

Glymatrix Technology Produces Longer Lasting Facial Filler

By Lara G. Owens, Contributing Editor

Photos courtesy of Berthold Rzany, M.D.



Nasolabial folds before Tx

Nasolabial folds after
EVOLENCE Tx

"Longevity is a major advantage because a once a year injection puts fillers in a more pleasant financial perspective for the patient."

With the help of a revolutionary production process, collagen is pushing its way back into the dermal filler market. OrthoNeurogena's new collagen fillers, EVOLENCE™ and the softer version EVOLENCE Breeze, are approved by the European Union and already on the move in Israel, Canada and parts of Asia while they undergo clinical trials for FDA approval in the U.S. EVOLENCE is designed to correct mild-to-severe facial folds, wrinkles and volume loss, while EVOLENCE Breeze (injected with a 30 gauge needle) is intended to correct fine-to-moderate wrinkles. Both products maintain significant benefits for at least one year. They are naturally produced by Glymatrix' technology, a technique developed by ColBar LifeScience Ltd. in Herzliya, Israel.

According to Belgium based dermatologist Koenraad De Boule, M.D., traditional bovine collagen fillers promise correction for only a few months, whereas correction with EVOLENCE is always lasting more than 12 months and up to 18 months in clinical trials. "Longevity is a major advantage because a once a year injection puts fillers in a more pleasant financial perspective for the patient." You also don't have the swelling and bruising of popular hyaluronic acid fillers. The new fillers provide a natural look and people can return to their daily activities quite fast," he explained. Another advantage of EVOLENCE products is that patients don't require an allergy test before treatment. "Glymatrix (glycation plus collagen matrix) technology uses porcine derived collagen, which is less immunogenic to human tissue than bovine collagen," he continued.



Koenraad De Boule, M.D.
Dermatologist
Director
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Dermatologist Said Hilton, M.D., in Germany, attributes the lack of allergenicity to the absence of chemical additives in EVOLENCE.



Said Hilton, M.D.
Dermatologist
Düsseldorf, Germany

"Chemical additives can be problematic in sensitive patients with allergies." Drs. De Boule and Hilton have each treated approximately 400 patients with EVOLENCE and EVOLENCE Breeze.

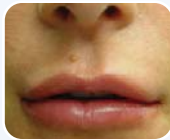
According to Menashe Y. Levy, Ph.D., ColBar's vice president of research and development, collagen is cross-linked in the body by two main pathways. "One is enzymatic in which lysyl oxidase facilitates the cross-linking of two lysine residues of adjacent collagen molecules. The other is a cascade of reactions mediated by glucose, ribose and other natural sugars. These two cross-linking processes govern the biological longevity of collagen in the body. Hyaluronic acid in the body is not cross-linked and that's why it has a very short biological life."

EVOLENCE is composed only of natural ingredients, making it biocompatible with the human body, according to Dr. Levy, "Glymatrix technology chemically, structurally and functionally mimics the extracellular matrix of the skin." Chemically, the collagen in EVOLENCE is cross-linked with non-toxic sugar moieties, similar to the natural process occurring in skin. Structurally, collagen cross-linked by Glymatrix technology forms a three-dimensional matrix that mimics the structure of the extracellular skin matrix and supports the normal housekeeping functions of the skin."

Photos courtesy of Koenraad De Boulle, M.D.



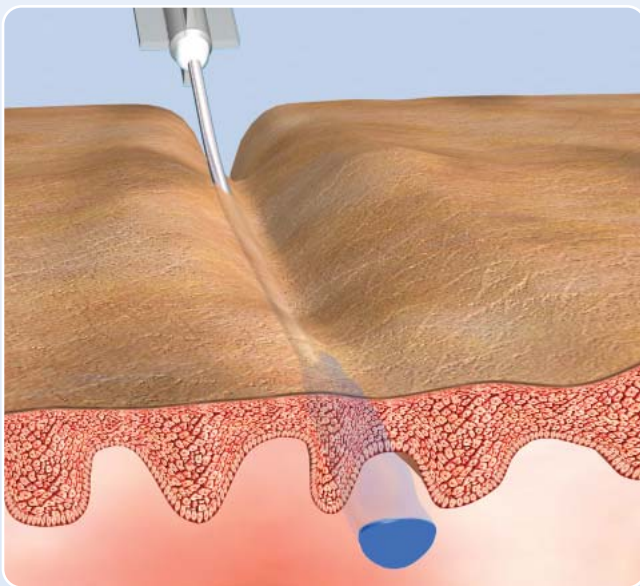
Lips before Tx



Lips after EVOLENCE Tx

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The key to EVOLENCE’s longevity lies in the Glymatrix cross-linking process. “Cross-linking of bovine and even human collagen products requires the use of glutaraldehyde, whose concentration is limited to avoid toxicity,” David Shoshani, M.D., ColBar’s vice president of medical affairs said. “This limits the amount of cross-linking that can be done with these traditional fillers. Rather than glutaraldehyde, Glymatrix uses ribose, a natural sugar and cross-linking agent, which allows us to create products with different biodurabilities. The more cross-linking in collagen, the stronger the collagen’s resistance to degradation and the greater its longevity as a filler.”



EVOLENCE treatment

Collagen fillers prepared by Glymatrix technology differ in other important ways from hyaluronic acid fillers, according to Dr. Levy. “Hyaluronic acid fillers are gel-like products while EVOLENCE fillers are three-dimensional fibrous matrices similar to those in the skin. Histology sections of injected hyaluronic acid implants show large fragmented particles dispersed in the dermis while sections of EVOLENCE products look more like the dermis. It allows penetration of fibroblasts, formation of vascular vessels, propagation of fibroblasts and formation of new collagen in the implant. We don’t see any of this with hyaluronic acid implants.” Dr. Levy added that since collagen “glues itself to tissues in the deep dermis, it is not as easily displaced from the injection site as hyaluronic acid.”

Dermatologist Berthold Rzany, M.D., who practices in Germany, participated in a clinical trial in which EVOLENCE was compared to hyaluronic acid fillers. “In the U.S., all fillers on the market have clinical trial data. But in Europe, you can put a filler on the market and say it’s comparable to this or that without proving anything. The advantage of EVOLENCE is that it has clinical trial data that shows it lasts at least 12 months in most patients. I treated deep nasolabial folds and the effects lasted up to 15 months in some patients. That means patients would have to come back once a year rather than two or three times per year, which is nice. It also seems to cause less erythema when you inject it, although the clinical trial data is needed to



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Photos courtesy of Koenraad De Boulle, M.D.



Nasolabial folds before Tx



Nasolabial folds after
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“With other products, swelling can last one to eight days whereas EVOLENCE induced swelling is gone the next day in 99% of patients.”

really judge that.” EVOLENCE is expected to be available in Germany in 2007.

EVOLENCE isn't limited to just folds and wrinkles. “The lips are also responding well,” Dr. De Boulle said. “If you use EVOLENCE Breeze to redefine a lip contour, the swelling and bruising are minimal. For me, EVOLENCE products are number one for the lip.” Dr. Hilton agreed adding, “With other products, swelling can last one to eight days whereas EVOLENCE induced swelling is gone the next day in 99% of patients. Patients are very happy about that.” Dr. Rzany, who has treated nearly 100 patients with one or both products, considers EVOLENCE Breeze to work especially well on the lips. “I inject Breeze quite superficially in the lips with a 30 gauge needle. I also use anesthesia because I know of no filler product that won't cause pain when injected into the lips.”

Based in Canada, Nowell Solish, M.D., also uses both products on the lips. “EVOLENCE is a good filler that is easy to inject, doesn't cause much swelling or bruising and has very little downtime in the lips,” he said. “A lot of other fillers used in the lips cause significant swelling and downtime. EVOLENCE seems to reduce the swelling and downtime significantly.”



Nowell Solish, M.D.
Dermatologist
Toronto, Canada

Injection of these products is not a problem for physicians experienced in injecting fillers, according to Dr. Rzany. “Injection is basically the same as for any injectable filler. I prefer the tunnel technique, but you can also use other techniques. I view injection

as an art because you have to look at the patient's characteristics, try to figure out what the patient wants and then do your best to achieve it,” he conveyed. Dr. Solish agreed and also added, “Because EVOLENCE and EVOLENCE Breeze don't require refrigeration, you can pull them out of the box and put them in, just as with hyaluronic acid fillers.”

Like hyaluronic acid fillers, the EVOLENCE products require anesthesia, according to Dr. Solish. “I use a local anesthetic, but when injecting the lips I may also use a small nerve block as I do with hyaluronic acid fillers. Pre-treatment depends on the patient's general level of comfort.” Dr. Rzany typically uses a topical anesthetic for 25 minutes under occlusion before injection. “Some patients also require a dental block,” he said. As for post treatment care, physicians cool the treated area. “I just ice it a bit and that's it,” reported Dr. Rzany. Dr. Solish added that swelling and bruising are temporary and so minimal that patients can go home and be fine the next day.

The physicians agreed that the future for these two products is bright. “I think EVOLENCE will find quite a big niche,” commented Dr. Rzany. “Restylane is a fine product, but it seems EVOLENCE has the advantage because it causes less erythema.” Dr. Solish hopes the ongoing clinical trials show the same results as the European studies. “EVOLENCE and EVOLENCE Breeze are user-friendly, require no allergy tests, have little downtime and hopefully will prove to last longer than their competitors,” he said. “I hadn't picked up a syringe of collagen in five years. Then these collagen fillers come along that last a year, have all the advantages of the old collagen but with less swelling and less bruising, and I had to reconsider.”