending on the goal the patient wishes to achieve. Injection volumes into the infraorbital hollows after repeat treatment tended to be lower, with the typical total injection volume to achieve optimal improvement being approximately 0.4 mL in each infraorbital area.
18. Correct to 100% of the desired volume effect. Do not overcorrect. The degree and duration of the correction depend on the character of the defect treated, the tissue stress at the implant site, the depth of the implant in the tissue, and the injection technique. Markedly indurated defects may be difficult to correct.
19. If immediate blanching occurs, the injection should be stopped and the area massaged until it returns to a normal color. Blanching may represent a vessel occlusion. If normal skin coloring does not return, do not continue with the injection. Treat in accordance with American Society for Dermatologic Surgery guidelines, which include hyaluronidase injection.[1]
20. When injection is completed, the treated site should be gently massaged so that it conforms to the contour of the surrounding tissues. If overcorrection occurs, massage the area with your fingers or against an underlying superficial bone and/or teeth to obtain optimal results.
21. With patients who have localized swelling, the degree of correction is sometimes difficult to judge at the time of treatment. In these cases, it is better to invite the patient back to the office for a touch-up treatment.
22. After the initial treatment, an additional touch-up treatment may be necessary to achieve the desired level of correction. If further treatment is needed, the same procedure should be repeated until a satisfactory result is obtained. The need for an additional treatment may vary from patient to patient and is dependent upon a variety of factors such as treatment goals, skin elasticity, and dermal thickness at the treatment site.
23. Patients may have mild to moderate injection-site responses after treatment in the lips, perioral area, and infraorbital hollows, which typically resolve within 14 days. Ice may be applied, using gentle pressure, for a brief period following treatment to minimize swelling and reduce pain.
24. The health care professional should instruct the patient to promptly report to her/him any evidence of problems possibly associated with the use of JUVÉDERM® VOLBELLA® XC.

[1] Jones DH, Fitzgerald R, Cox SE, et al. Preventing and treating adverse events of injectable fillers: evidence-based recommendations from the American Society for Dermatologic Surgery Multidisciplinary Task Force. *Dermatol Surg.* 2021;47(2):214-226.

C. Patient Instructions

It is recommended that the following information be shared with patients:

- Within the first 24 hours, patients should avoid strenuous exercise, extensive sun or heat exposure, and alcoholic beverages. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the injection-sites.
- To report an adverse reaction, phone the Allergan Product Support Department at 1-877-345-5372.

9. HOW SUPPLIED

JUVÉDERM® VOLBELLA® XC injectable gel is supplied in individual treatment syringes with 30-G or 32-G needles for single-patient use and ready for injection (implantation). The TSK *STERiGLIDE*® 27-G, 1½" cannula is not supplied with JUVÉDERM® VOLBELLA® XC but is available for purchase through Allergan®. The volume in each syringe is as stated on the syringe label and the carton. The contents of the syringe are sterile and non-pyrogenic. Do not resterilize. Do not use if package is opened or damaged.

10. SHELF LIFE AND STORAGE

JUVÉDERM® VOLBELLA® XC injectable gel must be used prior to the expiration date printed on the label.

Store at room temperature (up to 25°C/77°F). DO NOT FREEZE.

JUVÉDERM® VOLBELLA® XC injectable gel has a clear appearance. In the event that a syringe contains material that is not clear, do not use the syringe; notify Allergan Product Support immediately at 1-877-345-5372.

To place an order, contact Allergan® at 1-800-377-7790.

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