New Filler Approval: Juvederm Volbella

Karol A Gutowski, MD, FACS
Hot Topics
Disclosures

Angiotech/Surgical Specialties - Advisory Board
AxcelRx Pharmaceuticals - Advisory Board
Suneva Medical - Instructor

Will use brand names due to lack of distinguishing generic names
Juvederm Volbella XC

- Allergan
- Cross-linked hyaluronic acid injectable soft tissue filler
- Produced by *Streptococcus*
- 15 mg HA/mL + lidocaine
- (Ultra & Ultra Plus: 24 mg, Voluma: 20 mg)

**Indications:** Lips & perioral rhytides, >21 years old

**FDA Status:** Approved

**Availability:** October 2016
Presentation Level of Evidence

Levels of Evidence and Qualifying Studies (Therapeutic Studies):

I  High-quality, multi-centered or single-centered, randomized controlled trial with adequate power (N ≥ 100); or a systematic review of these studies

II Lesser-quality, randomized controlled trial; prospective cohort study; or systematic review of these studies

III Retrospective comparative study; case-control study; or a systematic review of these studies

IV Case series

V Expert opinion; case report or clinical example; or evidence based on physiology, bench research or "first principles"
Treatment & Costs

• Product cost  To be determined
• Disposables  None (injection cannula $5-10)
• Treatment  1 to 6 syringes (2.6 average)
• Sessions  1 or 2
• Patient cost  To be determined
Recent FDA Approvals

- 2013  Voluma  Cheek augmentation
- 2014  Restylane Silk  Lips & perioral lines
- 2015  Restylane Lyft  Facial folds
- 2015  Radiesse  Hands
- 2015  Juvederm  Lips & perioral lines
- 2016  Volbella  Lips & perioral lines
Match Filler to Need

**Lips**
**Goals:** Easy molding and spreadability
**Challenges:** Avoid visible edges and bumps

**Wrinkles/Folds**
**Goals:** Moldable, integrate well with movement
**Challenges:** Resist shearing and mild compressive forces

**Midface Volumization**
**Goals:** Volume restoration, 3-D contouring
**Challenges:** Resist shearing and compressive forces
Physical Properties

Viscoelasticity\(^1\)
- Affects how the filler behaves when subjected to shearing (lateral) forces created by facial movement

Cohesivity\(^1\)
- How well the filler behaves as a gel deposit once it is implanted in the face

Viscosity\(^1\)
- How well the filler flows when subjected to the high shear forces of injection
Hylacross vs Vycross Technology

**HYLACROSS™**
100% high-molecular weight HA chains

- Highly cross-linked

  - JUVEDERM® Ultra
  - JUVEDERM® Ultra Plus

**VYCROSS®**
Proprietary mixture of low- and high-molecular weight HA chains

- Tightly cross-linked

  - JUVEDERM VOLUMA® XC
## Juvederm Product Comparison

<table>
<thead>
<tr>
<th></th>
<th>JUVÉDERM® Ultra XC</th>
<th>JUVÉDERM® Ultra Plus XC</th>
<th>JUVÉDERM VOLBELLA® XC</th>
<th>JUVÉDERM VOLUMA® XC</th>
</tr>
</thead>
</table>
| **Indication** | • Moderate to severe facial wrinkles and folds (such as nasolabial folds)  
                • Injection into the lips and perioral area for lip augmentation in adults over the age of 21 | • Moderate to severe facial wrinkles and folds (such as nasolabial folds)  
                • Injection into the lips for lip enhancement and for correction of perioral rhytids in adults over the age of 21 | • Injection into the lips for lip enhancement and for correction of perioral rhytids in adults over the age of 21 | • Deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation to correct age-related volume deficit in the mid-face in adults over the age of 21 |
| **Implantation depth** | Mid-to-deep dermis  
                        Lip mucosa | Mid-to-deep dermis | Superficial to mid-dermis  
                        Lip mucosa | Subcutaneous  
                        Upper periosteal  
                        Deep dermis |
| **Total HA concentration** | 24 mg/mL | 24 mg/mL | 15 mg/mL | 20 mg/mL |
| **Formulation** | Smooth, viscous gel | Smooth, viscous gel | Smooth, viscous gel | Smooth, viscous gel |
| **Gel hardness/viscosity (G’ @ 5 Hz)** | 176 Pa | 244 Pa | 274 Pa | 353 Pa |
| **Cohesivity** | 72 gmF | 78 gmF | 18 gmF | 35 gmF |
| **Lidocaine** | 0.3% | 0.3% | 0.3% | 0.3% |
| **Needle gauge and length** | 30 G, ½” | TSK 27 G, ½” | 30 G, ½” | 25 G, ½” (2.0 mL syringe)  
                        27 G, ½” (1.0 mL syringe) |
| **Gel swelling potential** (max unconstrained water uptake) | 600-650% | 425-475% | 100-150% | 200-250% |
| **Duration** | Up to 1 year | Up to 1 year | Up to 1 year | Up to 2 years |
G’ & Cohesivity

G’ (Pa)

Elastic Modulus G’ (Pa)

Cohesivity (gmf)

Grams-force (gmf)

JUVEDERM® Ultra
JUVEDERM® Ultra Plus
JUVEDERM® VOLUMA® XC
JUVEDERM® VOLBELLA® XC

JUVEDERM® Ultra
JUVEDERM® Ultra Plus
JUVEDERM® VOLUMA® XC
JUVEDERM® VOLBELLA® XC
Water Absorption

Maximum Water Absorption*

Unconstrained Gel Swelling (%)

<table>
<thead>
<tr>
<th>Product</th>
<th>Unconstrained Gel Swelling (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JUVÉDERM® Ultra XC</td>
<td>622%</td>
</tr>
<tr>
<td>JUVÉDERM® Ultra Plus XC</td>
<td>454%</td>
</tr>
<tr>
<td>JUVÉDERM VOLBELLA® XC</td>
<td>127%</td>
</tr>
<tr>
<td>JUVÉDERM VOLUMA® XC</td>
<td>220%</td>
</tr>
</tbody>
</table>
Lift

- Bolus injection, subcutaneous plane (overlying skull), Sprague-Dawley rat model
- 3D Canfield imaging of projection; significant differences calculated across all time-points

Overall Significance Among Groups:

- JUVÉDERM VOLBELLA® XC < JUVÉDERM® Ultra Plus XC ≈ JUVÉDERM VOLUMA® XC

![Graph showing mean height over weeks post-injection for different products.](chart.png)
Moldability

Resistance to Deformation
Pre-clinical model

% decrease = (1 - 2) / 1

More Moldable

Less Moldable

% Decrease in Mean Height

- A significant decrease in moldability was observed at day 1 for all VYCROSS® products with an additional decrease for JUVEDERM VOLUMA® XC at day 2 compared to day 1.

Ultral Plus XC
VOLUMA XC
VOLBELLA XC

* P < .05 compared to day 0, within group
# P < .05 compared to day 1, within group
Error bars indicate +/- SD
N = 6
Pivotal Clinical Trial

Prospective multicenter, double blinded RCT
• Volbella XC n=168
• Restylane L = 56
• Optional touch up at 1 month (same in both groups)

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<thead>
<tr>
<th></th>
<th>Volbella XC¹ (N = 168)</th>
<th>Control² (N = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (median, range; mL)</td>
<td>2.6 (0.75-5.80)</td>
<td>2.6 (0.50-6.00)</td>
</tr>
<tr>
<td>Upper lip</td>
<td>1.0 (0.20-2.20)</td>
<td>0.9 (0.30-1.90)</td>
</tr>
<tr>
<td>Lower lip</td>
<td>0.8 (0.20-2.10)</td>
<td>0.7 (0.10-1.70)</td>
</tr>
<tr>
<td>Perioral lines</td>
<td>0.3 (0.05-1.60)</td>
<td>0.3 (0.05-1.30)</td>
</tr>
<tr>
<td>Oral commissures</td>
<td>0.5 (0.10-3.40)</td>
<td>0.6 (0.10-3.70)</td>
</tr>
<tr>
<td>Philtral columns</td>
<td>0.1 (0.03-0.75)</td>
<td>0.2 (0.10-0.20)</td>
</tr>
<tr>
<td></td>
<td>Volbella XC (N = 165)</td>
<td>Control (N = 53)</td>
</tr>
<tr>
<td>----------------</td>
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</tr>
<tr>
<td>Mean</td>
<td>1.1(^1)</td>
<td>1.0(^1)</td>
</tr>
<tr>
<td>SD</td>
<td>0.75</td>
<td>0.85</td>
</tr>
<tr>
<td>P-value(^b)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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</table>
Lip Lines

% of Subjects Improved ≥1-Point on POLSS

- Month 1: 77.5%
- Month 3: 65.4%
- Month 6: 61.3%
- Month 9: 65.8%
- Month 12: 66.2%
- Month 1 After Repeat Tx: 89.6%
Lip Satisfaction FACE Q

Mean FACE-Q Score

- Month 1: 96.6%
- Month 3: 96.1%
- Month 6: 92.6%
- Month 9: 86.5%
- Month 12: 79.7%
- Month 1 After Repeat Tx: 96.7%
Lip Fullness

% Subjects Improved ≥1-Point on LFS

- Month 1: 86.2%
- Month 3: 80.3%
- Month 6: 71.1%
- Month 9: 65.1%
- Month 12: 61.8%
- Month 1 After Repeat Tx: 94.3%

Volbella XC
Perioral Lines Maximal Contraction

% of Subjects Improved ≥1-Point on POLM

- Month 1: 61.3%
- Month 3: 50.6%
- Month 6: 37.5%
- Month 9: 38.0%
- Month 12: 30.9%
- Month 1 After Repeat Tx: 67.2%
Oral Commissure

% of Subjects Improved ≥1-Point on OCSS

Month 1: 68.2%
Month 3: 59.2%
Month 6: 52.8%
Month 9: 48.4%
Month 12: 53.3%
Month 1 After Repeat Tx: 78.1%²
Global Aesthetic Improvement

% of Subjects Improved or Much Improved on GAIS

- Month 1: 95.5%
- Month 3: 92.9%
- Month 6: 85.9%
- Month 9: 75.0%
- Month 12: 58.5%
- Month 1 After Repeat Tx: 100.0%

Volvella XC
Lip Lines FACE Q

Mean FACE-Q Score

- Month 1: 88.5%
- Month 3: 88.2%
- Month 6: 81.0%
- Month 9: 77.4%
- Month 12: 74.8%
- Month 1 After Repeat Tx: 89.3%

Vobella XC
• Safe & effective
• 2 to 3 syringes for full effect
• Expect 6 to 9 month results
  – Duration of effect depends on site
• Similar results as Restylane but lower G’?
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