Revanesse®

The Next Generation of Hyaluronic Acid Dermal Fillers

Revitalize
Rejuvenate
ReNew®

The Revanesse® Family of Products

The Revanesse® family of products incorporates the latest advancements in cross-linking technology, resulting in a high quality, safe, long lasting dermal filler. The Revanesse® family of products utilize the highest concentration of stabilized hyaluronic acid (HA) available in addition to the rejuvenating properties of non cross-linked HA. This line of products includes:

Revanesse® Pure
Revitalisation Implant

Revanesse®
Cross Linked Hyaluronic Acid

Revanesse® Ultra
Cross Linked Hyaluronic Acid ~ High Viscosity

Revanesse® Lips
Cross Linked Hyaluronic Acid

ReDexis®
Cross Linked Hyaluronic Acid with Dextranomers

ReDexis® Ultra
Cross Linked Hyaluronic Acid with Dextranomers

Revanesse® Pure
Revitalisation Implant

Revanesse® Pure is a biodegradable, non animal-based, non cross-linked, clear HA gel. It is quickly absorbed into the skin, replenishing HA that has been lost to ageing. With its hygroscopic properties Revanesse® Pure hydrates the skin and restores elasticity for firm, healthy looking skin. Revanesse® Pure helps to nourish and moisturize the entire surface of the dermis creating healthier looking skin. Treatments typically take 10-15 minutes and are repeated on a monthly basis for four consecutive months.

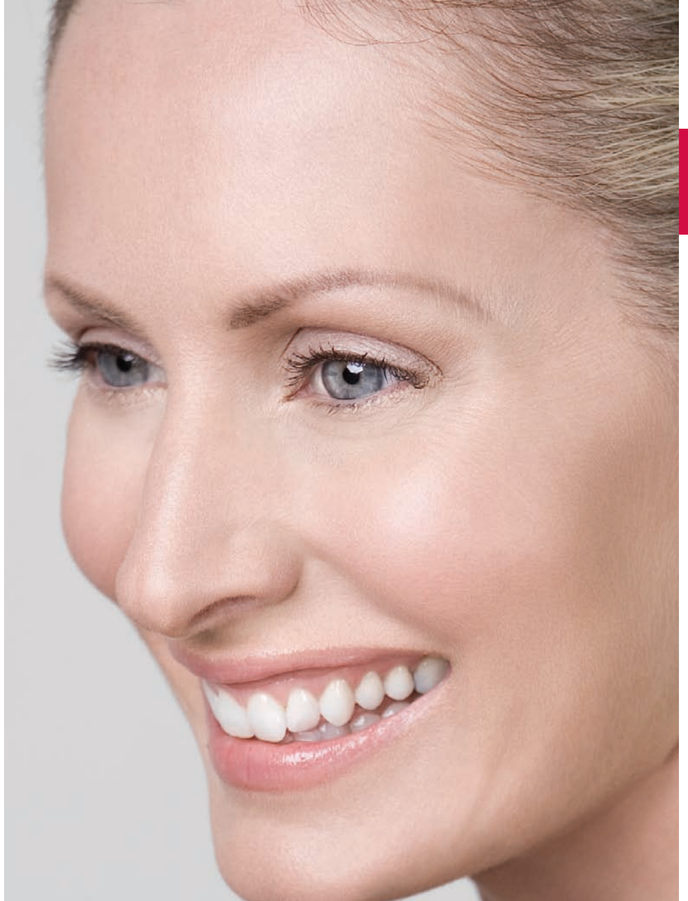
Revanesse®
Cross Linked Hyaluronic Acid

Revanesse® is a biodegradable, non animal-based, clear HA gel which is best used to fill superficial imperfections in the dermis such as fine lines, forehead wrinkles, crow's feet, peri-orbital lines and glabellar lines. Revanesse® uses ultra smooth monophasic HA gel which makes it easy to inject.

Revanesse® Ultra

Cross Linked Hyaluronic Acid ~ High Viscosity

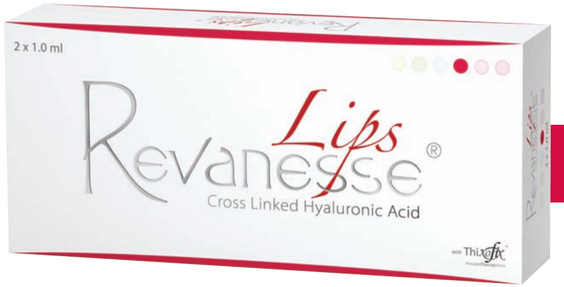
Revanesse® Ultra is a high viscosity, biodegradable, non animal-based, clear HA gel made using Prollenium's® patented cross-linking process. This process creates a thicker, longer lasting gel that improves the ability to treat deep and more pronounced lines and wrinkles such as nasolabial folds and oral commissures.



Revanesse® Lips

Cross Linked Hyaluronic Acid

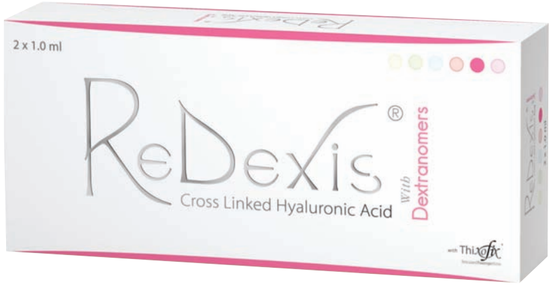
The unique and delicate properties of the lips require a specially formulated filler to ensure good post-injection results. Revanesse® Lips has been specifically engineered for lip augmentation and definition. The result of this special design is a filler which is easy to inject and mold after injection with fewer incidences of swelling.

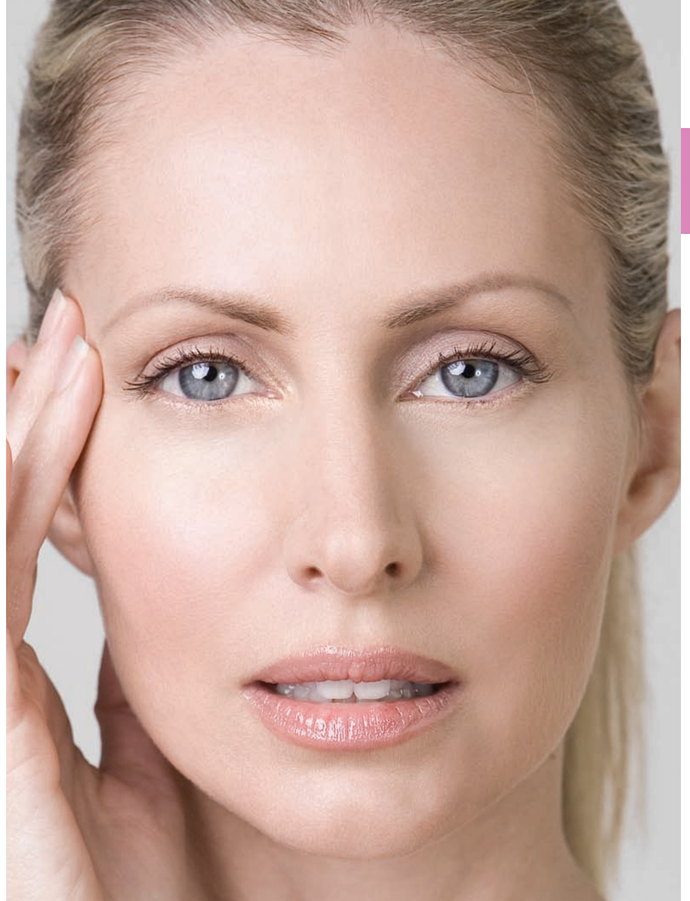


ReDexis®

Cross Linked Hyaluronic Acid with Dextranomers

ReDexis® is a biodegradable, non animal-based, HA gel with a unique ingredient – dextranomer beads – which gives it the ability to generate new tissue. These fully absorbable dextranomer beads create a scaffolding effect for collagen growth. The positive charge of the beads enables them to attract naturally occurring, negatively charged, collagen and elastin. The collagen and elastin then bind together, providing natural augmentation which lasts even after the HA has been broken down. ReDexis® is safe, effective, and ideal for treating deep wrinkles and folds.

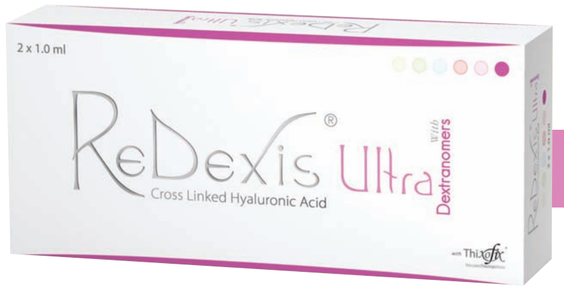




ReDexis® Ultra

Cross Linked Hyaluronic Acid with Dextranomers

ReDexis® Ultra is a fully absorbable, high viscosity dermal filler for subcutaneous injection and is designed for creating and shaping facial contours. This non animal based, HA gel utilizes the unique properties of dextranomer beads for collagen production. Its long lasting results are ideal for creating or restoring lost volume in areas such as the cheeks and the chin. Unlike other subcutaneous fillers currently on the market ReDexis® Ultra is easy to inject using only a 27G needle. An increased amount of dextranomer beads (50mg/ml) ensures maximum collagen production at the injection site for enduring results of up to 24 months.



Revanesse® Contour

Revanesse® Contour is a fully absorbable, high viscosity, clear HA gel specially formulated for body contouring and shaping. Revanesse® Contour is provided in a 10 ml syringe for large volume treatments and will break down naturally after approximately 24 months.

Safe & Effective

The HA used in the Revanesse® family of products is obtained through biosynthesis, making it safe and non pathogenic for humans. With less than 0.025 IU/mg of endotoxins and less than 2 ppm of protein*, it exceeds the highest standard of purity for HA.

The Revanesse® line of dermal fillers is completely free of all animal products, thus reducing the risk of an immunogenic reaction. The HA utilized in the Revanesse® product line is naturally integrated into the tissue keeping the skin looking healthy and natural. Because the Revanesse product line consists of non-permanent material, it allows clients the opportunity to reassess their needs throughout the course of their treatment as desired.

The safety of the Revanesse® family of fillers is our utmost concern. The following tests have been conducted on Revanesse®.

- 4 week muscle implantation
- Acute systemic injection test
- Biocompatibility test
- Cytotoxicity
- Guinea Pig maximization sensitization
- Identification: pH,osmoality, residual BDDE, sterility
- Intracutaneous reactivity
- Mutagenicity
- Protein
- Reverse mutation assay
- Tests for interactions with blood Haemolysis test
- Tests for local effect after implantation
- Acute toxicity
- Subchronic toxicity
- 26 week biocompatibility & toxicity study

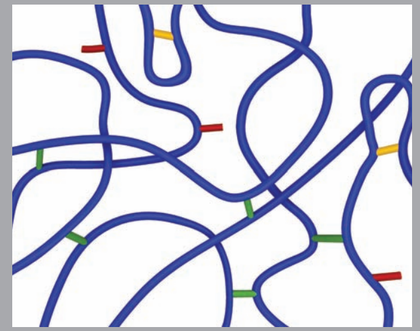
Testing by AppTec Inc., Pennsylvania, USA.

Thixofix® Cross-Linking Technology

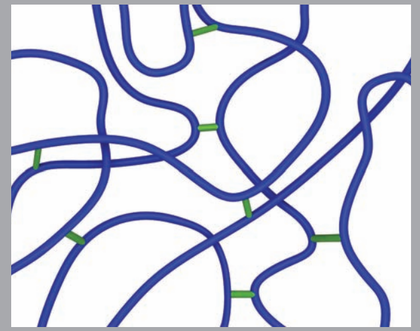
HA is a naturally-occurring polysaccharide found in the skin and other tissues and is a key component of the extra-cellular matrix. It helps to maintain hydration and contributes to the elastic properties of the skin.

Because there are many HA based fillers on the market, one may ask, “What makes the Revanesse® product line different?” The answer lies in our unique formula and patented Thixotropic cross-linking technology, which allows a highly viscous gel to be injected easily through a fine gauge needle without causing degradation to the modified HA particles.

Thixotropic fluids can, under pressure (such as the force used when injecting), increase their rate of flow then revert back to their original more highly viscous state once the pressure (i.e. the injection) has been stopped.



Other HA fillers have large amounts of dangling and ineffective internal links. These fillers require more BDDE and can lead to higher incidences of adverse reactions (such as swelling) and decreased durability in the skin.



Thixofix Technology requires less BDDE as dangling and ineffective links are minimized. This more effective cross linking technology results in a safe, long lasting product.

Effective Links

Dangling(Partially Reacted) Links

Ineffective Internal Links

Prollenium’s® precisely crafted cross-linking process is designed to maximize the effectiveness of the cross-linked HA chains present in the gel. Links between different HA polymer chains are promoted, while ineffective ‘dangling’ links and less effective links between portions of the same chain are minimized. This leads to a gel, which derives maximum benefit in terms of mechanical properties and durability, with a minimum amount of BDDE.

The state of the cross-linked HA, along with the size of the gel particles is tuned to produce a gel which flows readily through a fine needle, but which under low stress conditions after injection into the dermis has appropriate elastic properties to provide a soft, smooth feel to the augmented skin. The osmolality and pH of the gel is balanced to be compatible with the fluid in the skin, neither drawing in or releasing water. This minimizes problems of overfilling or the need for volume correction. As the filler is slowly degraded over time the cross-linked network is loosened and this allows for slow expansion of the gel particles that partly offsets the natural loss in dermal filler volume, maintaining the level of correction. The degree of cross-linking is also selected to provide a desirable level of durability in the skin.

Optimizing all these properties provides for a dermal filler with superior performance and patient satisfaction.

Thixofix®

ReticulatedThixotropicMatrix

Monophasic HA

Superior Results

HA dermal fillers typically fall into one of two categories: biphasic or monophasic. Biphasic HA products consist of particles of stabilized HA gel suspended in a non-stabilized HA fluid. In contrast, monophasic HA products, such as Revanesse®, are made entirely of stabilized, non-particle, HA gel. The benefit of this approach is two fold.

First, the body's breakdown of biphasic HA differs from that of monophasic HA. In biphasic products the fluid and gel phases behave differently. Biphasic HA experiences a rapid initial degradation of the non-stabilized HA carrier fluid and a slower degradation of the stabilized HA gel; to combat this effect the physician will over-correct to compensate for the initial rapid degradation. In contrast, monophasic HA degrades in a simple, consistent manner, allowing the physician to correct to the desired look thereby taking the guess work out of the final outcome. Additionally, monophasic HA remains cohesive when added to water (i.e. it stays together as a gel 'blob') while biphasic products are more dispersive and will separate to form visible micro particles. This explains why some patients treated with biphasic HA experience initial loss of volume with selected residual beading and patients treated with monophasic HA do not.,

Second, the entire volume of the syringe is filled with fine, soft gel particles packed together. This uniform composition leads to the desirable qualities of smoothness, uniformity, and accurate filling.

Biocompatible & Biodegradable

The Revanesse® product line integrates naturally into the tissue and allows vital nutrients such as oxygen and hormones to continue to pass through the skin. When properly injected there is no migration from the implant site.

As HA is naturally occurring in the body, these advanced filler products will eventually break down and be naturally absorbed by the body.

Durability

Once injected, HA is gradually broken degraded and absorbed by the body, which is why the process of cross-linking is crucial to the longevity of these products. The durability of HA fillers is directly related to the degree of cross-linking of the HA molecules.

The Revanesse® line of fillers employs our Thixofix™ Technology - one of the most advanced methods of cross-linking available- thereby ensuring long lasting results. This patented process also ensures that the products remain easy to inject while not sacrificing viscosity. Additionally, Revanesse® fillers exclusively use HA with a high molecular weight to achieve maximum durability and longevity. In ReDexis® the use of dextranomer beads further enhances the longevity of the product. Overall, this innovative engineering makes the Revanesse® product line unique and exceptionally durable.

Ease of Use

The greatest care has been taken to ensure that the Revanesse® line of fillers is easy to inject. We have designed our syringes to include extra wide finger flanges and broadened pistons that provide much greater ease of use. This new design allows the physician a much higher degree of flexibility when injecting.

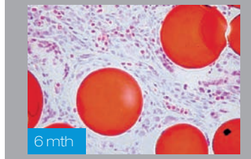
The strong shear-thinning behavior of our HA formulation enables even the highly viscous Revanesse® Ultra to be easily injected with fine gauge needles without compromising the integrity of the gel.

Benefits of Dextranomer Beads

The key ingredient in ReDexis® - positively charged Dextranomer beads – is made of biocompatible cross linked glucose molecules. These beads attract negatively charged GAG and elastin (soft tissue) to the injection site to help form new collagen. They then begin to bind together, forming a scaffold of new collagen. This new collagen will stay at the injection site, providing natural augmentation long after the HA has been broken down and absorbed. The end result is increased volume to the injection site and a longer lasting and more natural look than traditional fillers.

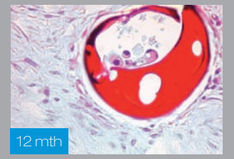
Histology Report

Dextranomer Beads used in ReDexis®/ReDexis® Ultra



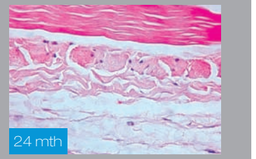
6 months: (Dextranomer beads are 100% present)

After 6 months the inter-material space is mainly composed of minute collagenous fiber bundles, varying from 1–10µm in width. Capillaries and fibroblasts are also present.



12 months: (Dextranomer beads are 40% present)

Extensive fibroblasts and collagen have formed in the inter-material space after 12 months.

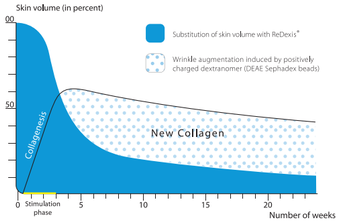


24 months: (No beads are detectable)

Complete absence of neutrophilic or lymphocytic infiltrate. Note: extensive formation of fibroblasts and collagen.

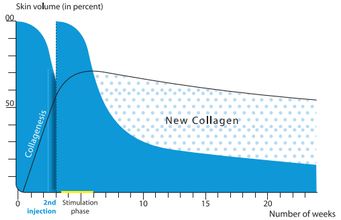
The pictures above are part of a histology test that was conducted on 3 NZW rabbits.

1st Injection



New collagen is formed after treatment with ReDexis®

2nd Injection



Follow up procedure after 2-3 weeks results in a significant increase in collagen formation.

Multi-Centre Study

A multicentre, double-blind, randomized prospective comparative evaluation of the efficacy and safety of Revanesse® Ultra versus Restylane® in patients undergoing cutaneous correction of nasolabial folds.

Study Investigators: Dr. Melvin Elson, Dr. Sheldon Pollack, Dr. Sylvia Garnis-Jones, Dr. Lisa Kellet

One hundred forty-two (142) patients had informed consent obtained for inclusion into the study, of which 130 patients were injected with both Revanesse® Ultra and Control. Of the 130 patients receiving treatment, all patients were included in safety analysis. The number of patients that completed the study (N=118) were all included in the primary efficacy analysis.

The effectiveness analysis is based on N = 118 patients for the 6 month period. The number of patients missing for follow-ups was very limited (9%) and there was no affect on the study results or the conclusions drawn from those study results.

Conclusions

Effectiveness

Revanesse® Ultra met the primary effectiveness endpoint of equivalency when compared to Control using the WSRS after 6 months.

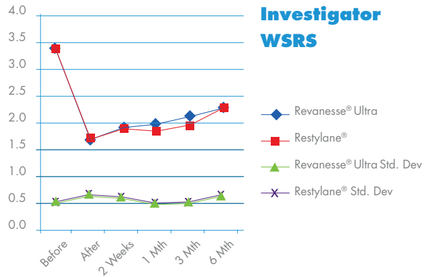
Revanesse® Ultra also met all the secondary endpoints determining that the efficacy of Revanesse® Ultra is comparable to Control using both the Investigator and Patient GAIS as well as Patient WSRS as the measurement tools.

Each of the three blinded Investigators independently rated Revanesse® Ultra in the same manner that resulted in the conclusions. Furthermore, the single blinded Investigator assessed efficacy using photographic based WSRS and GAIS, which also showed that Revanesse® Ultra is equivalent to Control at 6 months. The amount of Revanesse® Ultra injected was similar to Control.

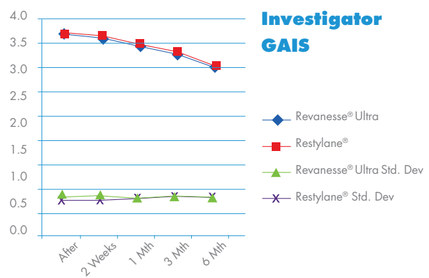
Safety

The clinical trial established Revanesse® Ultra as being a safe device for soft tissue augmentation for the treatment of NLFs. The adverse events that were reported were not unexpected with most being mild in nature, short in duration and not requiring treatment.

It is important to note that there were no reports of granulomas, erosion, necrosis, infection or hematomas during the course of the study.



Wrinkle Severity Rating Scale



Global Aesthetic Improvement Scale

Patient and Physician Satisfaction

Figure 1

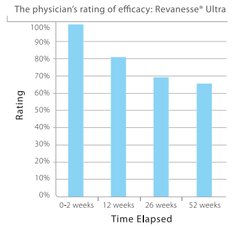


Figure 2

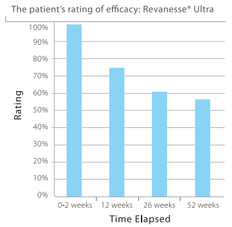


Figure 3

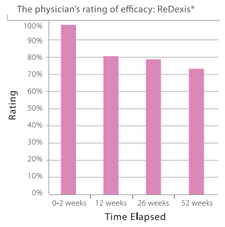
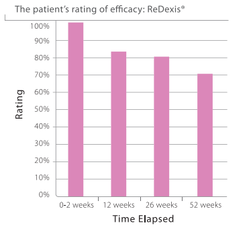


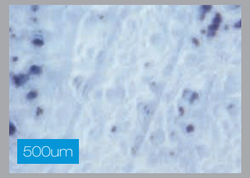
Figure 4



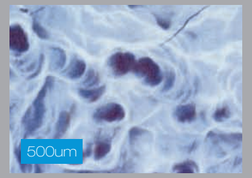
Results based on a 120 patient single centre study conducted in Germany. The result of this study suggest that the combination of positively charged dextran beads and a highly bio-compatible liquid polymer medium like reticulated hyaluronic acid, with or without dextranomer beads induced significant and safe tissue augumentation. Revanesse® Ultra and ReDexis® fulfil the expectations of a safe and efficient tissue augmentation material.

Chemical/Physical Characterization

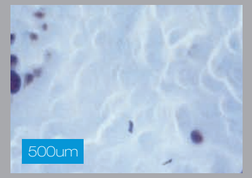
A 500µm microscopy photo reveals the smaller particle size and more uniform dispersion of the particles of Revanesse® vs. other popular HA based fillers. This results in a more homogenous gel that is smoother to inject and easier to mold.



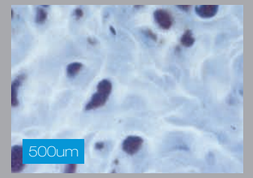
Revanesse ® Ultra



Juvederm ®



Restylane ®



Captique ®

Product Outline

	Revanesse® Pure	Revanesse®	Revanesse® Ultra	Revanesse® Lips	ReDexis®	ReDexis® Ultra
Indication	Bio-Revitalization	Small to Medium Lines & Wrinkles	Mid to Deep Lines & Wrinkles	Lip Augmentation	Mid to Deep Lines & Wrinkles	Subcutaneous Volumetric Contouring
Composition – Stabilised HA	14mg/ml non cross linked	25mg/ml	25mg/ml High Viscosity	25mg/ml	25mg/ml	17mg/ml
Composition – DEAE Sephadex					25mg/ml	50mg/ml
Degree of Cross Linking	–	**	****	***	***	***
Needle Used – Mid	30 G or 32 G	30 G	30 G			
Needle Used – Deep		27 G	27 G	27 or 30 G	27 G	27 G
Injection Depth	Superficial Dermis	Mid Dermis	Mid-Deep Dermis	-	Subcutaneous	Subcutaneous/Periosteum
Duration	+	6 months	9-12 months	6 months	12-18 months	18-24 months

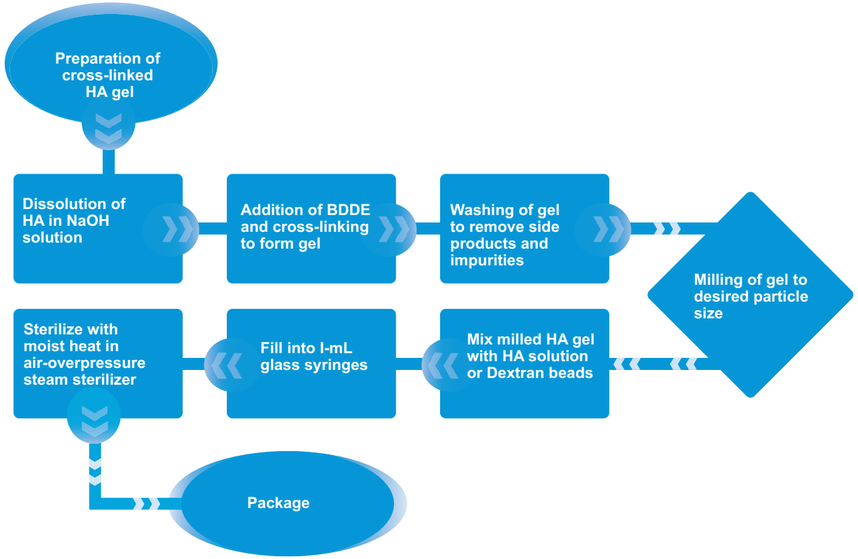
+ Revanesse® Pure is not intended to be used as a dermal filler as it is a Bio-Revitalization implant.

Revanesse® vs. Other Fillers

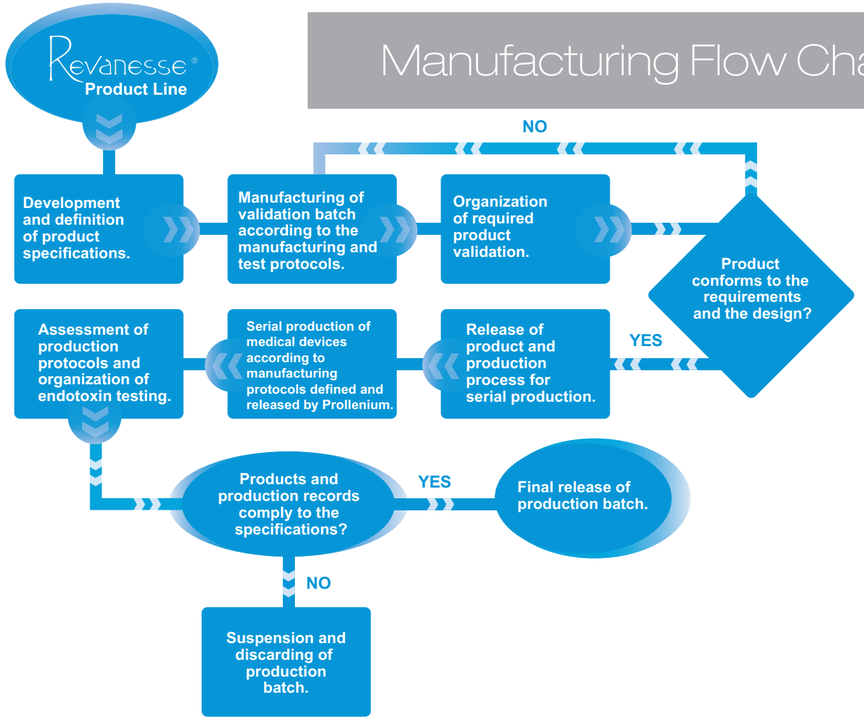
	Stabilised Hyaluronic Acid	Other Ingredients	Source	Syringe Size
Revanesse®	25mg/ml	-	Non Animal	1.0ml
Revanesse® Ultra	25mg/ml	-	Non Animal	1.0ml
ReDexis®	25mg/ml	25mg sephadex	Non Animal	1.0ml
ReDexis®Ultra	17mg/ml	50mg sephadex	Non Animal	1.0ml
Juvederm® Ultra/Plus	24mg/ml	-	Non Animal	0.8ml
Restylane®	20mg/ml	-	Non Animal	1.0ml
Perlane®	20mg/ml	-	Non Animal	1.0ml
Radiesse®	-	CaHa	Non Animal	1.3ml

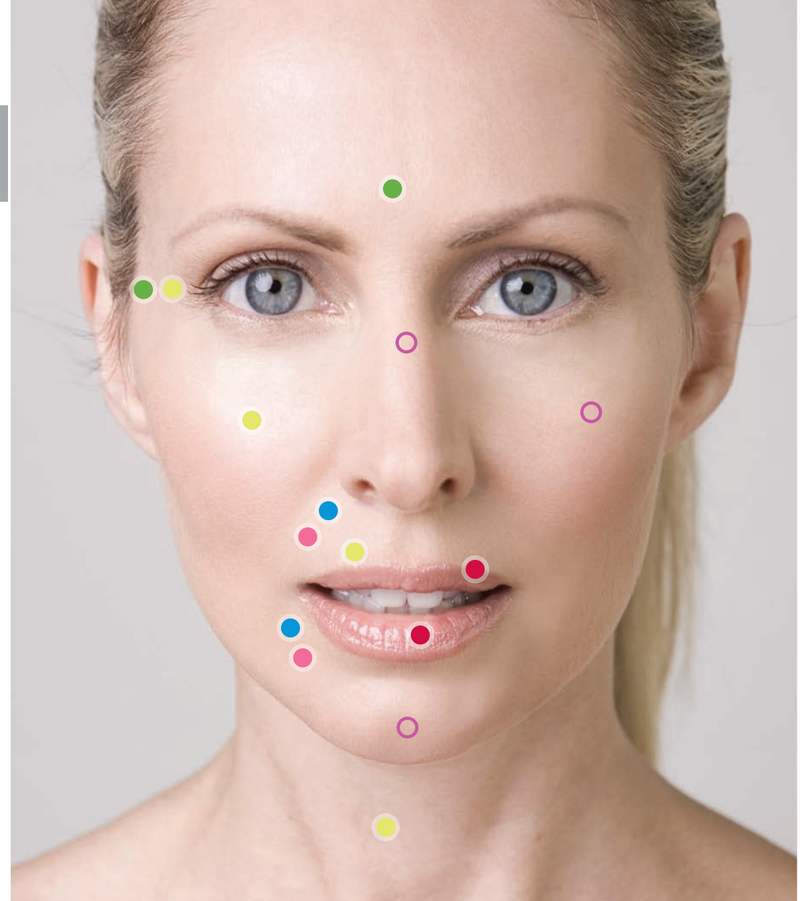
- Juvederm® is a registered trademark of Allergan Inc.
- Restylane® Touch and Perlane are registered trademark of HA North American Sales.
- Radiesse® is a registered trademark of Bioform Medical Inc.

Product Synthesis Flow Chart



Manufacturing Flow Chart





Revanesse® Pure* Revitalisation Implant ▸ 1

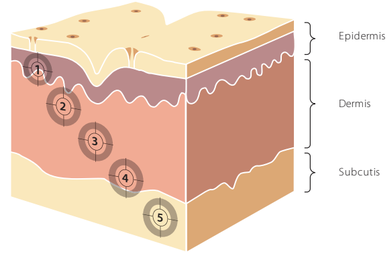
Revanesse® Cross Linked Hyaluronic Acid ▸ 2 & 3

Revanesse® Ultra Cross Linked Hyaluronic Acid – High Viscosity ▸ 3 & 4

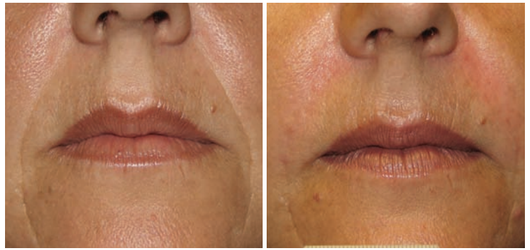
Revanesse® Lips Cross Linked Hyaluronic Acid ▸ —

ReDexis® for Dermatologists Cross Linked Hyaluronic Acid ▸ 5

ReDexis® Ultra for Dermatologists Cross Linked Hyaluronic Acid ▸ 5

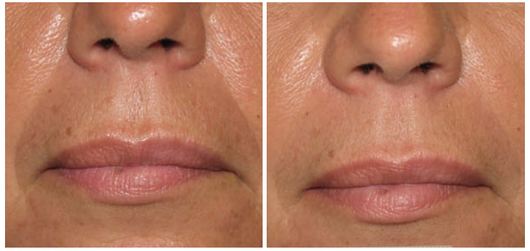


Before & After



BEFORE

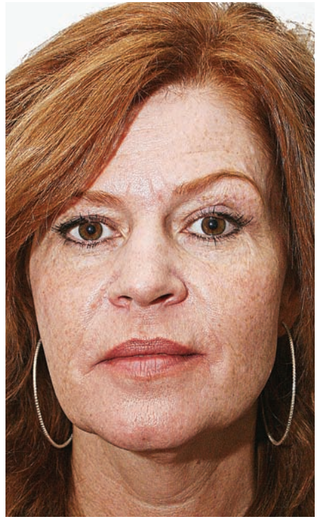
AFTER



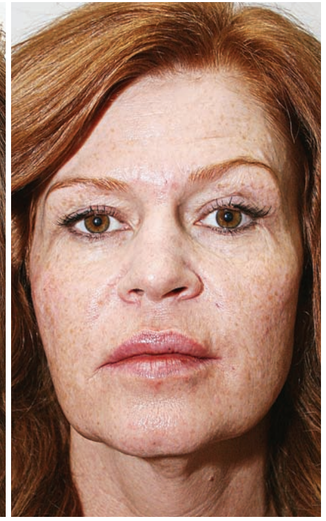
BEFORE

AFTER

Patients treated with 1ml of Revanesse® in each nasolobial fold. Pictures taken after 6 months.



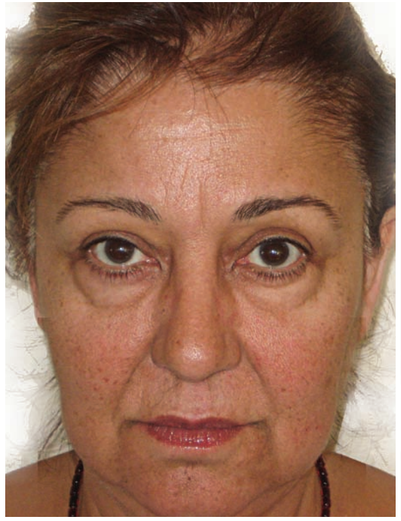
BEFORE



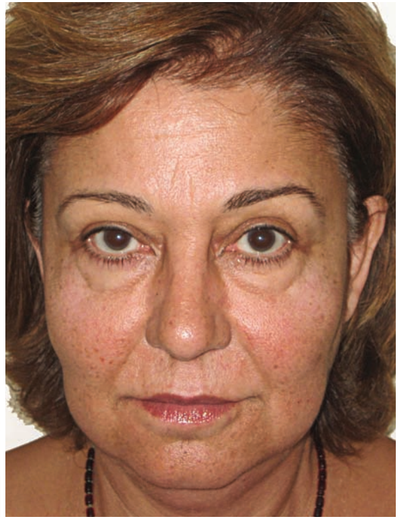
AFTER

Patient treated with 3ml of Revanesse®. Patient also received IPL treatment for pigmentation

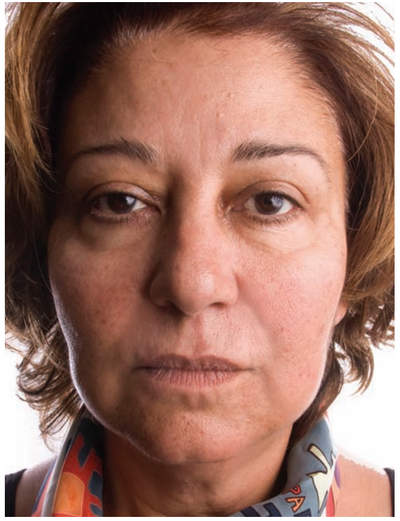
Augmentation after multiple syringes of Revenasse® Ultra results in a more aesthetically pleasing outcome.



BEFORE

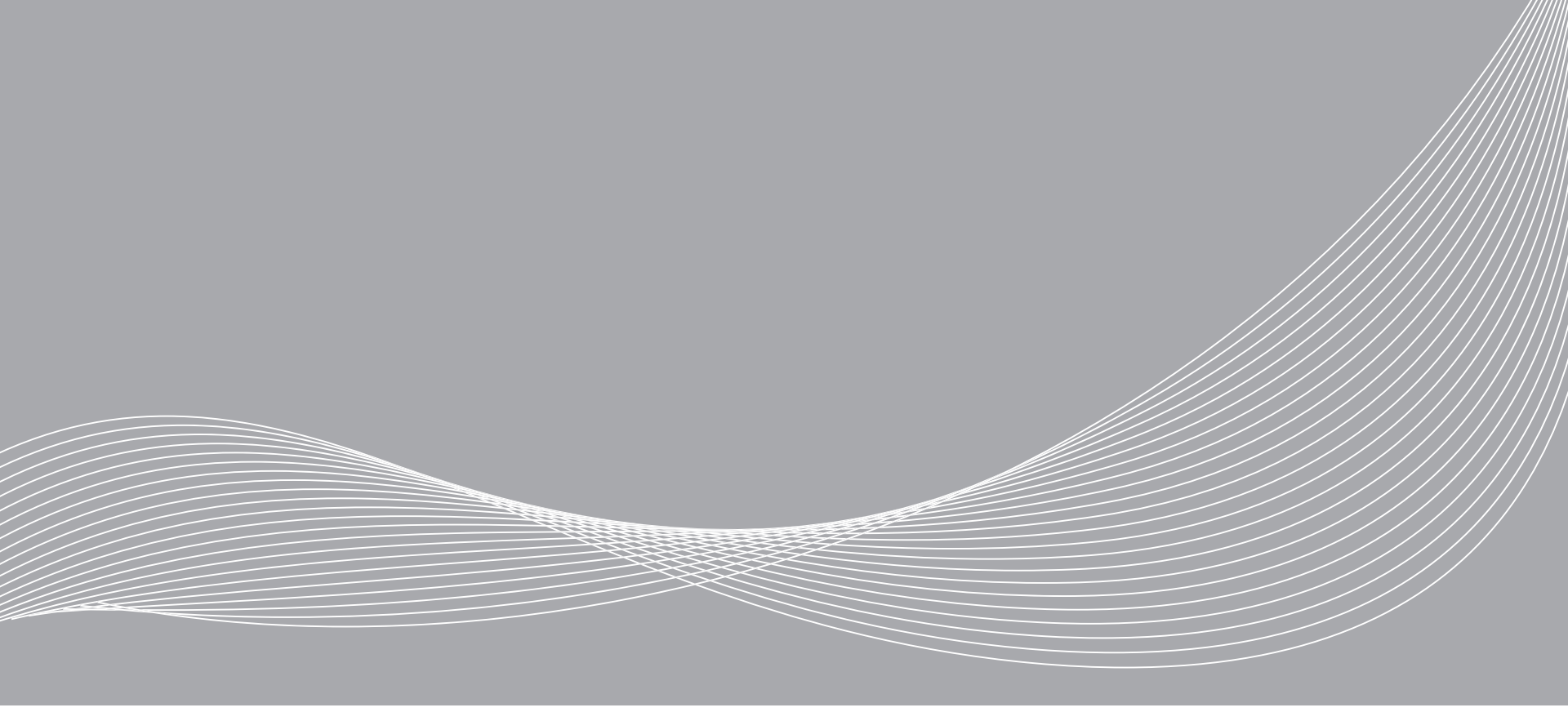


AFTER 4 SYRINGES



AFTER 8 SYRINGES*

Patient also received IPL treatment for pigmentation



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