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soft-tissue fillers, for example, after insertion of the needle, and just before injection, the plunger rod can be withdrawn slightly to aspirate and verify the needle is not intravascular, inject the product slowly, and apply the least amount of pressure necessary.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 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 (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 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.
### Table 2. Injection Site Reactions by Duration After Initial Occurrence in >5% of Treated Subjects

<table>
<thead>
<tr>
<th>Injection Site Reaction</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abcess</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>30.6%</td>
<td>5.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>1.2%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>0.4%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>0.2%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
<tr>
<td>bruising</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>30.6%</td>
<td>5.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>1.2%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>0.4%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>0.2%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
<tr>
<td>chapped lips</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>30.6%</td>
<td>5.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>1.2%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>0.4%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>0.2%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
<tr>
<td>Edema</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>30.6%</td>
<td>5.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>1.2%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>0.4%</td>
<td>19.0%</td>
<td>0%</td>
<td>5.8%</td>
<td>0.2%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

### Table 3. Injection Site Reactions by Severity and Duration After Initial Treatment in Subjects Treated with JUVÉDERM® VOLBELLA® XC

#### Table 3. Injection Site Reactions by Severity and Duration After Initial Treatment in Subjects Treated with JUVÉDERM® VOLBELLA® XC

<table>
<thead>
<tr>
<th>Injection Site Reaction</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abcess</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
<tr>
<td>bruising</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
<tr>
<td>chapped lips</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
<tr>
<td>Edema</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

### Table 4. Treatment-Related Adverse Events by Severity After Initial Treatment Occurring in >5% of Treated Subjects

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>JUVÉDERM® VOLBELLA® XC (%)</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection Site</td>
<td>35.1%</td>
<td>28.0%</td>
</tr>
<tr>
<td>Swelling</td>
<td>17.9%</td>
<td>10.1%</td>
</tr>
<tr>
<td>Infected Site</td>
<td>11.9%</td>
<td>7.7%</td>
</tr>
<tr>
<td>Pain</td>
<td>8.9%</td>
<td>7.7%</td>
</tr>
<tr>
<td>Injection Site</td>
<td>8.4%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Redness</td>
<td>4.2%</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

### Table 5. Treatment-Related Adverse Events by Duration After Initial Treatment Occurring in >5% of Treated Subjects

#### Table 5. Treatment-Related Adverse Events by Duration After Initial Treatment Occurring in >5% of Treated Subjects

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>JUVÉDERM® VOLBELLA® XC (%)</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection Site</td>
<td>91.0%</td>
<td>85.7%</td>
</tr>
<tr>
<td>Swelling</td>
<td>86.2%</td>
<td>80.0%</td>
</tr>
<tr>
<td>Infected Site</td>
<td>84.8%</td>
<td>80.5%</td>
</tr>
<tr>
<td>Pain</td>
<td>80.9%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Injection Site</td>
<td>76.5%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Redness</td>
<td>70.5%</td>
<td>65.4%</td>
</tr>
</tbody>
</table>

### Table 6. Injection Site Reactions by Severity and Duration After Initial Treatment in Subjects Treated with JUVÉDERM® VOLBELLA® XC

#### Table 6. Injection Site Reactions by Severity and Duration After Initial Treatment in Subjects Treated with JUVÉDERM® VOLBELLA® XC

<table>
<thead>
<tr>
<th>Injection Site Reaction</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
<th>Any ISR (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abcess</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
<tr>
<td>bruising</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
<tr>
<td>chapped lips</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
<tr>
<td>Edema</td>
<td>24.1</td>
<td>4.8%</td>
<td>19.0%</td>
<td>0%</td>
<td>4.0%</td>
<td>0.8%</td>
<td>19.0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

### Table 7. Treatment-Related Adverse Events by Severity and Duration After Initial Treatment Occurring in >5% of Treated Subjects

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>JUVÉDERM® VOLBELLA® XC (%)</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection Site</td>
<td>91.0%</td>
<td>85.7%</td>
</tr>
<tr>
<td>Swelling</td>
<td>86.2%</td>
<td>80.0%</td>
</tr>
<tr>
<td>Infected Site</td>
<td>84.8%</td>
<td>80.5%</td>
</tr>
<tr>
<td>Pain</td>
<td>80.9%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Injection Site</td>
<td>76.5%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Redness</td>
<td>70.5%</td>
<td>65.4%</td>
</tr>
</tbody>
</table>

### Table 8. Treatment-Related Adverse Events by Duration After Initial Treatment Occurring in >5% of Treated Subjects

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>JUVÉDERM® VOLBELLA® XC (%)</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection Site</td>
<td>91.0%</td>
<td>85.7%</td>
</tr>
<tr>
<td>Swelling</td>
<td>86.2%</td>
<td>80.0%</td>
</tr>
<tr>
<td>Infected Site</td>
<td>84.8%</td>
<td>80.5%</td>
</tr>
<tr>
<td>Pain</td>
<td>80.9%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Injection Site</td>
<td>76.5%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Redness</td>
<td>70.5%</td>
<td>65.4%</td>
</tr>
</tbody>
</table>
Among the 139 subjects who were treated with JUVÉDERM® VOLBELLA® XC at initial treatment and received repeat treatment with repeat treatment with JUVÉDERM® VOLBELLA®, 114 treated the infraorbital hollows during the primary phase of the study. The follow-up period consisted of safety and effectiveness follow-up visits. After initial treatment (or touch-up treatment if performed), subjects were eligible for a repeat treatment with JUVÉDERM® VOLBELLA® XC at which time all subjects completed the study.

The overall total median volume of JUVÉDERM® VOLBELLA® XC injected was equal to or greater than 0.1 mL for all treated subjects. Individual subjects received a median volume of 1.0 mL in the upper lip, 0.8 mL in the lower lip, 0.3 mL in the perioral lines, 0.5 mL in the oral commissures, and 0.1 mL in the philtral columns. Injection volumes into the lips and perioral area after repeat treatment tended to be lower, with the typical total median injectable volume to achieve optimal correction being approximately 1.6 mL. Similar injection volumes were used in subjects treated with the control device.

In general, injections into the vermilion body of the upper and lower lip were subdermal, and injections into the vermilion border, Cupid’s bow, philtral columns, and oral commissures were intradermal. A tunneling technique, partial dermal plane technique, fanning technique, or combination was used to achieve optimal results.

The primary endpoint of the study was the mean change from baseline to month 3 in mean lip fullness based on Evaluating Investigators’ assessment of subjects’ perioral lines using the validated Perioral Lines Severity Scale (POLSS) and subjects’ satisfaction with their lips using the validated Satisfaction with Lips module of the FACE-Q.

Additional effectiveness measures included Evaluating Investigators’ assessments of subjects’ self-perception of improvement in perioral lines severity at maximal contraction using the Perioral Lines at Maximal Contraction (POLMC) scale, and assessment of lip smoothness. Subjects performed self-assessments of lip lines using the Perioral Lines module of the FACE-Q, lip shape, and natural look and feel of the lips. The Treating Investigators also assessed injection ease and product moldability. Safety measures included incidence, severity, and duration of ISRs and AEs, assessments of procedural pain and impact to daily activities, and reporting of adverse events, reactions, and infections, vaccinations, or dental procedures. Typically, the reported inflammation was non-irritating and resolved on its own.

Recurrent 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 exposure to products, vaccines, or dental procedures. Typically, the reported inflammation was non-irritating and resolved on its own at the time of last contact. (see WARNINGS section).

American Indian or Alaska Native 1.2% (2/180)

Asian 1.8% (3/164)

Caucasian 97.6% (164/168)

Female 56.9% (94/163)

Gender

Race

Table 9. Subject Demographics and Pretreatment Characteristics (N = 224)

<table>
<thead>
<tr>
<th>Treatment Characteristic</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>6.0% (13/216)</td>
</tr>
<tr>
<td>Control</td>
<td>6.0% (13/216)</td>
</tr>
<tr>
<td>Baseline Overall LFS Score</td>
<td></td>
</tr>
<tr>
<td>Very Marked</td>
<td>3% (6/176)</td>
</tr>
<tr>
<td>Marked</td>
<td>3% (6/176)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3% (6/176)</td>
</tr>
<tr>
<td>Mild</td>
<td>3% (6/176)</td>
</tr>
<tr>
<td>None</td>
<td>3% (6/176)</td>
</tr>
<tr>
<td>Baseline Overall LFS Score</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>3% (6/176)</td>
</tr>
<tr>
<td>Control</td>
<td>3% (6/176)</td>
</tr>
</tbody>
</table>

Pivotal Study Design

A prospective, double-blind, randomized, controlled, multicenter clinical study was conducted to evaluate the safety and effectiveness of JUVÉDERM® VOLBELLA® XC versus control for injection into the upper and lower lips and perioral area (vermilion, vermilion border, philtral columns, Cupid’s bow, perioral lines, and/or oral commissures) for lip augmentation and perioral Rhytids. The total number of subjects was 224. All 224 subjects were randomized and underwent treatment with either JUVÉDERM® VOLBELLA® XC (N = 168) or control (N = 56) at the outset of the study. An optional touch-up treatment was performed approximately 1 month after the initial treatment, if deemed necessary by the Treating Investigator.

The follow-up period consisted of safety and effectiveness follow-up visits at 1, 3, 6, 9, and 12 months after the last treatment. Subjects were then eligible for a repeat treatment with JUVÉDERM® VOLBELLA® XC, with injections repeated every 3 months for up to 2 repeat treatments, at which time all subjects completed the study.

Study Endpoints

The primary effectiveness measure for the study was the analysis of non-inferiority of JUVÉDERM® VOLBELLA® XC relative to placebo for the terms of change from baseline to month 3 in mean lip fullness based on Evaluating Investigators assessment using the validated 5-point Allergan Lip Fullness Scale (POLSS) and subjects’ satisfaction with their lips using the validated Satisfaction with Lips module of the FACE-Q.

Secondary measures included Evaluating Investigators’ assessment of subjects’ perioral lines using the validated Perioral Lines Severity Scale (POLSS) and subjects’ satisfaction with their lips using the validated Satisfaction with Lips module of the FACE-Q.

A total of 139 subjects were treated with JUVÉDERM® VOLBELLA® XC and 10 for subjects treated with control. With 80.3% (121/151) of subjects treated with JUVÉDERM® VOLBELLA® XC.
Investigator assessment. After repeat treatment, the responder rate was similar to that after 56.3.

Table 10. Effectiveness Results Through 1 Year

<table>
<thead>
<tr>
<th>Month</th>
<th>JUVÉDERM® XC</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Week</td>
<td>90.4% (101/112)</td>
<td>92.5% (107/116)</td>
</tr>
<tr>
<td>3 Months</td>
<td>89.5% (101/112)</td>
<td>92.6% (107/116)</td>
</tr>
<tr>
<td>6 Months</td>
<td>85.4% (101/117)</td>
<td>88.5% (110/125)</td>
</tr>
<tr>
<td>9 Months</td>
<td>85.4% (101/117)</td>
<td>88.5% (110/125)</td>
</tr>
<tr>
<td>1 Year</td>
<td>83.1% (101/121)</td>
<td>86.6% (110/128)</td>
</tr>
</tbody>
</table>

At 1 year, 74.8% (92/123) of subjects treated with JUVÉDERM® XC maintained improvement in perioral lines severity at rest. At 3 months, improvements in perioral lines severity at rest were observed in 65.4% (82/124) of subjects treated with JUVÉDERM® XC. At 1 year, 66.2% (45/68) of subjects treated with JUVÉDERM® XC reported improvement in satisfaction with their lips, based on the Satisfaction with Lip module of the FACE-Q questionnaire, 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, based on the maximum correction with a mean score of 59.6.

Table 11. Subject Demographics and Pretreatment Characteristics (N = 224)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>JUVÉDERM® XC</td>
<td>113</td>
<td>111</td>
<td>224</td>
</tr>
<tr>
<td>Control</td>
<td>112</td>
<td>111</td>
<td>223</td>
</tr>
</tbody>
</table>

During the follow-up period, JUVÉDERM® VOLBELLA® XC demonstrated improvement in perioral lines following 3 months of treatment. The responder rate was similar to that after 51 months.

Table 12. Effectiveness Results Through 1 Year Based on AHIIS Responder Rates Using Observed Data

<table>
<thead>
<tr>
<th>Month</th>
<th>JUVÉDERM® VOLBELLA® XC</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Week</td>
<td>86.5% (102/118)</td>
<td>88.0% (100/114)</td>
</tr>
<tr>
<td>3 Months</td>
<td>86.5% (102/118)</td>
<td>88.0% (100/114)</td>
</tr>
<tr>
<td>6 Months</td>
<td>77.0% (95/124)</td>
<td>77.0% (95/124)</td>
</tr>
<tr>
<td>9 Months</td>
<td>77.0% (95/124)</td>
<td>77.0% (95/124)</td>
</tr>
<tr>
<td>1 Year</td>
<td>73.4% (95/129)</td>
<td>73.4% (95/129)</td>
</tr>
</tbody>
</table>

At Month 3, the GAIS responder rate was 86.1% (87/101) based on the GAIS responder rate in subjects treated with JUVÉDERM® VOLBELLA® XC demonstrating a clinically and statistically significant improvement in the appearance of infraorbital hollowing compared to the no-treatment control group at Month 3. The principal effectiveness criteria were met in that the treatment group 5 responder rate of 83.1% was statistically significantly greater (p ≤ 0.0001) than the no treatment control group (15.6%) based on the 1T population with multiple imputation. The mean improvement was clinically significant (≥ 1 point) for the majority of subjects demonstrating improvement through 1 year (Table 12).

Through 1 year in the JUVÉDERM® VOLBELLA® XC group, improvements in upper and lower lip fullness were similar to those observed in overall lip fullness. Subjects treated with JUVÉDERM® VOLBELLA® XC reported improvement in satisfaction with lips, based on the Satisfaction with Lip module of the FACE-Q questionnaire, 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, based on the maximum correction with a mean score of 59.6.

Additional effectiveness measures included volume change of each infraorbital area as assessed by 3D facial digital imaging. Subjects self-reported improvements in the appearance of 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 and vasculature, effective patient assessment, safe injection technique, and identification and management of potential adverse events, including vascular complications. Health care practitioners should contact Allergan for educational and training resources.

Completion of device-specific use training is required and will be verified prior to use of JUVÉDERM® VOLBELLA® XC for the treatment of infraorbital hollows.

Prior to treatment, the patient’s medical history should be obtained and the patient should be apprised of the indications, contraindications, warnings, precautions, treatment regimens, adverse reactions, and method of administration. Patients should also be advised that supplemental touch-up treatments may be required to achieve and maintain maximum correction.

Before and after treatment, health care practitioners are encouraged to conduct vision assessments, including visual acuity, blink and ocular motility.

Dental professionals are encouraged to be prepared with the following in the event of an intravascular injection:

• an emergency protocol is available, as recommended by the American Society for Dermatologic Surgery guidelines
• identifying a local ophthalmologist or ophthalmology subspecialist to be available in the event of an ophthalmic adverse event related to a dermal filler injection.

STEP 2: Insert needle or cannula
Hold the syringe body and firmly insert the hub of the needle (provided in the JUVÉDERM® package) or cannula (provided separately) into the Luer-Lok® end of the syringe.

STEP 3: Tighten the needle or cannula
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 is not correct as shown in Figure D, it is not attached correctly. Retighten it until the needle or cannula is seated in the proper position.

STEP 4: Remove the needle or cannula 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 cap from the needle or cannula.
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.

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

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 STERILIDE® 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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