JUVÉDERM®
VOLLURE™ 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® VOLLURE™ 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 17.5 mg/mL and 0.3% w/w lidocaine in a physiologic buffer.

2. INTENDED USE/INDICATIONS

JUVÉDERM® VOLLURE™ XC injectable gel is indicated for injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (such as nasolabial folds) in adults over the age of 21.

3. CONTRAINDICATIONS

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

4. WARNINGS

- JUVÉDERM® VOLLURE™ XC injectable gel must not be injected into blood vessels. Introduction of the product 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soft-tissue fillers; for example, after insertion of the needle, and just before injection, the plunger rod can be withdrawn slightly to aspirate and verify the needle is not intravascular, inject the product slowly, and apply the least amount of pressure necessary.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 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 #13).
- 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® VOLLURE™ 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 risks of potential complications, this product should only be used by health care practitioners who have appropriate training, experience, and who are knowledgeable about the anatomy at and around the site of injection.
- 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 (132 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 facial wrinkles and folds have not been established in controlled clinical studies.
- As with all transcutaneous procedures, dermal filler implantation carries a risk of infection. Standard precautions associated with injectable materials should be followed.
- JUVÉDERM® VOLLURE™ 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, 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® VOLLURE™ 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® VOLLURE™ 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® VOLLURE™ 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.
- If laser treatment, chemical peeling, or any other procedure based on active dermal response is considered after treatment with JUVÉDERM® VOLLURE™ 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® VOLLURE™ XC

In a multicenter, randomized, double-blind, within-subject controlled clinical trial to evaluate the safety and effectiveness of JUVÉDERM® VOLLURE™ XC versus the control (an FDA-approved cross-linked hyaluronic acid dermal filler which is legally marketed with similar indications) for the correction of moderate to severe nasolabial folds (NLFs), 123 subjects received treatment with JUVÉDERM® VOLLURE™ XC in 1 NLF and control in the other NLF. Touch-up treatment, if needed to achieve optimal correction, occurred approximately 30 days after the initial injection. Subjects were allowed an asymmetry correction treatment between 9 and 15 months after the initial treatment and a repeat treatment 12 to 18 months after initial treatment.

Subjects used preprinted diary forms to record specific signs and symptoms of injection site responses (ISRs) experienced during the 30 days following the initial treatment, touch-up treatment (if performed), asymmetry correction (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 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 subjects who completed post-treatment diary forms after initial treatment are summarized in Table 1 and Table 2, respectively. Subjects reported the severity of their ISRs as mild, moderate, or severe. Most of the individual ISRs were mild to moderate in severity and lasted less than 1 week after initial treatment, asymmetry correction, and repeat treatment with JUVÉDERM® VOLLURE™ XC; some of the ISRs lasted 8-30 days. The most common ISRs that lasted for 8-30 days after initial treatment were: firmness (42.6%, 46/108), lumps/bumps (36.0%, 36/100), and discoloration (24.2%, 8/33). For most of the individual ISR types, subjects reported significantly fewer severe ISRs for JUVÉDERM® VOLLURE™ XC than for the control product. The incidence of ISRs reported after the asymmetry correction/repeat treatment was generally lower than that reported after initial treatment (Table 3).

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

Injection Site Response	JUVÉDERM® VOLLURE™ XC				Control			
	Total % (n/N[a])	Mild[b] % (n/N)	Moderate[b] % (n/N)	Severe[b] % (n/N)	Total % (n/N[a])	Mild[b] % (n/N)	Moderate[b] % (n/N)	Severe[b] % (n/N)
Firmness	88.5% (108/122)	30.6% (33/108)	50.0% (54/108)	19.4% (21/108)	92.6% (113/122)	14.2% (16/113)	43.4% (49/113)	42.5% (48/113)
Swelling	86.1% (105/122)	42.9% (45/105)	40.0% (42/105)	17.1% (18/105)	92.6% (113/122)	17.7% (20/113)	38.9% (44/113)	43.4% (49/113)
Tenderness to Touch	84.4% (103/122)	52.4% (54/103)	31.1% (32/103)	16.5% (17/103)	94.3% (115/122)	28.7% (33/115)	37.4% (43/115)	33.9% (39/115)
Lumps/Bumps	82.0% (100/122)	47.0% (47/100)	39.0% (39/100)	14.0% (14/100)	90.0% (110/122)	27.3% (30/110)	33.6% (37/110)	39.1% (43/110)
Redness	73.8% (90/122)	43.3% (39/90)	41.1% (37/90)	15.6% (14/90)	86.9% (106/122)	34.0% (36/106)	44.3% (47/106)	21.7% (23/106)
Pain After Injection	72.1% (88/122)	51.1% (45/88)	33.0% (29/88)	15.9% (14/88)	79.5% (97/122)	32.0% (31/97)	35.1% (34/97)	33.0% (32/97)
Bruising	56.6% (69/122)	43.5% (30/69)	31.9% (22/69)	24.6% (17/69)	59.0% (72/122)	30.6% (22/72)	38.9% (28/72)	30.6% (22/72)
Itching	31.1% (38/122)	73.7% (28/38)	7.9% (3/38)	18.4% (7/38)	45.1% (55/122)	61.8% (34/55)	23.6% (13/55)	14.5% (8/55)
Discoloration	27.0% (33/122)	54.5% (18/33)	30.3% (10/33)	15.2% (5/33)	29.5% (36/122)	44.4% (16/36)	36.1% (13/36)	19.4% (7/36)

[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 injection site response.

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

Injection Site Response	JUVÉDERM® VOLLURE™ XC					Control				
	Total % (n/N[a])	1-3 Days[b] % (n/N)	4-7 Days[b] % (n/N)	8-14 Days[b] % (n/N)	15-30 Days[b] % (n/N)	Total % (n/N[a])	1-3 Days[b] % (n/N)	4-7 Days[b] % (n/N)	8-14 Days[b] % (n/N)	15-30 Days[b] % (n/N)
Firmness	88.5% (108/122)	29.6% (32/108)	27.8% (30/108)	20.4% (22/108)	22.2% (24/108)	92.6% (113/122)	21.2% (24/113)	30.1% (34/113)	23.0% (26/113)	25.7% (29/113)
Swelling	86.1% (105/122)	55.2% (58/105)	23.8% (25/105)	19.0% (20/105)	1.9% (2/105)	92.6% (113/122)	39.8% (45/113)	34.5% (39/113)	18.6% (21/113)	7.1% (8/113)
Tenderness to Touch	84.4% (103/122)	62.1% (64/103)	23.3% (24/103)	10.7% (11/103)	3.9% (4/103)	94.3% (115/122)	45.2% (52/115)	33.9% (39/115)	15.7% (18/115)	5.2% (6/115)
Lumps/Bumps	82.0% (100/122)	40.0% (40/100)	24.0% (24/100)	19.0% (19/100)	17.0% (17/100)	90.2% (110/122)	32.7% (36/110)	26.4% (29/110)	17.3% (19/110)	23.6% (26/110)
Redness	73.8% (90/122)	58.9% (53/90)	26.7% (24/90)	10.0% (9/90)	4.4% (4/90)	86.9% (106/122)	57.5% (61/106)	28.3% (30/106)	9.4% (10/106)	4.7% (5/106)
Pain After Injection	72.1% (88/122)	80.7% (71/88)	8.0% (7/88)	10.2% (9/88)	1.1% (1/88)	79.5% (97/122)	71.1% (69/97)	19.6% (19/97)	6.2% (6/97)	3.1% (3/97)
Bruising	56.6% (69/122)	55.1% (38/69)	31.9% (22/69)	8.7% (6/69)	4.3% (3/69)	59.0% (72/122)	47.2% (34/72)	34.7% (25/72)	9.7% (7/72)	8.3% (6/72)
Itching	31.1% (38/122)	71.1% (27/38)	15.8% (6/38)	10.5% (4/38)	2.6% (1/38)	45.1% (55/122)	63.6% (35/55)	21.8% (12/55)	10.9% (6/55)	3.6% (2/55)
Discoloration	27.0% (33/122)	72.7% (24/33)	3.0% (1/33)	15.2% (5/33)	9.1% (3/33)	29.5% (36/122)	61.1% (22/36)	19.4% (7/36)	13.9% (5/36)	5.6% (2/36)

[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. Severity and Duration of Injection Site Responses after Asymmetry Correction/Repeat Treatment Occurring in > 5% of Subjects in the JUVÉDERM® VOLLURE™ XC Group

Injection Site Response	Incidence (n/N[a])	Severity[b]			Duration[c]			
		Mild	Moderate	Severe	1-3 Days	4-7 Days	8-14 Days	15-30 Days
Firmness	69.2% (63/91)	22.2% (14/63)	47.6% (30/63)	30.2% (19/63)	11.1% (7/63)	28.6% (18/63)	22.2% (14/63)	38.1% (24/63)
Swelling	67.0% (61/91)	36.1% (22/61)	47.5% (29/61)	16.4% (10/61)	29.5% (18/61)	41.0% (28/61)	13.1% (8/61)	16.4% (10/61)
Tenderness to Touch	64.8% (59/91)	39.0% (23/59)	44.1% (26/59)	16.9% (10/59)	40.7% (24/59)	33.9% (20/59)	10.2% (6/59)	15.3% (9/59)
Redness	62.6% (57/91)	45.6% (26/57)	42.1% (24/57)	12.3% (7/57)	42.1% (24/57)	33.3% (19/57)	10.5% (6/57)	14.0% (8/57)
Lumps/Bumps	58.2% (53/91)	28.3% (15/53)	52.8% (28/53)	18.9% (10/53)	20.8% (11/53)	34.0% (18/53)	3.8% (2/53)	41.5% (22/53)
Pain After Injection	52.7% (48/91)	39.6% (19/48)	50.0% (24/48)	10.4% (5/48)	54.2% (26/48)	29.2% (14/48)	6.3% (3/48)	10.4% (5/48)
Bruising	44.0% (40/91)	45.0% (18/40)	32.5% (13/40)	22.5% (9/40)	22.5% (9/40)	45.0% (18/40)	15.0% (6/40)	17.5% (7/40)
Itching	20.9% (19/91)	68.4% (13/19)	26.3% (5/19)	5.3% (1/19)	63.2% (12/19)	15.8% (3/19)	10.5% (2/19)	10.5% (2/19)
Discoloration	20.9% (19/91)	63.2% (12/19)	31.6% (6/19)	5.3% (1/19)	47.4% (9/19)	21.1% (4/19)	5.3% (1/19)	26.3% (5/19)

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

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

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

ISRs that were ongoing at the end of the 30-day diary were considered adverse events (AEs). AEs were also reported by the Evaluating Investigator (EI) at follow-up visits. After initial/touch-up treatment, a total of 55 AEs were reported in 23.6% (29/123) of the NLFs treated with JUVÉDERM® VOLLURE™ XC, and 52 AEs were reported in 22.0% (27/123) of the NLFs treated with control. For JUVÉDERM® VOLLURE™ XC, AEs reported in > 5% of NLFs after initial/touch-up treatment are listed in Table 4; the control product had similar rates of AEs.

Table 4. AEs After Initial/Touch-up Treatment Occurring in > 5% of NLFs

Adverse Event	JUVÉDERM® VOLLURE™ XC	Control
	% (n/N)	% (n/N)
Injection Site Induration	10.6% (13/123)	8.9% (11/123)
Injection Site Mass	8.1% (10/123)	7.3% (9/123)
Injection Site Swelling	7.3% (9/123)	9.8% (12/123)

AEs after initial/touch-up treatment occurring in ≤ 5% of NLFs included injection site bruising, erythema, pain, discoloration, pruritus, reaction, and facial asymmetry.

In general, AEs at the NLFs were mild or moderate in severity for both products, with 49.1% (27/55) mild and 29.1% (16/55) moderate for JUVÉDERM® VOLLURE™ XC. Some AEs at the NLFs were severe (21.8%, 12/55). The majority of the AEs at the NLFs required no action to be taken (94.5%, 52/55) and resolved without sequelae (98.2%, 54/55). AEs at the NLFs after initial/touch-up treatment that required treatment included swelling treated with antihistamines and NSAIDs, injection site erythema treated with antibiotics, and skin mass that was biopsied and treated with steroids. One subject had mild injection site swelling that occurred after initial/touch-up treatment and was ongoing at the end of the study. This AE did not require treatment.

Three adverse events at the JUVÉDERM® VOLLURE™ XC NLFs occurred weeks to months after the injection procedure. These events included mild swelling, moderate skin mass, and severe itching. Swelling was treated with fexofenadine hydrochloride and ibuprofen, the skin mass was treated with triamcinolone, and the itching did not require any treatment. All 3 events resolved without sequelae.

All asymmetry corrections (if needed) and repeat treatments were performed with JUVÉDERM® VOLLURE™ XC. In general, AEs at the NLFs after asymmetry correction/repeat treatment were similar to those after initial/touch-up treatment. Within the JUVÉDERM® VOLLURE™ XC randomization group, after asymmetry correction/repeat treatment, 20 AEs were reported in 10.8% (10/93) of NLFs, with the most common AE being injection site induration (firmness) in 7.5% (7/93) of NLFs. All other AEs occurred in < 5% of NLFs and included injection site mass, pain, bruising, erythema, discoloration, and swelling. A majority of the AEs after asymmetry correction/repeat treatment in NLFs originally treated with JUVÉDERM® VOLLURE™ XC were mild (20.0%, 4/20) or moderate (45.0%, 9/20) in severity, required no action to be taken (100%, 20/20), and resolved without sequelae (65.0%, 13/20). Some AEs after asymmetry correction/repeat treatment were severe (35.0%, 7/20). After asymmetry correction/repeat treatment, seven AEs were ongoing at the end of the study and included injection site induration, mass, swelling, bruising, and discoloration. These AEs did not require treatment.

There were no serious adverse events related to the treatment reported in the study.

On the validated *Recovery Early Symptoms* module of the FACE-Q® questionnaire, the majority of subjects reported feeling not at all or only a little bothered by all 17 symptoms 3 days after initial treatment with JUVÉDERM® VOLLURE™ XC. Subjects reported less discomfort (9.9% for JUVÉDERM® VOLLURE™ XC vs 25.7% for control), tenderness (11.5% vs 30.5%), soreness (10.8% vs 28.9%), and swelling (15.1% vs 40.0%) after treatment with JUVÉDERM® VOLLURE™ XC compared to treatment with the control. For all other symptoms (bruising, tightness, numbness, stinging, burning, throbbing, tingling, itching, tired, feverish, lightheaded, headaches, and pain), subjects reported similar results between JUVÉDERM® VOLLURE™ XC and control.

B. European Clinical Study

A prospective, randomized, multicenter study was conducted with 70 subjects treated with JUVÉDERM® VOLLURE™ XC for correction of moderate to severe nasolabial folds. Enrolled subjects exhibited moderate to severe NLF severity scores on the validated 5-point photonumeric NLFSS, the same scale as that used for the US pivotal study discussed above. Subjects received treatment with JUVÉDERM® VOLLURE™ XC in both NLFs and received a touch-up treatment at Day 14 if optimal correction was not achieved after the initial treatment. Subjects were followed for up to 12 months after the last treatment, returning to the investigational site at regular intervals (Months 1, 9, and 12) throughout the study for safety and effectiveness evaluations. All subjects in the study had the option to receive a repeat treatment at the Month 12 visit; the subjects were followed for up to 1 month after the repeat treatment.

Subjects were monitored throughout the study for any adverse events (AEs) by the investigator. AEs that were related to the study device/procedure were recorded. Expected AEs, listed in the Directions for Use (DFU), were only reported as AEs if the events were assessed to be more severe or more prolonged than routinely observed. After repeat treatment, subjects completed a 30-day safety diary to record the severity and duration of any injection site responses (ISRs). No device/procedure-related AE was observed after the initial/touch-up treatment. Forty-one subjects completed the 30-day safety diary after repeat treatment. The most frequently reported ISRs in the diaries were swelling (87.8%, 36/41), firmness (80.5%, 33/41), and tenderness to touch (78.0%, 32/41). The majority of ISRs were mild or moderate and resolved within 3 days (Table 5). One device/procedure-related AE was observed after repeat treatment. The subject experienced redness around the mouth, swelling, and lower sensibility requiring treatment with corticoid ointment; the AE symptoms resolved in 51 days.

Table 5. Injection Site Responses by Severity and Duration after Repeat Treatment with JUVÉDERM® VOLLURE™ XC Occurring in > 5% of Subjects from European Study

ISR	Incidence (n/N[a])	Severity[b]			Duration[c]			
		Mild	Moderate	Severe	1-3 Days	4-7 Days	8-14 Days	15-30 Days
Swelling	87.8% (36/41)	55.6% (20/36)	27.8% (10/36)	16.7% (6/36)	86.1% (31/36)	11.1% (4/36)	2.8% (1/36)	0% (0/36)
Firmness	80.5% (33/41)	57.6% (19/33)	30.3% (10/33)	12.1% (4/33)	75.8% (25/33)	15.2% (5/33)	9.1% (3/33)	0% (0/33)
Tenderness	78.0% (32/41)	65.6% (21/32)	25.0% (8/32)	9.4% (3/32)	87.5% (28/32)	12.5% (4/32)	0% (0/32)	0% (0/32)
Redness	58.5% (24/41)	66.7% (16/24)	29.2% (7/24)	4.2% (1/24)	83.3% (20/24)	16.7% (4/24)	0% (0/24)	0% (0/24)
Lumps/Bumps	56.1% (23/41)	47.8% (11/23)	30.4% (7/23)	21.7% (5/23)	56.5% (13/23)	26.1% (6/23)	8.7% (2/23)	8.7% (2/23)
Bruising	53.7% (22/41)	40.9% (9/22)	31.8% (7/22)	27.3% (6/22)	40.9% (9/22)	50.0% (11/22)	9.1% (2/22)	0% (0/22)
Pain	51.2% (21/41)	76.2% (16/21)	14.3% (3/21)	9.5% (2/21)	95.2% (20/21)	4.8% (1/21)	0% (0/21)	0% (0/21)
Itching	12.2% (5/41)	60.0% (3/5)	40.0% (2/5)	0% (0/5)	80.0% (4/5)	0% (0/5)	0% (0/5)	20.0% (1/5)
Discoloration	4.9% (2/41)	100% (2/2)	0% (0/2)	0% (0/2)	50.0% (1/2)	0% (0/2)	0% (0/2)	50.0% (1/2)

[a] N denotes the number of subjects who recorded in the diaries.

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

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

C. Postmarket Surveillance

JUVÉDERM® VOLLURE™ XC has been marketed in the United States since 2017. Outside the United States, JUVÉDERM® VOLLURE™ XC is known as JUVÉDERM® VOLIFT® with Lidocaine and has been marketed since 2011.

The following AEs were received from postmarket surveillance on the use of JUVÉDERM® VOLLURE™ XC with a frequency of 5 events or more and were not observed in the clinical study; this includes reports received globally from all sources including

scientific journals and voluntary reports. All AEs obtained through postmarket surveillance are listed in order of number of reports received: edema, non-inflammatory nodule, inflammatory reaction, pain, inflammatory nodule/granuloma, lack/loss of correction, allergic reaction, hematoma, unsatisfactory result, vascular occlusion, skin discoloration, infection, anxiety, device migration, neurological symptoms such as increase or decrease in sensation, dermatitis, varied injuries, blister, abscess, flu-like symptoms, angioedema, headache, drainage, necrosis, herpes, dry skin, overcorrection, scarring, vision abnormalities, bleeding, acne, cysts, malaise, lymphadenopathy, autoimmune disorder exacerbation, dizziness, telangiectasia, extrusion, calcification, depression, syncope, and anaphylactic reaction. In addition, 1 report of stroke after injections in an unspecified area with multiple dermal fillers were reported.

In many cases the symptoms resolved without any treatment. Reported treatments for these events included the use of (in alphabetical order): analgesics, anesthetics, anti-allergy medications, antibiotics, antifungal, antihistamines, anti-inflammatory medications, antiviral, arnica, aspiration, ACE inhibitors, drainage, hyaluronidase, hyperbaric oxygen treatment, ice, laser treatment, massage, nitrates, oral and topical corticosteroids, petroleum jelly, ultrasound therapy, vasodilators, and warm compress. Outcomes for these reported adverse events ranged from resolved to ongoing at the time of last contact.

Vision abnormalities have been reported following injection of JUVÉDERM® VOLLURE™ XC into the cheek, chin, nasolabial folds, oral commissures, pre-jowl area, lips, mouth, and/or periorbital area, with a time to onset ranging from immediate to 2 months following injection. Reported treatments include antibiotics, anti-inflammatories, hyaluronidase, massage, steroids, warm compress, and vasodilators. Outcomes ranged from resolved to ongoing at the time of last contact (see WARNINGS section).

Delayed-onset inflammation near the site of dermal filler injections is one of the known adverse events associated with dermal fillers. Cases of delayed-onset inflammation have been reported to occur at the dermal filler treatment site following viral or bacterial illnesses or infections, vaccinations, or dental procedures. Typically, the reported inflammation was responsive to treatment or resolved on its own.

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

7. CLINICAL STUDIES

A. Pivotal Study for JUVÉDERM® VOLLURE™ XC

Pivotal Study Design

A multicenter, randomized, within-subject controlled, double-blind pivotal clinical trial was conducted to evaluate the safety and effectiveness of JUVÉDERM® VOLLURE™ XC versus control for the correction of moderate to severe nasolabial folds (NLFs). Subjects were randomized to undergo treatment with JUVÉDERM® VOLLURE™ XC in 1 NLF and with control in the other NLF. Subjects returned on days 3 and 14 after treatment for safety and effectiveness assessments. Approximately 30 days after the initial treatment, subjects underwent an optional touch-up treatment, if deemed necessary, to achieve optimal correction. The primary effectiveness endpoint was at 6 months after subjects' last treatment (initial or touch-up, if performed).

The follow-up period consisted of safety and effectiveness follow-up visits at 1, 3, 6, 9, 12, 15, and 18 months after the last treatment. After the month 9, 12, and 15 visits, subjects could request a single, unilateral treatment to correct clinically significant asymmetry (defined as at least 1-point difference in NLF severity between NLFs, based on the EI assessment). The Treating Investigator treated asymmetry using JUVÉDERM® VOLLURE™ XC in the more severe NLF only, regardless of which treatment was originally used in that NLF. Subjects completed another 30-day safety diary after asymmetry correction; repeated the days 3, 14, and 30 follow-up visits; and continued with any remaining study follow-up visits. After the month 12 and 15 visits, subjects were eligible to receive a repeat treatment with JUVÉDERM® VOLLURE™ XC if the NLF severity for both NLFs had returned to baseline or worse, based on the EI's assessment. All subjects were eligible for a repeat treatment at month 18, with follow-up for 1 month after repeat treatment; at which time, all subjects completed the study.

Study Endpoints

The primary effectiveness measure was the EI's live assessment of NLF severity using the validated 5-point photonumeric Nasolabial Fold Severity Scale (NLFSS). A responder was defined as a subject with ≥ 1-point improvement on the NLFSS since baseline. The primary effectiveness endpoints were to demonstrate that the observed responder rate for JUVÉDERM® VOLLURE™ XC was statistically greater than 50% at 6 months, and to demonstrate non-inferiority of JUVÉDERM® VOLLURE™ XC relative to control in terms of the mean of difference in improvement (reduction) in NLF severity at month 6.

The secondary effectiveness endpoints included observed NLFSS responder rates based on EI's assessment of NLF severity and subject's assessment of facial appearance using the validated *Appraisal of Nasolabial Folds* module of the FACE-Q® questionnaire at 12 months.

Other effectiveness measures included assessment of primary and secondary effectiveness variables at other time points, EI's assessment of product smoothness and natural look of the NLF region, subjects' satisfaction with treatment, subject's evaluation of NLF preference for overall treatment outcome, subject's desire for repeat treatment, and Treating Investigator's evaluation of injection ease and product moldability.

Safety endpoints included incidence rates, severity and duration of ISRs and AEs, subjects' assessment of procedural pain, and the *Recovery Early Symptoms* module of the FACE-Q® questionnaire.

Subject Demographics

Subject demographics and pretreatment characteristics are presented in Table 4.

Table 4. Subject Demographics and Pretreatment Characteristics (N = 123)

Characteristic	Attribute	Total (N = 123)
		n (%)
Age (years)	Median	54
	Range	33-83
Gender	Female	117 (95.1%)
	Male	6 (4.9%)
Race	White	91 (74.0%)
	Black or African American	26 (21.1%)
	Asian	3 (2.4%)
	American Indian/Alaska Native	2 (1.6%)
	Other	1 (0.8%)
Fitzpatrick Skin Phototype	I	14 (11.4%)
	II	27 (22.0%)
	III	31 (25.2%)
	IV	20 (16.3%)
	V	18 (14.6%)
	VI	13 (10.6%)
Mean Baseline NLF Severity Score[a]	JUVÉDERM® VOLLURE™ XC	2.6
	Control	2.6

[a] NLF severity was ranked on a 5-point scale from None (0) to Extreme (4).

Treatment Characteristics

A total of 123 subjects were randomized and received treatment with JUVÉDERM® VOLLURE™ XC and control. Of the 123 treated, 63 subjects received touch-up treatment, 45 received asymmetry correction, and 85 received repeat treatment. Multiple injection techniques were used to achieve optimal results, with the most common being serial puncture, tunneling, and fanning. Most of the injections were in the intradermal plane. Subjects received a median volume of 1.7 mL per NLF (JUVÉDERM® VOLLURE™ XC or control) during the initial and touch-up treatments combined. Subjects received a median volume of 0.6 mL of JUVÉDERM® VOLLURE™ XC per NLF during the repeat treatment.

Effectiveness Results

Follow-up After Initial Treatment

The co-primary effectiveness endpoints in this study were met. The mean NLFSS score at baseline for the subjects was 2.6; the score improved to 1.2 for JUVÉDERM® VOLLURE™ XC and 1.3 for control, as assessed by the EI at month 6 after the last study treatment. The responder rate at month 6 was 93.2% (109/117) for the NLFs treated with JUVÉDERM® VOLLURE™ XC compared to 86.3% (101/117) for NLFs treated with control.

Throughout the follow-up period, JUVÉDERM® VOLLURE™ XC continued to provide clinically significant improvement in NLF severity (≥ 1-point improvement on the NLFSS), with a majority of the NLFs treated with JUVÉDERM® VOLLURE™ XC demonstrating improvement through 18 months (Table 5).

Table 5. Effectiveness Results Through 18 Months

Time Point After Initial/Touch-up Treatment	JUVÉDERM® VOLLURE™ XC
	% (n/N)
6 Months	93.2% (109/117)
9 Months	84.6% (99/117)
12 Months	57.5% (65/113)
15 Months	61.7% (50/81)
18 Months	59.4% (57/96)

At 6 months, 95.7% (112/117) of subjects reported improvement in their JUVÉDERM® VOLLURE™ XC treated NLFs, based on the *Appraisal of Nasolabial Folds* module of the FACE-Q® questionnaire, with a mean score increasing from 32.1 at baseline to 72.8. At 18 months, 61.8% (55/89) of subjects reported improvement in their JUVÉDERM® VOLLURE™ XC treated NLFs over baseline, with a mean score of 50.3. These mean scores indicate that subjects treated with JUVÉDERM® VOLLURE™ XC reported being less bothered with the depth of their NLF, with the look of their NLF when relaxed and when smiling, with how old their NLF makes them look, and with how their NLF looks compared with other people their age, when compared with their pretreatment assessments of these questions in the FACE-Q® module.

Subjects reported a high level of satisfaction with JUVÉDERM® VOLLURE™ XC treated NLF throughout the study, with 75.2% (91/121) of the subjects very satisfied (score of 7-10 on a 0-to-10 scale) with JUVÉDERM® VOLLURE™ XC at day 3 compared to 61.1% (74/121) for control. A majority of the subjects (67.8%, 40/59) continued to be very satisfied with the results of their JUVÉDERM® VOLLURE™ XC treated NLF at the month 18 visit.

JUVÉDERM® VOLLURE™ XC was found to be effective in all Fitzpatrick Skin Phototypes, for males and females, and across the studied age range.

Follow-up After Repeat Treatment

Repeat treatment with JUVÉDERM® VOLLURE™ XC was administered to 85 subjects. 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 94.0% (79/84) of subjects showing a ≥ 1-point improvement in NLF severity, based on the EI assessment. More than 90% of subjects (79/84) in the JUVÉDERM® VOLLURE™ XC randomization group were very satisfied with their NLF 1 month after the repeat treatment.

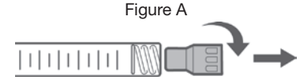
8. INSTRUCTIONS FOR USE

A. To Attach Needle to Syringe

STEP 1: Remove tip cap

Hold syringe and pull tip cap off the syringe, as shown in Figure A.

Figure A



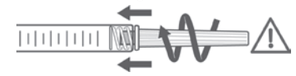
STEP 2: Insert needle

Hold the syringe body and firmly insert the hub of the needle (provided in the JUVÉDERM® VOLLURE™ XC package) into the LUER-LOK® end of the syringe.

STEP 3: Tighten the needle

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

Figure B



NOTE: If the position of the needle 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 C

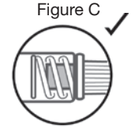


Figure D

STEP 4: Remove the needle cap

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

Figure E

B. Health Care Professional Instructions

1. JUVÉDERM® VOLLURE™ XC injectable gel is a smooth, cross-linked, cohesive, injectable gel formulation, injected using a 30-G ½" needle into the mid to deep dermis for versatility in the correction of moderate to severe facial wrinkles and folds (such as nasolabial folds).
2. 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" implantations may be required to achieve and maintain maximum correction.
3. The patient's soft-tissue deficiencies should be characterized with regard to etiology, distensibility, stress at the site, and depth of lesion. Pretreatment photographs are recommended.
4. Supplementary anesthesia may be used for additional pain management during and after injection.

5. 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.
6. After insertion of the needle, and just before injection, the plunger rod should be withdrawn slightly to aspirate and verify the needle is not intravascular.
7. 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.
8. The injection technique may vary with regard to the angle and orientation of the bevel, the depth of injection, and the quantity administered. Different techniques such as serial puncture, tunneling, fanning, cross-hatching or a combination has been used to achieve optimal results. Injecting the product too superficially may result in visible lumps and/or discoloration.
9. Inject JUVÉDERM® VOLLURE™ XC by applying even pressure on the plunger rod while slowly moving the needle. 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. The wrinkle should be lifted and reduced by the end of the injection.
10. If the needle is blocked, do not increase the pressure on the plunger rod. Instead, stop the injection and replace the needle.
11. The typical total volume to achieve optimal correction of moderate to severe nasolabial folds is 1.7 mL per treatment site. To maintain optimal correction, approximately one-third of the volume per treatment site is needed at repeat treatment.
12. 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 volume and technique. Markedly indurated defects may be difficult to correct.
13. 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] (See WARNINGS section.)
14. When the 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 treated area against the underlying superficial bone or between your fingers to obtain optimal results.
15. 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.
16. After the initial treatment, an additional treatment may be necessary to achieve the desired level of correction. 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 wrinkle severity, skin elasticity, and dermal thickness at the treatment site.
17. Patients may experience mild to moderate injection site responses, which typically resolve within 1 week. If the treated area is swollen immediately after the injection, an ice pack can be applied to the site for a brief period.
18. The health care professional should instruct the patient to promptly report any evidence of problems possibly associated with the use of JUVÉDERM® VOLLURE™ XC.

[1] Alam, M, Gladstone H, Kramer EM, et al. ASDS guidelines of care: injectable fillers. *Dermatol Surg*. 2008;34(suppl 1):S115-S148.

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® VOLLURE™ XC injectable gel is supplied in individual treatment syringes with 30-G needles for single-patient use and ready for injection (implantation). 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® VOLLURE™ XC injectable gel must be used prior to the expiration date printed on the label.

Store at room temperature (up to 25ºC/77ºF). DO NOT FREEZE.

JUVÉDERM® VOLLURE™ 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.

Allergan Aesthetics
an AbbVie company
Irvine, CA 92612 USA
1-800-624-4261
Made in France

hcp.Juvederm.com
05/2023 022764 20079127