WELCOME TO THE ERA OF DYNAMIC AESTHETICS

RESILIENT BEAUTY

*Resilient Hyaluronic Acid
Everyday as we smile, speak, yawn and blink...

- Forehead lifting
- Brow frowning
- Cheek raising
- Nose wrinkling
- Lip stretching

...our facial expressions convey many messages\textsuperscript{1,2}

\textbf{The face is naturally dynamic}
The long chains of natural hyaluronic acid self-organise in a 3D mobile network conferring its viscoelastic capacities. Thanks to these properties, hyaluronic acid maintains tissue architecture, volume and hydration\(^3,4\)

**Classical method**

Crosslinking requires harsh conditions
The long hyaluronic acid chains are degraded\(^5\)
To create a monophasic cohesive gel with the subsequent shorter chains, larger amounts of BDDE\(^*\) must be added\(^6\)

\(^*\) BDDE: 1,4-Butanediol Diglycidyl Ether.
The specific crosslinking conditions better preserve the length of the hyaluronic acid chains. Less BDDE is needed to create the gel, also supported by the natural interactions between the long chains.

Gel consisting of hyaluronic acid long chains stabilised by natural and mobile interactions supported by a lower crosslinker rate (1.9-4.0%).

Maintains natural viscoelastic properties: Dynamic structure.
In order to assess the behavior of TEOSYAL®RHA gel in a dynamic environment, TEOXANE Laboratories together with the University of Grenoble have developed an exclusive dynamic rheology method based on 2 combined characteristics:

**Stretch**

*Behavior of gel when pulled away* in a superficial layer, such as the lips or nasolabial folds

**Strength**

*Resistance of gel to compression* in a deep layer, such as the cheeks or chin

Illustrative diagrams of rheologic properties of TEOSYAL®RHA gels (test developed with the University of Grenoble, France)

Under stretching or compression, TEOSYAL®RHA adapts to its environment and keeps its performance

*A, B, C and D are commonly used competitors products to treat wrinkles. E and F are commonly used competitors volumizers. Teosyal®RHA keeps its mechanical properties on a large range of strain or stress contraints (dynamic G’) - Report Rheological characterizations of hyaluronic acid gels. Rheonova (University of Grenoble, France). Data on file - Patent pending*
UNIQUE RESILIENCE SCIENTIFICALLY PROVEN BY DYNAMIC RHEOLOGY

Unparalleled stretch and strength properties

**Stretch and strength values**

**Unparalleled stretch**

**and strength properties**
Randomized, controlled, double-blinded, single-center, pilot clinical trial
Including 90 patients, 180 moderate-to-severe nasolabial folds were evaluated over
a 9-month period to assess the efficacy and safety of TEOSYAL® RHA vs reference
products

Patients
• 90 healthy patients, 39 to 70 years old
• Primary inclusion criteria: 2 symmetrical moderate to severe nasolabial folds

Methodology
• Injections were carried out by six European doctors and assessed by trained
  physicians
• Split-face injections
• Touch-up at D14, if required
• Evaluations at 1, 6, 9 and 12 months

Efficacy
• Primary endpoint
  – Wrinkles improvement evaluated by the Wrinkle Severity Rating Scale (WSRS)
• Secondary endpoints
  – Aesthetic improvement on the Global Aesthetic Improvement Scale (GAIS)
  – Duration of filling effect
  – Patients and physicians satisfaction

Safety
• Pain at injection using a 10 cm Visual Analog Scale (VAS)
• Common Treatment Reactions and Adverse Events collection

* Juvederm® Volift and Juvederm® Ultra4 are products of Allergan.
## Patients and injections characteristics in the European RHA trial

<table>
<thead>
<tr>
<th></th>
<th>TEOSYAL® RHA2 vs Juvederm® Volift*</th>
<th>TEOSYAL® RHA3 vs Juvederm® Ultra4*</th>
<th>TEOSYAL® RHA4 vs TEOSYAL® PureSense UltraDeep</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td><strong>Depth of injection</strong></td>
<td>Mid to deep dermis</td>
<td>Deep dermis</td>
<td>Deep dermis to subcutaneous</td>
</tr>
<tr>
<td><strong>Wrinkles</strong></td>
<td>Moderate</td>
<td>Severe</td>
<td>Severe</td>
</tr>
<tr>
<td><strong>WSRS</strong></td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Besides this European trial, TEOXANE Laboratories are conducting a **large, prospective clinical program**, including **more than 500 patients** in Europe and the USA.
TEOSYAL® RHA reduces wrinkles in mobile areas over the long term vs reference products\(^9,11\)

\[\text{Mean improvement WSRS* score} \]

\[\begin{array}{c|c|c|c|c|c}
\hline
 & \text{Juvéderm Volift}\(^\ddagger\) & \text{TEOSYAL® RHA2} & \text{Juvéderm Ultra4}\(^\ddagger\) & \text{TEOSYAL® RHA3} & \text{TEOSYAL® Puresense UltraDeep} & \text{TEOSYAL® RHA4} \\
\hline
\text{1.1} & 1.1 & 1.7 & 1.8 & 1.6 & 1.8 \\
\text{p=NS**} & & & & & \\
\hline
\end{array}\]

\[\text{WSRS* score improvement between baseline and 9 months after treatment^9}\]

\[\text{Percentage of product left (%)} \]

\[\begin{array}{c|c|c|c|c|c|c}
\hline
 & \text{Juvéderm Volift}\(^\ddagger\) & \text{TEOSYAL® RHA2} & \text{Juvéderm Ultra4}\(^\ddagger\) & \text{TEOSYAL® RHA3} & \text{TEOSYAL® Puresense UltraDeep} & \text{TEOSYAL® RHA4} \\
\hline
\text{39.1%} & 70.6% & 58.7% & 75.9% & 68.9% & 88.3% \\
\text{p=NS**} & & & & & \\
\hline
\end{array}\]

\[\text{Volume of product remaining in nasolabial folds at 9 months vs baseline^11}\]

\(^*\) WSRS: Wrinkles Severity Rating Scale. ** NS: Not significant. *** GAIS: Global Aesthetic Improvement Scale.
\(^\ddagger\) No Unexpected Adverse Device Effect (UADE), nor device related Serious Adverse Event (SAE) was reported, and there was no difference in pain during injection nor in safety (Common Treatment Reactions and Adverse Events) between Teosyal RHA and control products. \(^\ddagger\ddagger\) Juvederm® Volift and Juvederm® Ultra4 are products of Allergan. \(^9\) TEOXANE. 9-month interim report. Internal data. December 19, 2014. \(^10\) TEOXANE. 6-month interim report. Independent CRO analysis. October 28, 2014. \(^11\) TEOXANE. 9-month interim report. Internal data. January 22, 2015.
Most patients express GAIS*** score improved or very improved in all treatment groups\textsuperscript{9}.

All tested products have a good safety profile\textsuperscript{9,10}.

88.6\% of patients are very or totally satisfied\textsuperscript{9}.
Deep wrinkles

Volume in extended areas

Deep wrinkles

Volume in extended areas

TEOSYAL® RHA
RESILIENT HYALURONIC ACID
“The filler becomes part of the dermal structure rendering it more natural especially in mobile areas where the skin stretches – the likelihood of developing lumps like with other products decreases”.
Dr. Hassan Galadari, Dermatologist, UAE

“You’ve got an aesthetic improvement without feeling the product in the skin and soft tissue – That’s great”.
Dr. Wolfgang Redka-Swoboda, Surgeon, Germany

“It works great on lines. It seems to take them away immediately, which is unusual”.
Dr. Wayne Carey, Dermatologist, Canada

<table>
<thead>
<tr>
<th>Hyaluronic acid concentration (mg/mL)</th>
<th>15</th>
<th>23</th>
<th>23</th>
<th>23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crosslinker rate</td>
<td>1.9%</td>
<td>3.1%</td>
<td>3.6%</td>
<td>4.0%</td>
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<tr>
<td>Lidocaine concentration</td>
<td>0.3%</td>
<td>0.3%</td>
<td>0.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Needle</td>
<td>30G 1/2”</td>
<td>30G 1/2”</td>
<td>27G 1/2”</td>
<td>27G 1/2”</td>
</tr>
</tbody>
</table>

Characteristics of TEOSYAL®RHA gels

A new, exclusive crosslinking method preserving HA long chains in a mobile network

Unique resilience properties of the gel

Immediate and long-lasting efficacy in dynamic areas of the face\textsuperscript{9,10}

For highly satisfied doctors and patients