JUVÉDERM® VOLUX™ 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 THIS PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.

1. DEVICE DESCRIPTION

JUVÉDERM® VOLUX™ XC injectable gel is a sterile, biodegradable, non-pyrogenic, viscoelastic, clear, colorless, homogeneous gel implant. It consists of hyaluronic acid (HA) produced by *Streptococcus* species of bacteria crosslinked with BDDE, formulated to a concentration of 25 mg/mL with 0.3% w/w lidocaine in a physiologic buffer.

2. INTENDED USE/INDICATIONS

JUVÉDERM® VOLUX™ XC injectable gel is indicated for subcutaneous and/or supraperiosteal injection for improvement of jawline definition in adults over the age of 21 with moderate to severe loss of jawline definition.

3. CONTRAINDICATIONS

- JUVÉDERM® VOLUX™ XC is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.
- JUVÉDERM® VOLUX™ XC contains trace amounts of gram-positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.
- JUVÉDERM® VOLUX™ 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® VOLUX™ XC injectable gel into the vasculature may lead to embolization, occlusion of the vessels, ischemia, or infarction. Take extra care when injecting the product, for example, after insertion of the needle, and just before injection, the plunger rod can be withdrawn slightly to aspirate and verify the needle is not intravascular, inject the product slowly and apply the least amount of pressure necessary.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 (AEs) associated with the intravascular injection of injectable gels 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: 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 #17).
- 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 (ISRs) consist mainly of short-term inflammatory symptoms and generally resolve within 2 weeks. Refer to the ADVERSE EVENTS section for details.

5. PRECAUTIONS

- JUVÉDERM® VOLUX™ XC injectable gel is packaged for single-patient use. Do not resterilize. Do not use if package is open or damaged.
- In order to minimize the risk 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 AEs, including intravascular complications.
- Health care professionals are encouraged to discuss all potential risks of soft tissue injections with their patients prior to treatment and ensure that patients are aware of signs and symptoms of potential complications.
- Based on preclinical studies and a toxicological risk assessment, patients should be limited to 20 mL of any JUVÉDERM® injectable gel per 60 kg (132 lbs) body mass per year. The safety of injecting greater amounts has not been established.
- This product is intended for improving jawline definition. The safety and effectiveness for the treatment of anatomic regions in other areas of the body have not been established in controlled clinical studies.
- Injection of more than 9 mL of JUVÉDERM® VOLUX™ XC for improvement of jawline definition has not been studied.
- As with all transcutaneous procedures, injections of this product carry a risk of infection. Standard precautions associated with injectable materials should be followed.
- JUVÉDERM® VOLUX™ XC 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, and in patients under 22 years has not been established.
- The safety in patients with known susceptibility to keloid formation, hypertrophic scarring, or pigmentation disorders has not been studied.
- JUVÉDERM® VOLUX™ XC 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 AEs with use of injectable gel implants, including JUVÉDERM® VOLUX™ 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® VOLUX™ 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 Surveillance at 1-877-345-5372.

- JUVÉDERM® VOLUX™ 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 jawline.
- If laser treatment, chemical peeling, or any other procedure based on active dermal response is considered after treatment with JUVÉDERM® VOLUX™ 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® VOLUX™ XC

In the randomized, controlled, multicenter clinical study to evaluate the safety and effectiveness of JUVÉDERM® VOLUX™ XC for improving jawline definition, 156 participants were randomized to treatment and received injections in the jaw area (pre- and post-jowl sulci, chin, marionette lines, and mandible) during the primary phase of the study. Touch-up treatments occurred approximately 30 days after initial injection, if needed. After the 6-month blinded "no-treatment" control period, control participants were offered treatment; 42 control participants elected to receive treatment. Treatment group participants were offered a maintenance treatment 12 months after the last treatment. A total of 87 treatment group participants opted for the maintenance treatment.

Participants used electronic diaries to record specific signs and symptoms of ISRs experienced during the 30 days after the initial, touch-up, and maintenance treatments. Participants were instructed to rate each ISR listed on the diary as Mild, Moderate, Severe, or None.

- Mild ISRs were defined as symptoms causing little, if any, discomfort leading to little, if any, effect on daily activities.
- Moderate ISRs were defined as symptoms causing some discomfort leading to some effect on daily activities.
- Severe ISRs were defined as symptoms causing great discomfort leading to compromised performance of daily activities.

The severity and duration of all ISRs reported by > 5% of participants after initial treatment (from both the treatment and control groups) are summarized in Table 1. Most ISRs were mild or moderate (75%, 147/196 for any ISRs after initial treatment), and their duration was short lasting (14 days or less). A total of 35% (69/196) of ISRs lasted between 15 to 30 days. The incidence, severity, and duration of ISRs reported after the touch-up and maintenance treatments were similar to those reported after initial treatment.

Table 1. ISRs by Severity and Duration After Initial Treatment with JUVÉDERM® VOLUX™ XC Occurring in > 5% of Treated Participants

ISR	Total % (n/N[a])	Severity[b]			Duration[c]			
		Mild % (n/N[a])	Moderate % (n/N[a])	Severe % (n/N[a])	1-3 Days % (n/N[a])	4-7 Days % (n/N[a])	8-14 Days % (n/N[a])	15-30 Days % (n/N[a])
Any ISR	85.2% (167/196)	32.7% (64/196)	42.3% (83/196)	10.2% (20/196)	20.4% (40/196)	14.3% (28/196)	15.3% (30/196)	35.2% (69/196)
Tenderness	80.1% (157/196)	42.3% (83/196)	36.2% (71/196)	1.5% (3/196)	29.1% (57/196)	21.4% (42/196)	18.4% (36/196)	11.2% (22/196)
Lumps/Bumps	79.1% (155/196)	40.3% (79/196)	32.7% (64/196)	6.1% (12/196)	20.9% (41/196)	12.8% (25/196)	12.8% (25/196)	32.7% (64/196)
Pain	78.1% (153/196)	44.9% (88/196)	31.1% (61/196)	2.0% (4/196)	41.3% (81/196)	21.4% (42/196)	10.2% (20/196)	5.1% (10/196)
Swelling	77.6% (152/196)	42.9% (84/196)	31.1% (61/196)	3.6% (7/196)	37.2% (73/196)	23.5% (46/196)	11.7% (23/196)	5.1% (10/196)
Firmness	73.5% (144/196)	41.8% (82/196)	29.1% (57/196)	2.6% (5/196)	33.7% (66/196)	15.3% (30/196)	12.2% (24/196)	12.2% (24/196)
Bruising	69.4% (136/196)	38.8% (76/196)	25.0% (49/196)	5.6% (11/196)	24.5% (48/196)	18.9% (37/196)	19.4% (38/196)	6.6% (13/196)
Redness	67.9% (133/196)	41.8% (82/196)	24.5% (48/196)	1.5% (3/196)	44.9% (88/196)	13.8% (27/196)	7.1% (14/196)	2.0% (4/196)
Itching	33.2% (65/196)	27.0% (53/196)	6.1% (12/196)	0%	21.4% (42/196)	4.6% (9/196)	5.1% (10/196)	2.0% (4/196)
Discoloration	32.7% (64/196)	23.5% (46/196)	8.2% (16/196)	1.0% (2/196)	20.9% (41/196)	4.6% (9/196)	5.6% (11/196)	1.5% (3/196)

[a] N denotes the number of participants who recorded responses in the diaries after initial treatment.
[b] Maximum severity reported in the diary.
[c] Duration is calculated based on the difference between the first and last date of occurrence +1.

Adverse Events (AEs) were defined as "any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device."

AEs were reported by the Treating Investigator at follow-up visits. Among the 198 participants who received an initial treatment with JUVÉDERM® VOLUX™ XC, 16 participants (8.1%, 16/198) had 20 treatment-related AEs. These AEs included mastication disorder (2.0%, 4/198), injection site nodule (1.5%, 3/198), injection site bruising (1.0%, 2/198), injection site hypersensitivity (0.5%, 1/198), injection site mass (0.5%, 1/198), injection site pain (0.5%, 1/198), injection site swelling (0.5%, 1/198), injection site infection (0.5%, 1/198), oral herpes (0.5%, 1/198), temporomandibular joint syndrome (0.5%, 1/198), muscle tightness (0.5%, 1/198), muscle twitching (0.5%, 1/198), and headache (0.5%, 1/198). There were 15 mild and 5 moderate adverse events. The severity and duration of all treatment-related AEs after initial treatment (for the treatment and the treated control groups) are summarized in Table 2. Among the 87 participants who received maintenance treatment, 3 participants (3.4%, 3/87) had 4 treatment-related AEs, which included injection site nodule (2.3%, 2/87) and mastication disorder (1.1%, 1/87). Most AEs were mild and resolved within 7 days without sequelae. There were 3 participants that required medical intervention, which may have included antibiotics, oral and intralesional steroids, antihistamines, diuretics, or hyaluronidase to resolve the

AEs. The treatment-related AEs lasting longer than 30 days and with a delayed onset (> 30 days) are summarized in Table 3 and Table 4.

Table 2. Severity and Duration of Treatment-Related AEs in the Treated Period (JUVÉDERM® VOLUX™ XC Treated Population)

	Participants (N=198) n (%)	Treatment-Related AEs
Severity		
Total	16 (8.1%)	20
Mild	12 (6.1%)	15
Moderate	4 (2.0%)	5
Severe	0 (0.0%)	0
Duration		
Total	16 (8.1%)	20
≤ 7 Days	10 (5.1%)	13
8-14 Days	0 (0.0%)	0
15-30 Days	0 (0.0%)	0
> 30 Days	7 (3.5%)	7
Ongoing	0 (0.0%)	0

N: number of participants (from both control and treatment groups) who received initial treatment
n: number of participants with at least one treatment-related AE

Table 3. Treatment-Related AEs with Duration Greater than 30 Days in the Treated Period (JUVÉDERM® VOLUX™ XC Treated Population)

AE	Severity	Time to Onset (Days after last treatment)	Duration (Days)	Outcome
Injection site nodule	Mild	4	176	Recovered/Resolved
Injection site mass	Mild	1	163	Recovered/Resolved
Injection site nodule	Mild	13	48	Recovered/Resolved
Injection site hypersensitivity reaction	Moderate	17	118	Recovered/Resolved
Injection site nodule	Mild	2	106	Recovered/Resolved
Injection site nodule	Moderate	76	80	Recovered/Resolved
Muscle twitching	Mild	8	33	Recovered/Resolved

Table 4. Treatment-Related AEs with Onset Days Greater than 30 Days After Last Treatment (JUVÉDERM® VOLUX™ XC Treated Population)

AE	Severity	Time to Onset (Days after last treatment)	Duration (Days)	Outcome
Injection site swelling	Mild	251	6	Recovered/Resolved
Injection Site nodule	Moderate	76	80	Recovered/Resolved

The incidence of treatment-related AEs in different subgroups is summarized in Table 5. The differences observed in the percentages of participants who experienced treatment-related AEs within the different subgroups were not statistically significant.

Table 5. Treatment-Related AEs by Different Subgroups

Subgroup	Participants (%)	Events
Total Treatment-related AE (N=198)	16 (8.1%)	20
≤ Median Volume (N=103)	12 (11.7%)	15
> Median Volume (N=95)	4 (4.2%)	5
Fitzpatrick Skin Phototype I/II (N=67)	3 (4.5%)	4
Fitzpatrick Skin Phototype III/IV (N=104)	8 (7.7%)	11
Fitzpatrick Skin Phototype V/VI (N=27)	5 (18.5%)	5
Needle Only (N=106)	10 (9.4%)	11
Cannula (N=92)	6 (6.5%)	9
Male (N=22)	1 (4.5%)	1
Female (N=176)	15 (8.5%)	19
≤ Median Age (59) (N=99)	7 (7.1%)	9
> Median Age (59) (N=99)	9 (9.1%)	11

N: number of participants in each group

Other Safety Assessments

Jaw Functional Limitation Scale

Participant assessments on the Jaw Functional Limitation Scale in the JUVÉDERM® VOLUX™ XC Treated and Maintenance Treatment populations showed a median score of zero at baseline and all postbaseline timepoints in overall score and scores for the 3 subscales of mastication, mobility, and verbal and nonverbal communication, indicating that treatment did not affect jaw function.

EI Assessment of Facial Sensation

To determine facial sensitivity, 2-point discrimination and light-touch tests were performed by the Evaluating Investigator. The 2-point discrimination test assessed the distances for which participants indicated they felt 2 distinct points of pressure in the left and right pre-jowl and post-jowl areas. The light touch assessment determined the smallest filament number for which participants felt the presence of the filament in the left and right pre-jowl and post-jowl areas. For both the JUVÉDERM® VOLUX™ XC Treated and Maintenance Treatment populations, the assessments showed that the treatment did not affect facial sensation.

Pronunciation Video Recordings

The pronunciation video recordings were comprised of 5 assessments: pronunciation of individual words, pronunciation of words in a sentence, the number and preciseness of “tuh” iterations performed in 10 seconds, and the naturalness of a spoken paragraph. Participants were video recorded reading a script of words and sentences, and the videos were then assessed by an independent speech and language pathologist. The results showed that JUVÉDERM® VOLUX™ XC treatment did not affect the pronunciation for both the Treated and Maintenance Treatment populations.

Vision Assessments

Snellen visual acuity assessments in the Treated and Maintenance Treatment populations showed that over 90% of participant eyes had the same or better visual acuity at all post-treatment assessments.

Only 2 eyes in one participant from the JUVÉDERM® VOLUX™ XC Treated population and no eyes in the JUVÉDERM® VOLUX™ XC Maintenance Treatment population showed a ≥ 3line worsening in visual acuity at any assessment. These results were not related to intravascular injection and were deemed not clinically significant by the Treating Investigator.

Confrontational visual fields and ocular motility assessments showed that 100% of eyes were full to confrontation and had full duction and version, with no changes from pre-treatment at all assessments.

B. Postmarket Surveillance

The following AEs were received from postmarket surveillance on the use of JUVÉDERM® VOLUX™ XC outside the United States and were not observed in the clinical study; this includes reports received globally from all sources, including scientific journals and voluntary reports. These AEs, with a frequency of 5 events or more, are listed in order of prevalence: swelling, inflammatory reaction, non-inflammatory nodule, pain, inflammatory nodule, abscess, infection, redness, hematoma, neurological symptom, migration, allergic reaction, loss/lack of correction, vascular occlusion, discoloration, minor inflammatory reaction, autoimmune disorder exacerbation, necrosis, itching, scar, cyst, and bleeding.

In many cases, AEs resolved without any treatment. Reported treatments for these events included (in alphabetical order): Antibiotics, anti-inflammatory drugs, analgesics, antiseptics, antihistamines, anti-bacterial drugs, anti-stress and sleeplessness drugs, anti-edema drugs, antithrombotics, anticoagulants, calcium supplements, cold compress, drainage, hyaluronidase, hair growth stimulators, immunosuppressive drugs, immunotherapy, massage, muscle relaxants, NSAIDs (non-steroidal anti-inflammatory drugs), opioids, proton-pump inhibitors, rectal ointment, steroids, surgery, sedatives, ultrasound, and Vitamin B.

Adverse reactions should be reported to Allergan Product Surveillance at 1-877-345-5372.

7. CLINICAL STUDIES

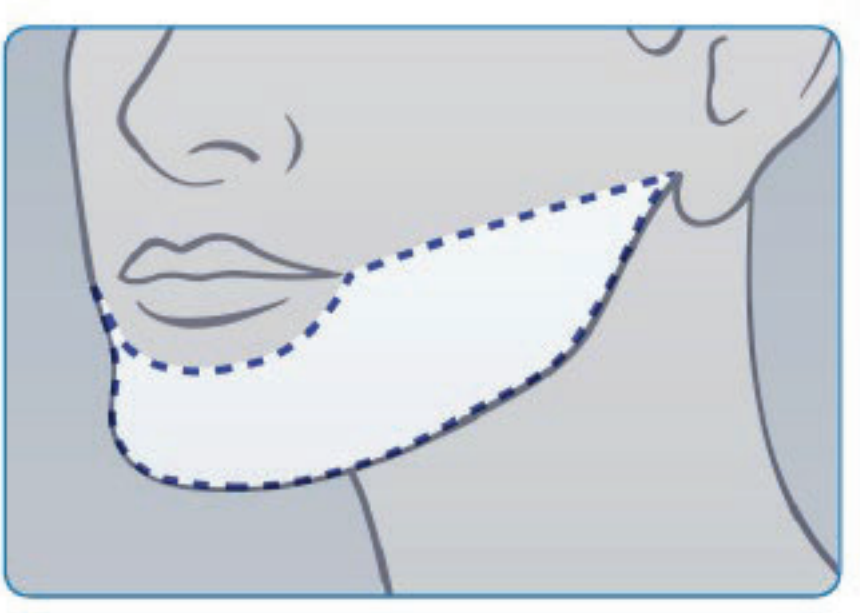
A. Pivotal Study for JUVÉDERM® VOLUX™ XC

Pivotal Study Design

A randomized, multicenter, evaluator-blind, controlled pivotal clinical study was conducted to evaluate the safety and effectiveness of JUVÉDERM® VOLUX™ XC for improving jawline definition. At the outset of the study, 157 participants were randomized to the treatment group and 49 participants were randomized to the delayed-treatment control group.

Treatment group participants underwent treatment with JUVÉDERM® VOLUX™ XC (treatment area is depicted in Figure 1), followed by an optional touch-up treatment 1 month after initial treatment, if deemed necessary to achieve optimal improvement, with follow-up visits at 1, 3, 6, 9, and 12 months after the last treatment. Maintenance treatment was offered to treatment group participants at 12 months, with follow-up visits 1 and 3 months after treatment. Control group participants attended a follow-up visit at 1, 3, and 6 months during the “no treatment” control period. Thereafter, control participants were offered study treatment and optional touch-up with post-treatment follow-up visits at 1, 3, 6, 9, and 12 months after last treatment.

Figure 1. Treatment Area for Jawline Definition



Study Endpoints

The primary effectiveness measure for the study was the blinded Evaluating Investigator's photo assessment of the participant's jawline using the validated 5-point Allergan Loss of Jawline Definition Scale (ALJDS). A responder was defined as a participant with ≥ 1-point improvement in jawline definition compared with the pre-treatment score on the ALJDS for both sides of the jawline. Effectiveness of JUVÉDERM® VOLUX™ XC was demonstrated if the responder rate at 6 months for treatment group participants was significantly greater than that for the control group participants, and the treatment group responder rate was statistically greater than or equal to 50%.

Secondary measures included Evaluating Investigator and participant assessments using the Global Aesthetic Improvement Scale (GAIS) and participant assessment of satisfaction using the validated *Satisfaction with Lower Face and Jawline* module of the FACE-Q® questionnaire.

Other effectiveness measures included participant assessments using the validated *Appraisal of Lines – Marionette* module of the FACE-Q® questionnaire, 3D facial digital imaging analyses for linear depth and volumetric changes of the jawline profile, participant satisfaction with treatment, and participant willingness to recommend treatment.

Participant Demographics

Participant demographics and pretreatment characteristics of the treatment and control groups are presented in Table 6.

Table 6. Participant Demographics and Pretreatment Characteristics

	JUVÉDERM® VOLUX™ XC	Control
	(N = 157) % (n/N)	(N = 49) % (n/N)
Sex		
Female	89.8% (141/157)	79.6% (39/49)
Male	10.2% (16/157)	20.4% (10/49)
Age		
Median	60	57
Range	26-79	37-81
Race		
White	84.1% (132/157)	85.7% (42/49)
Black or African American	13.4% (21/157)	12.2% (6/49)
American Indian or Alaska Native	0.6% (1/157)	0%
Multiple	1.9% (3/157)	2.0% (1/49)
Ethnicity		
Hispanic or Latino	19.7% (31/157)	22.4% (11/49)
Not Hispanic or Latino	80.3% (126/157)	77.6% (38/49)
Fitzpatrick Skin Type		
I/II	34.4% (54/157)	28.6% (14/49)
III/IV	51.6% (81/157)	59.2% (29/49)
V/VI	14.0% (22/157)	12.2% (6/49)
Baseline Allergan Loss of Jawline Definition Scale (ALJDS) Score		
Moderate	21.7% (34/157)	26.5% (13/49)
Severe	72.6% (114/157)	73.5% (36/49)
Extreme	5.7% (9/157)	0%

Treatment Characteristics

Of the 156 treatment group participants, 156 participants received initial treatment, 129 participants received touch-up treatment, and 87 participants received maintenance treatment. Injections were administered using 27-G ½" needles and 25-G 1½" cannulas. The most common injection techniques to achieve optimal results were tunneling, serial puncture, and bolus injections. In the treatment group, the median total injection volume was 4.35 mL at initial treatment, 2.0 mL at touch-up treatment, and 3.0 mL at maintenance treatment The amount used ranged from 1.0 to 9.3 mL for initial and touch-up treatments combined.

Effectiveness Results

Follow-up After Initial Treatment

JUVÉDERM® VOLUX™ XC provided a clinically and statistically significant improvement in jawline definition compared to the no-treatment control group at 6 months after treatment. The primary effectiveness endpoint was met in that the treatment group ALJDS responder rate was significantly greater (p = 0.0001) than the control group responder rate, and the treatment group responder rate was also statistically greater than 50%. Most treatment group participants maintained a clinically significant improvement in jawline definition (≥ 1-point improvement on the ALJDS) through the 12-month follow-up period (Table 7). The ALJDS responder rates at 6 months were analyzed for the different subgroups and any differences observed within the subgroups were not considered statistically significant (Table 8 and Table 9).

Table 7. Effectiveness of JUVÉDERM® VOLUX™ XC for Jawline Definition through 12 Months

Timepoint After Initial/Touch-up Treatment	Treatment Group Responder Rate % (n/N[a])	Control Group Responder Rate % (n/N[a])
1 Month	78.7% (118/150)	22.7% (10/44)
3 Months	76.0% (111/146)	30.4% (14/46)
6 Months	69.9% (102/146)	39.1% (18/46)
9 Months	64.9% (87/134)	N/A[b]
12 Months	61.3% (84/137)	N/A[b]

[a] Number of participants with data at baseline and the specified timepoint.

[b] No control group results were available at Month 9 and Month 12 since the control period ended at Month 6. At Month 6, the control participants were given the option to get the treatment.

Table 8. ALJDS Responder Rates at Month 6 by Sex and FST Subgroups

	Sex		Fitzpatrick Skin Type (FST)		
	Male	Female	I/II	III/IV	V/VI
Treatment Group Responder Rate, % (n/N)	78.6% (11/14)	68.9% (91/132)	62.7% (32/51)	72.0% (54/75)	80.0% (16/20)
95% CI (%)	49.20 - 95.34	60.30 - 76.70	48.08 - 75.87	60.44 - 81.76	56.34 -94.27

Table 9. ALJDS Responder Rates at Month 6 by Route of Administration and Age Subgroups

	Route of Administration		Age	
	Cannula	Needle Only	<= Median Age	> Median Age
Treatment Group Responder Rate, % (n/N)	73.5% (50/68)	66.7% (52/78)	76.1% (54/71)	64.0% (48/75)
95% CI (%)	61.43 - 83.50	55.08 - 76.94	64.46 - 85.39	52.09 - 74.77

The Evaluating Investigators rated the majority of treatment group participants (89.0%, 130/146) as showing improvement in overall aesthetic appearance at 6 months based on the GAIS, with the majority continuing to show improvement through 12 months (79.9%, 107/134).

At 6 months, 88.4% (129/146) of treatment group participants reported improvement in the overall aesthetic appearance of their jawline area on the GAIS. Most treatment group participants continued to report improvement on the GAIS at 12 months (74.3%, 104/140).

Per the *Satisfaction with Lower Face and Jawline* module of the FACE-Q® questionnaire, the majority of treatment group participants (82.3%, 116/141) were satisfied with the appearance of their lower face and jawline through 12 months following treatment with JUVÉDERM® VOLUX™ XC. Within the *Satisfaction with Lower Face and Jawline* module of the FACE-Q® questionnaire, participants reported the following:

- 81.5% (119/146) of participants at 6 months were satisfied with how sculpted (well-defined) their jawline looked compared to 12.2% (19/156) at baseline
- 70.5% (103/146) of participants at 6 months were satisfied with how smooth their lower face looked (i.e., no jowls or folds of fatty skin) compared to 7.7% (12/156) at baseline
- 73.1% (106/145) of participants at 6 months were satisfied with how nice their lower face looked compared to 9.0% (14/156) at baseline

The 3D facial digital analyses showed that treatment group participants had an overall mean change of 4.6 mm in linear depth and overall mean volume change of 6.0 cc at 6 months. These changes in the treatment group participants continued to be observed at 12 months, with an overall mean change of 4.4 mm in linear depth and overall volume change of 6.4 cc. The control group participants had an overall mean change of 2.5 mm in linear depth and overall mean volume change of -2.6 cc at 6 months.

Patient reported outcomes only reported by the treatment group:

The following two measures were only performed on the treatment group and were not collected from the control group as they had not received a treatment during the control period.

The majority of treatment group participants (78.8%, 115/146) reported being satisfied or definitely satisfied with the overall result of treatment at 6 months. At 12 months, 68.1% (96/141) of treatment group participants reported being satisfied or definitely satisfied with the overall result of treatment.

At 6 months, 89.7% (131/146) of treatment group participants were willing to recommend the treatment to a friend, with the majority continuing to recommend treatment at 12 months (87.2%, 123/141).

Follow-up After Maintenance Treatment
Maintenance treatment with JUVÉDERM® VOLUX™ XC was administered to 87 participants. The effectiveness profile after maintenance treatment was similar to that after initial treatment. The ALJDS responder rate after maintenance treatment was 70.3% (45/64) at 1 month and 63.6% (49/77) at 3 months.

8. INSTRUCTIONS FOR USE

A. To Attach Needle or Cannula to Syringe

STEP 1: Remove tip cap
Hold syringe and pull tip cap off the syringe, as shown in Figure A.

FIGURE A

STEP 2: Insert needle
Hold the syringe body and firmly insert the hub of the needle (provided in the JUVÉDERM® VOLUX™ XC package) or cannula into the LUER-LOK® end of the syringe.

STEP 3: Tighten the needle
Tighten the needle or cannula by turning it firmly in a clockwise direction (see Figure B) until it is seated in the proper position, as shown in Figure C.

NOTE: If the position of the needle or cannula cap is as shown in Figure D, it is not attached correctly. Continue to tighten until the needle is seated in the proper position.

FIGURE B

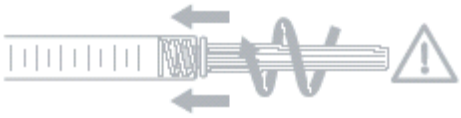


FIGURE C

FIGURE D

STEP 4: Remove the needle cap
Hold the syringe body in one hand and the needle or cannula cap in the other. Without twisting, pull in opposite directions to remove the needle or cannula cap, as shown in Figure E.

FIGURE E

B. Health Care Professional Instructions

1. JUVÉDERM® VOLUX™ XC injectable gel is a highly crosslinked, smooth gel formulation that can be injected using a fine gauge needle (e.g., 27-G) or cannula (e.g., 25-G) to improve jawline definition.

2. The TSK STERiGLIDE™ 25-G 1½" cannula was used in the clinical trial and is the only cannula recommended for use with JUVÉDERM® VOLUX™ XC.

3. Educational resources are available through the Allergan Medical Institute, which provides training in facial anatomy and vasculature, effective patient assessment, safe injection techniques, and identification and management of potential AEs, including vascular complications. Health care practitioners may contact Allergan for educational and training resources.

4. Prior to treatment, the patient's medical history should be obtained, and the patient should be fully apprised of the indications, contraindications, warnings, precautions, treatment responses, adverse reactions, and method of administration. Patients also should be advised that supplemental touch-up injections may be required to achieve and maintain optimal effect.

5. Before and after treatment, health care practitioners are encouraged to conduct vision assessments, including visual acuity, extraocular motility, and visual field testing.

6. Health care practitioners are encouraged to be prepared with the following in the event of an intravascular injection:

    - Ensuring supplies are immediately available, as recommended by the American Society for Dermatologic Surgery guidelines[1]
    - Identifying a local ophthalmologist or ophthalmology subspecialist to be available in the event of an ophthalmic AE related to soft tissue filler injection
    - Conducting a basic neurologic examination in the event of an ophthalmic AE due to the association of such events with central nervous system deficits

7. The patient's treatment goals should be characterized by improvement of jawline definition. Pretreatment photographs are recommended.

8. Supplementary anesthesia may be used for additional pain management during and after injection.

9. After ensuring that the patient has thoroughly washed the treatment area with soap and water, the area should be prepped with alcohol or other antiseptic. Prior to injecting, depress the plunger rod until the product flows out of the needle.

10. After insertion of the needle/cannula, and just before injection, retract the plunger rod to slightly aspirate and verify the needle/cannula 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.

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[1]Jones, Derek; Fitzgerald, Rebecca; Cox, Sue Ellen; et al. Preventing and Treating Adverse Events of Injectable Fillers: Evidence-Based Recommendations from the American Society for Dermatologic Surgery Multidisciplinary Task Force, Dermatologic Surgery: February 2021 - Volume 47 - Issue 2 - p 214-226

11. 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.

12. The injection technique may vary with regard to the angle and orientation of the bevel, injection depth, and the quantity administered. Tunneling, serial puncture, and bolus injections are the most common technique used to achieve optimal results. Injecting the product too superficially may result in visible lumps and/or discoloration.

13. Inject JUVÉDERM® VOLUX™ XC by applying even pressure on the plunger rod. It is important that the injection be stopped before the needle/cannula is pulled out of the skin to prevent material from leaking out or being placed too superficially in the skin.

14. If the needle/cannula is blocked, do not increase the pressure on the plunger rod. Instead, stop the injection and replace the needle/cannula.

15. The typical volume to achieve optimal improvement in jawline definition is 6.8 mL, which was the median total volume injected for initial and touch-up treatments combined and may vary depending on the goals the patient wishes to achieve. Injection volumes after maintenance treatment tended to be lower, with the typical injection volume to maintain optimal effect being 3.0 mL.

16. Inject to 100% of the desired correction. Do not over-inject. The degree and duration of the effect depend on the character of the area being 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 treat.

17. 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]

18. When injection is completed, the treated site should be gently massaged so that it conforms to the contour of the surrounding tissues. If over-injection occurs, massage the area with your fingers or against the underlying superficial bone to obtain optimal results.

19. With patients who have localized swelling, the degree of effect is sometimes difficult to judge at the time of treatment. In this case, it is better to invite the patient back to the office for a touch-up treatment.

20. After the initial treatment, an additional treatment may be necessary to achieve the desired level of effect. 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.

21. Patients may experience mild to moderate ISRs after treatment, which typically resolve within 2 weeks. Ice using gentle pressure for a brief period following treatment to minimize swelling and reduce pain.

22. The health care professional should instruct the patient to promptly report to her/him regarding any evidence of problems possibly associated with the use of JUVÉDERM® VOLUX™ XC.

C. Patient Instructions

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

- Avoid applying makeup for 12 hours after treatment. 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, notify Allergan Product Surveillance at 1-877-345-5372.

9. HOW SUPPLIED

JUVÉDERM® VOLUX™ XC injectable gel is supplied in individual treatment syringes with 27-G needles for single-patient use and ready for injection (implantation). The TSK STERiGLIDE™ 25-G 1½" cannula is not supplied with JUVÉDERM® VOLUX™ XC but is available for purchase through Allergan. The volume in each syringe is as stated on the syringe label and on the carton. The contents of the syringe are sterile and non-pyrogenic. Do not resterilize. Do not use if package is open or damaged.

10. SHELF LIFE AND STORAGE

JUVÉDERM® VOLUX™ XC injectable gel should not be used after the expiration date printed on the label.

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

JUVÉDERM® VOLUX™ XC injectable gel has a clear appearance. In the event that a syringe contains material that is not a clear, colorless gel without visible particulates, do not use the syringe; notify Allergan Product Surveillance immediately at 1-877-345-5372.

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

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