Clinical Guide to Restylane®
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Introduction to esthetic treatment

Esthetic treatment

Esthetics is a branch of philosophy concerned with beauty and taste, while treatment can be defined as the treatment of a disease or disability, or a healing power or quality. The term esthetic treatment can therefore be interpreted to mean a treatment for the restoration of beauty. In this short overview the focus will be on the use of esthetic treatment as a means of restoring or improving facial beauty.

Since ancient times, women and men have used various means to improve or restore their facial beauty or mask the signs of skin aging. At certain ages or under certain conditions more effective methods have been sought to achieve the desired effect. Esthetic treatments have therefore been developed to provide more effective alternatives for those wishing to improve their facial appearance.

Structure and function of the skin

Successful esthetic treatment requires a thorough understanding of the structure and function of the skin. The total surface of the skin measures approximately 2 m² and weighs about 2 kg. The skin has a multitude of functions acting as a physical barrier against ultraviolet (UV) radiation, water, chemicals, bacteria, fungi and trauma. It also has an immunological function and regulates body temperature. Sensory nerve endings in the skin detect pain, touch, cold and heat, while vitamin D – critical for the mineralization of bones – is synthesized in the skin through the action of UV radiation. The skin may also play a role in reproductive function as sexual attractiveness is influenced by both the visual appearance and smell of the skin.

The skin comprises three layers: the epidermis, dermis and subcutis (Figure 1).

The epidermis is subdivided into the basal cell layer, squamous cell layer, granular layer, clear layer and outer cornified layer (stratum corneum). The thickness of the epidermis varies across the body; for example, the epidermis of the eyelid is about 0.05 mm thick, while on the soles of the feet it is about 2 mm thick. The cellular population of the epidermis consists largely of keratinocytes, with smaller populations of melanocytes (responsible for skin pigmentation) and Langerhans’ cells (immunologically active cells). The keratinocytes of the basal cell layer undergo cell division and differentiate as they migrate upwards through the strata, becoming flattened, losing their nuclei and filling with keratin. At the stratum corneum flakes of dead cells are found surrounded by lipids. These are called cornocytes and form the principal skin barrier against water loss. Cell turnover from the basal layer to the stratum corneum takes approximately 4 weeks in a healthy individual. Due to the lack of vascularization within the epidermis, nutrients and water must passively diffuse or be actively transported from the dermal layer located beneath.

The upper part of dermis is denoted papillary dermis, comprising fine elastic fibers, and below it the thicker reticular dermis. The dermis varies in thickness from 0.5 mm on the eyelids to 3 mm on the back. The cell population in this layer consists mainly of fibroblasts which synthesize and maintain components of the extracellular matrix. These components bind water to produce a viscoelastic gel that allows nutrients, hormones and waste products to pass through. The extracellular matrix also gives strength and flexibility to the skin, and acts as a ’shock absorber’. Some of the important components of the extracellular matrix include collagen, which prevents the skin from tearing when stretched, elastin that gives the skin its elasticity, and hyaluronic acid, which binds water and creates volume in the skin. Other components of the dermis include mast cells, lymphocytes, lymph vessels, sebaceous glands, free sensory nerve endings, hair shafts and bulbs, and sweat glands. The dermis is vascularized by a network of capillaries within its deeper layers.

The third layer of the skin is the subcutis, which consists of subcutaneous fat. In addition to acting as a reservoir for energy, this layer has a mechanical protective role.

<table>
<thead>
<tr>
<th>Epidermis (0.15-0.50mm)</th>
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<tbody>
<tr>
<td>Dermis (1-3mm)</td>
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<tr>
<td>Subcutaneous tissue</td>
</tr>
<tr>
<td>Muscle tissue</td>
</tr>
<tr>
<td>Bone tissue</td>
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</tbody>
</table>

Figure 1. Cross section through the skin.

Restylane Vital™
Restylane Touch™
Restylane®
Restylane Perlane™
Restylane SubQ™
Mechanisms of skin aging
Skin aging is a complex process involving many different mechanisms. These can be divided into intrinsic mechanisms (e.g. the biological clock), which affect all three layers of the skin, and extrinsic mechanisms related to environmental and lifestyle factors. The visual signs of skin aging are mostly related to extrinsic factors with photaging of the skin by UV radiation from over-exposure to the sun being a major cause. Other important factors are smoking (which damages the vasculature of the skin), alcohol, food intake and sleeping habits. The most effective methods to counteract skin aging are avoiding overexposure to the sun, and not smoking. Photaging mainly affects the epidermis and dermis, as UV radiation seldom reaches the subcutis. Epidermal changes from UV exposure include roughening of the skin’s surface texture, increased scaling and changes to skin pigmentation. In the dermis, collagen and elastin are degraded, affecting the function of endogenous hyaluronic acid. The net result is that skin elasticity and water-binding capacity decrease, and subcutaneous fat undergoes partial atrophy and redistribution. Thus, the visual signs of aging, such as alterations in skin texture and pigmentation, wrinkles and sagging of the skin, directly correspond to the effects of UV radiation on different layers of the skin.

Approaches to esthetic treatment
Given the diverse nature of the processes which contribute to skin aging, successful esthetic treatment for facial rejuvenation requires the choice of treatment to be tailored to the underlying damage. This highlights the importance of understanding the mechanisms of skin aging when choosing the right procedure or combination of procedures for esthetic treatment. For example, a face-lift procedure might tighten up the texture of aging skin, but will not counteract any three-dimensional changes that have taken place in the surrounding tissues such as bone resorption and fat atrophy/redistribution. Additionally, changes in skin pigmentation occurring over time will not be addressed by a face-lift. A number of non-invasive treatments are available for facial rejuvenation. Lasers have been used to correct pigmentation changes, activate components in the dermis and remove small superficial vessels and wrinkles. Under certain circumstances lasers can also be used for lipolysis and dermabrasive therapy of the skin. Lasers are also used in photodynamic therapy to activate a photosensitizer that destroys diseased cells. This approach was originally used for the treatment of pre-malignant skin conditions and basal cell carcinoma, but has also proved effective in cosmetic applications. Intensive pulsed light has been used for hair removal and for the treatment of small superficial vessels and pigmentation changes in the skin.

Skin peeling is a procedure aimed at removing old skin components and stimulating the function of newly formed skin components in order to achieve facial rejuvenation. This procedure is also useful to treat superficial changes in skin pigmentation. Usually several treatments sessions are required and some procedures (e.g. chemical peeling) require extended pre-treatment periods and significant downtime can be expected following treatment.

Other non-invasive techniques include monopolar radio frequencies to deliver energy for the removal of wrinkles and folds, an effect that has been attributed to the tightening of collagen in the dermis. Botulinum toxin has also proved effective for the treatment of dynamic wrinkles as well as modulating facial expression, by causing relaxation of the facial muscles. However, a major disadvantage of these non-invasive techniques is that they do not directly address the loss of skin volume or hydration, or fat atrophy that may have occurred as a result of aging. In these circumstances it is necessary to augment the skin with a filler material.

The first products developed for facial tissue augmentation were permanent dermal fillers and contained substances such as silicone, followed in the early 1980s by bovine collagen implants. More recently, animal-derived hyaluronic acid products and a diverse range of semi-permanent and permanent dermal fillers have become available. Some of these products are associated with a relatively high frequency of complications while those of animal origin require pre-testing to avoid hypersensitivity reactions. Permanent and semi-permanent fillers should be used with great caution since the risk of eliciting a foreign body response persists as long as the filler is present within the tissue. Furthermore, aging-related changes in the tissue surrounding the dermal filler may lead to the development of local facial asymmetries.

Restylane®: a new approach to facial tissue augmentation
The introduction in the mid-1990s of stabilized hyaluronic acid-based gels of non-animal origin founded on the patented NASHA™ technology of Q-Med AB, Uppsala, Sweden, set a new gold standard in facial tissue augmentation. Various injectable NASHA™ based gels including Restylane®, Restylane Perlane®, Restylane Lipp™, Restylane SubQ™ and Restylane Touch™, have been developed as instant esthetic treatments for facial soft-tissue augmentation. The Restylane range of products are characterized by a non-permanent, but long-lasting duration of action, and have demonstrated good efficacy and safety profiles during extensive clinical testing. Since NASHA™ based gels are stabilized to result in minimal modification of the hyaluronic acid, these dermal fillers have a high degree of biocompatibility. Many biodegradable dermal fillers shrink gradually upon degradation, but NASHA™ based gels have the unique property of maintaining their volume throughout this process. Due to isovolemic degradation, the gel molecules are able to take up more water as it is broken down. Variations in particle size and cohesive properties of different Restylane dermal fillers allows for true tissue tailoring, with the type of filler matched to the tissue layer into which it will be placed. This results in superior lifting capacity and minimal matrix disturbance.

The diverse collection of products in the Restylane range provides numerous options for facial tissue augmentation (i.e. increase of the skin/tissue volume), including the correction of lines and folds, contouring of three-dimensional topography and enhancement of individual facial esthetics. In addition to facial tissue augmentation, the NASHA™-based product range Restylane Vital™ rejuvenates the skin by improving skin structure. The treatments restore skin hydrobalance and improve elasticity to create a fresh and natural look.

A thorough understanding of the structure and function of the skin and the mechanisms involved in skin aging has allowed for the development of highly effective esthetic treatment. The ability to determine the type and extent of skin damage in a particular patient enables tailoring of treatments specifically to the individual. The Restylane range of NASHA™ based products offers effective and biocompatible solutions for tissue augmentation and rejuvenation, and as clinical experience with these products increases, further beneficial effects of hyaluronic acid placement in the skin will continue to emerge.
NASHA™ technology

In 1998, Q-Med AB patented the NASHA™ technology, a science-based technological platform that makes it possible to design products with special properties to address different intended uses and patient needs.

The cornerstones of the NASHA™ technology are to:

- Use pure hyaluronic acid of non-animal origin. The hyaluronic acid (HA) is manufactured biotechnologically by using cultured bacteria to obtain a very pure and consistent material.

- Stabilize the hyaluronic acid raw material. A minimal modification (< 1 %) is introduced to the hyaluronic acid molecule to obtain the desired physical form and to increase its residence time in the body.

The stabilization of HA thus onsets the development of Q-Med’s NASHA™ gel implants, characterized by long duration and superior tissue biocompatibility. Both properties are distinctive advantages for medical and esthetic applications.

Hyaluronic acid

HA exists naturally in living organisms and is identical between species and tissues. HA was first isolated in 1934 from the vitreous of bovine eyes. In the last two decades its applications have extended to many biomedical areas, including the treatment of joint pain, fertility and medical esthetic applications.

HA is a polysaccharide made up of repeating disaccharide units, comprising D-glucuronic acid and N-acetylglucosamine.

Independent of its origin hyaluronic acid contains only these two sugar units. The identical structure of the HA molecule within and between species, is of significance from a biological perspective – HA is thus an ideal material for medical use, due to its inherent biocompatibility.

Approximately 56% of the body’s HA is found in the skin. The dermis comprises a matrix of collagen and elastin fibers, suspended in an HA-rich extracellular matrix. The environment created by HA offers resistance to compression and protects the structures underlying the skin from physical damage. HA also performs a lubricating function, and enables the skin to accommodate changes in shape and volume that occur when bones and joints move.

The distribution of endogenous HA in the skin and throughout the body changes over time. Less accessible HA and thereby a diminished capacity for water-binding of the HA molecule leads to loss of volume of the skin, wrinkle formation and the characteristic signs of aging.
Biocompatibility

Q-Med uses biotechnologically obtained HA as raw material in the manufacturing process of esthetic and medical gel implants. The HA used in the manufacturing process of Q-Med gel implants is produced by bacterial cells. By using bacteria as a source for HA the risk of having products contaminated with, for example, viruses or proteins from animal sources has been abrogated. In addition, the carefully controlled fermentation process, by which the HA is produced, will minimize the presence of potentially harmful components, such as proteins, endotoxins and other impurities. The HA thus obtained is characterized by a high degree of purity.

The biocompatibility of Q-Med esthetic and medical implants has been tested in accordance with the guidelines of the ISO 10993 standard on Biological Evaluation of Medical Devices. These tests have shown that the gel implants have a very good safety profile. They do not cause any local or systemic toxic effects, they are not genotoxic, and they are not sensitizing or irritating.

Half-life in the skin, stabilization and isovolemic degradation

The half-life of HA is <24 hours in the skin. This is why the body’s own HA is not effective as implant material. Stabilization of the HA molecule is thus essential to achieve the desired effectiveness of a medical esthetic implant.

Q-Med’s esthetic and medical gel implants, such as Restylane contain stabilized HA - manufactured with Q-Med’s patented NASHA™ technology. Using this technology, HA molecules are modified to a very minor degree (<1%). Stabilization results in a 3-dimensional hyaluronic acid gel matrix through a minimum degree of binding between neighboring HA molecules. Gel particles of different sizes are thereafter produced for different esthetic and medical applications. Q-Med’s NASHA™ technology thus allows the manufacture of products with physical characteristics that match the intended uses. (Figure 2)

Restylane gel injected in tissues as esthetic implant, results in tangible, long-lasting (up to 1 year) volume enhancement effects, as a consequence of the unique stabilization process and the structural characteristics of the resulting gel particles. The removal of the gel implant in time occurs through the degradation of the three-dimensional gel matrix. HA chains are slowly released from the gel and biodegraded by the same mechanisms as those that degrade the body’s own HA. This occurs very slowly, by a process called isovolemic degradation, which preserves implant volume over time (Figure 3).
**Key benefits – NASHA™ technology**

**Non-permanent products**

NASHA™ products consist of a crystal clear gel of stabilized hyaluronic acid. The gel is biocompatible and readily becomes integrated into the tissue. It is non-permanent, i.e. it is biodegraded by the body's own mechanism and will thus disappear naturally over time.

**Superior lifting capacity**

NASHA™ gels are characterized by a superior skin lifting capacity, i.e. the ability to lift the skin under a wrinkle or a fold to achieve the desired esthetic effect. This is achieved by the structure and properties of NASHA™ gels. The treatment will result in increased dermal volume and plump tissue which characterize young skin.

**Skin rejuvenation**

Kerscher et al studied the rejuvenating influence of Restylane Vital™ on aged facial skin and found that the treatment generated a significant increase in cutaneous elasticity and also a significant decrease in skin surface roughness.

**Tissue-tailored for maximum esthetic effect**

The gel particle size in Restylane products, is carefully designed for injection into different dermal layers, to support different esthetic applications. This so-called tissue-tailoring concept enables the gel to match the density of the target tissue for which it is intended, resulting in a long-lasting esthetic enhancement. The versatility of the Restylane gel product range allows you to optimize the esthetic enhancement effect for each individual patient. (**Figure 4**)

**Scientifically documented efficacy**

Q-Med has through several scientifically documented clinical studies obtained an extensive amount of data demonstrating the efficacy and the duration of the NASHA™ gels. Clinical trials show that the duration of the esthetic enhancement lasts considerably longer than several other non-permanent esthetic treatments. The response is individual and depends on the injected NASHA™ gel and the desired esthetic effect.

**Compliance with international safety standards**

- NASHA™ gels contain stabilized hyaluronic acid of non-animal origin. Therefore there is essentially no risk of inflammatory reactions due to the presence of potentially harmful contaminants such as viruses, proteins and endotoxins, as is the case when using products containing hyaluronic acid from animal sources.

- All Q-Med’s esthetic and medical implants are moist heat sterilized for maximum safety and comply with international EU safety standards. The manufacturing process for the Restylane product range complies with the internationally recognized ISO 13485:2003 standard, and the local requirements of markets where the products are registered. Restylane was the first HA-based dermal filler approved by the FDA.

- NASHA™ gels are associated with a minimal rate of transient adverse events (0.04 -0.15 %), after > 10 million reported treatments worldwide. The most commonly observed adverse events are injection-related reactions such as swelling, erythema, tenderness and pain, which resolved spontaneously within 1-2 weeks. There have been no reported implant rejection problems.

- The clinical documentation obtained through investigator initiated studies (IIS) and Investigator Sponsored Studies (ISS) on the safety of NASHA™ gels is readily available to all customers.

**Product development through science**

- Q-Med has a well developed Research and Development (R&D) department constantly working on product innovation and optimization of treatment techniques.

- All NASHA™ gels are specially designed in order to meet the patient's needs and the anatomy and physiology of the skin. Gel particle size, structure and characteristics are carefully adjusted to match the different layers of the skin and the various intended uses, in order to achieve maximum esthetic results.
Figure 4. Tissue-tailoring concept.
Restylane® range of products overview

Restylane® was the first hyaluronic acid product to be approved by the FDA for esthetic use. It is specifically designed to reduce the appearance of moderate facial wrinkles and folds, such as frown and glabellar lines. It may also be used to treat smile lines and marionette lines at the corners of the mouth.

Restylane Perlane™ is used for the correction of deeper wrinkles and folds such as nasolabial folds. It is also a powerful tool for shaping facial contours, and provide minor to moderate contouring of the cheek or eyebrow area, accentuating the existing features.

Restylane Touch™ is designed to reduce the appearance of fine, superficial lines such as the periorbital and perioral lines. It can also be used to reduce scars.

Restylane Lipp™ is designed to meet the specific, highly dynamic demands of the anatomy of the lip. It is structured to withstand the strains associated with the full range of mouth movements. Restylane Lipp is designed to provide lip enhancement over time.

Restylane SubQ™ is designed for volumetric contouring of facial features. It is injected deeply to add volume, which supports the overlying tissue to provide facial fullness and restore symmetry. This treatment is ideal for patients with flattened facial features, or those with an unbalanced or asymmetrical face. It is also suitable for patients reluctant to undergo facelift surgery or the insertion of permanent implants.

Restylane Vital™ is a smooth NASHA™ gel designed to restore and maintain skin hydrobalance. It improves the elasticity and smoothness of the skin. Restylane Vital is ideal for rejuvenation of mature and photodamaged skin.

Restylane Vital should be given in a treatment cycle of 3 sessions 4 weeks apart, to be repeated after 6 months.

Restylane Vital™ Light is designed for younger, thinner skin which requires a lighter rejuvenating effect. Restylane Vital Light is a smoother and more fluid gel which adjusts well to delicate skin. Restylane Vital Light is therefore suitable for areas with thin skin such as neck, décolletage and the back of hands.

Restylane Vital Light should be given in a treatment cycle of 3 sessions 2-4 weeks apart, to be repeated after 4-6 months. Individual treatment programs can be designed according to the quality of the skin area treated.

<table>
<thead>
<tr>
<th>Product</th>
<th>Recommended indications</th>
<th>Where to inject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restylane®</td>
<td>Moderate facial wrinkles</td>
<td>Mid dermis</td>
</tr>
<tr>
<td>Restylane Perlane™</td>
<td>Deep wrinkles and folds, facial contouring</td>
<td>Deep dermis/ upper subcutaneous layer</td>
</tr>
<tr>
<td>Restylane Touch™</td>
<td>Fine superficial lines</td>
<td>Upper dermis</td>
</tr>
<tr>
<td>Restylane Lipp™</td>
<td>Lip enhancement</td>
<td>Deep dermis/ upper subcutaneous layer</td>
</tr>
<tr>
<td>Restylane SubQ™</td>
<td>Facial contouring/chin and cheek augmentation</td>
<td>Deep subcutaneous layer or supraperiosteal</td>
</tr>
<tr>
<td>Restylane Vital™</td>
<td>Rejuvenation of mature and photodamaged skin</td>
<td>Dermis, preferably deeper</td>
</tr>
<tr>
<td>Restylane Vital™</td>
<td>Rejuvenation of thin skin areas and younger skin</td>
<td>Mid-dermis</td>
</tr>
</tbody>
</table>
Indications that can be treated with Restylane®

Upper face
- Worry lines
- Glabellar lines
- Eye brow
- Forehead

Middle face
- Tear trough
- Periorbital lines
- Cheek augmentation
- Nose
- Nasal bridges
- Ear lobes

Lower face
- Nasolabial folds
- Perioral lines
- Smile lines & oral commissures
- Lip enhancement
- Chin augmentation

Skin rejuvenation
- Face
- Neck
- Décolletage
- Hands
The treatment session

Initial consultation
- Inform the patient about the procedure and the possible outcome as well as of the possibility of side effects. Answer any questions or address any concerns they may have. A brief medical history should be taken with special reference to any bleeding disorders or previous skin therapies, e.g. tissue augmenting or laser and peeling procedures.
- Discuss the appropriate indications, risks, benefits and expected responses to the treatment.
- Advise the patient that the treatment takes approximately 30 minutes and that the final result may take a few days to see as there may be some initial redness or swelling.
- Advise the patient of the necessary precautions before commencing the procedure.
- A patient brochure is available from Q-Med for additional information to read.

Inform the patient about Restylane®
- Emphasize that the Restylane range of products consist of stabilized non animal hyaluronic acid gel which is almost identical to the body’s own hyaluronic acid.
- The Restylane range of products cover many areas of interest when considering facial treatment such as restoring hydrobalance and increasing elasticity of large skin areas, correction of lines and folds, contouring of the three dimensional topography and enhancement of facial esthetics as requested on an individual basis.

Managing patient expectations
- It is recommended that the reason for the patient seeking treatment and the suitability of the treatment modality for the site and indication be discussed.
- Pre- and post-treatment photos are recommended.
- Inform the patient that touch ups may be necessary within 2-4 weeks to achieve optimal results.
- Recommend a maintenance plan similar to other beauty regimes. Timing depends on indication treated, the patient’s intrinsic and extrinsic factors and the degree of perfection expected by the patient.

Pain management
- Assess the patient’s need for pain management. Offer a variety of choices such as using ice, EMLA or anesthesia and discuss the risks and benefits with each patient. For lip enhancement a dental block may be advisable.

Treatment with the Restylane range of products
- It is strongly recommended that a signed informed consent form is obtained from the patient prior to a treatment. These can be obtained from Q-Med in several languages.
- Remove any make up and clean the treatment site with an antiseptic solution.
- Remove the patient record label (removable label on the syringe) and attach it in the patient record form, this ensures traceability in case of any adverse events or other issues that may come up. Record forms are available from Q-Med in several languages.
- There is a variety of injection techniques available to choose from. Which technique to use will depend on a variety of factors such as indication to be treated, individual patient needs, and personal preference on the practitioner part. The various injection techniques available are discussed further on this clinical guide for Restylane.

Combination treatments
- For combination treatments such as with botulinum toxin, laser or chemical peeling, a treatment plan needs to be set up to avoid suboptimal results of the Restylane treatment.

Post treatment
- Provide the patient with a post treatment checklist. These can be obtained from Q-Med.
- Provide the patient with contact details in case of questions or concerns that may arise after leaving the clinic.
Injection techniques

There are various techniques available. The following techniques recommended for use with the Restylane® range of products have been selected based on usage during clinical trials with the Restylane range of products or as recommended in peer reviewed journals. A number of important factors must be considered when selecting the technique to be used, including the area to be treated, depth of the injection, volume of the product injected, and technical features related to the needle. Certain techniques may require the use of several needles in order to maintain patient comfort throughout the treatment. As with all injection procedures/techniques, before injecting, the air should be removed from the syringe up to the point where a droplet is visible at the tip of the cannula/needle.

Basic techniques

Serial puncture technique
Multiple injections are closely spaced punctures along fine lines, wrinkles and folds. The serial placements of the product within the skin should join together into a smooth continuous line. There should be no spaces between the injected material. (Figure A)

Linear/serial threading technique
The full length of the needle is inserted in the middle of the wrinkle. Restylane is injected while pulling the needle slowly backwards (retrograde). The “threads”, each approximately 10 mm long, are injected along the length of a facial defect or area of desired enhancement. Together the threads will form one single string, lifting the wrinkle to the desired level of correction. Serial threading combines the serial puncture and linear threading techniques. (Figure B)
Advanced techniques

For large areas and facial shaping

**Fanning technique**
Insert the needle at the periphery of the area intended to be augmented as when using the linear threading technique. After injecting one line do not withdraw the needle from the skin. Instead, change the direction of the needle and inject as before along a new line and repeat this in a fan-shaped pattern. In this way a relatively large area can be covered while minimizing the number of puncture sites through the skin. *(Figure C)*

**Cross-hatching technique**
Insert the needle at the periphery of the area intended to be augmented and inject as when using the linear threading technique. Withdraw the needle from the skin and insert it 5-10 mm adjacent to the first puncture site and inject in the same way. This procedure can then be repeated from different sites around the area to be treated and at slightly different levels. *(Figure D)*
Advanced techniques

For volumetric contouring

Transdermal injection technique using a blunt cannula
Create a transdermal aperture using an 18G needle or a number 11 blade scalpel to facilitate entry of the cannula. Insert the cannula through the aperture. Determine the position of the cannula tip prior to injecting the product. Tent the overlying tissue with the tip of the cannula to ensure the correct depth for injection. Inject small aliquots in a retrograde fashion while withdrawing the cannula creating tunnels along the way, with the cannula facing downwards. Do not apply excessive pressure to the syringe at any time. If resistance is encountered the cannula/needle should be partially withdrawn and repositioned or fully withdrawn and checked for function. Do not inject superficially. Avoid injecting when removing the cannula. Leave a clear/empty zone from the point of incision. (Figure E)

Transdermal injection technique using a sharp needle
Inject using a perpendicular technique, i.e. vertically insert the needle down to the bone/periosteum. Aspirate before injecting to make sure not injecting intravascularly. Inject a small bolus slowly and while retracting the needle, taking care not to inject to close to the skin (to superficially) Stop injecting the product, withdraw the needle and move to an adjacent site. Repeat the process. (Figure E)

Micropuncture technique
Inject very small amounts intradermally (mid to deeper part of dermis) of micro deposits about 1 cm apart. Repeat the procedure over the selected skin area. (Figure F)

Short linear threading technique
Insert approximately two thirds of the needle in mid-dermis. While retracting the needle in a retrograde direction, gently press the plunger for three separate depositions of product. Avoid depositing product to close to each other. Adjust plunger pressure to the needed extrusion force for each product used (the force to extrude Restylane Vital Light is lower than for Restylane Vital). (Figure G)

For skin rejuvenation

Transdermal injection technique using a blunt cannula / sharp needle

Figure E

Figure F

Figure G
Skin rejuvenation using the Restylane® Injector

The Restylane® Injector assist in the delivery of Restylane Vital Light and gives predictable treatment results. This unique injection device enables an even volume distribution over large skin areas giving a controlled dosage of 10 µl of gel per injection site. As the Restylane Injector is preloaded with 2 ml of Restylane Vital Light, one injector can deliver approximately 200 doses.

1. Apply needle
   a. Hold the Restylane® Injector at the product reservoir and unscrew the protective cap.
   b. Attach the needle firmly to the Restylane Injector, by pushing and screwing the needle hub into the luer-lock connection until stop.

2. Wind the Restylane Injector
   Hold the Restylane® Injector with one hand around the body and twist the knob clockwise until it stops (approximately 20 full turns).
3. Prime the Restylane Injector
   Remove the needle cap, hold the Restylane® Injector upright and press the dose activator until you hear a click. Repeat this procedure (normally 15-25 times) until a droplet is visible on tip of needle.

4. Rotate needle
   If you prefer the needle tip in a specific position, this can be achieved by twisting the product reservoir.

5. Injection
   a. Prepare the skin for treatment.
   b. Hold the Restylane Injector comfortably, for example as if holding a pen, with the index finger on the dose activator.
   c. Insert the needle at the desired depth in the dermis.
   d. Press the dose activator (you will now hear a click).
   e. Wait until you hear a second click indicating that the full dose is delivered, which typically takes up to 3 seconds.
   f. Promptly move to the next site and immediately insert the needle to minimize any product waste.

6. Rewinding
   After approximately 50 injections the Restylane Injector needs to be rewound. The need for rewinding will be indicated when delivery of dose takes more than 3 seconds or when the dose activator no longer responds when pressed. Normally, the Restylane Injector needs to be rewound 2-4 times during a treatment session.

7. Disposal
   After approximately 200 deposits the product reservoir is empty and the injector can be disposed. Remove the needle and place it in a container for sharp objects.
Pain management

Each patient’s need for pain relief should be assessed prior to treatment. In some cases pain relief is not necessary when injecting into the skin for the correction of wrinkles and folds. However, each individual experiences pain differently and should be able to choose what suits them best.

Patient comfort techniques include anesthesia (topical, infiltrative, and nerve blocking), distraction techniques including carrying on a dialogue with the patient or using ice to numb the area of injection.

For certain indications Q-Med strongly recommends anesthesia such as lidocaine when injecting the lips, for volumetric contouring or rejuvenation of large skin areas.

**Zygomatic facial nerve block**
To anesthetize the outer cheek and orbital area locate the zygomatic facial nerve(s,) which usually exit below the lateral orbital retaining ligaments, and inject 1-2 ml of lidocaine with epinephrine 10-20 mg/ml. *(Figure A)*

**Infra orbital and/or mental nerve block**
To anesthetize the central cheek and upper lip feel the gingival of the upper teeth to locate the canine eminence (corresponding to the socket of the canine tooth). Just lateral to it or between the 3rd and 4th tooth at the mucosal fold you inject 0.5-1.0 ml of lidocaine with epinephrine 10-20 mg/ml. For the lower lip and/ or chin locate the mucosal fold between the premolars (4th and 5th tooth) and inject as above. *(Figure B)*

**Topical anesthesia**
The application of an anesthetic cream to the area to be treated can reduce discomfort. It is usually not sufficient to use only topical anesthesia when giving full lip treatment, but it can be used when treating only the lip line. For sufficient numbing of the area, the patient needs to sit with the anesthetic cream for at least 30 minutes prior to injection. *(Figure C)*

**Ice**
Ice is often used in combination with pain relief such as anesthesia or distraction techniques to further numb the area as well as cause increased vasoconstriction of the injection site. Recommend the patient to invest in an ice pack for post treatment care for at home comfort once the anesthesia wears off. *(Figure D)*
RESTYLANE INSTRUCTIONS FOR USE

Composition:
- Hyaluronic acid, stabilized
- Phosphates buffered saline, pH 7 ± 20 mg/mL

Description
RESTYLANE® is a clear, transparent and viscous gel supplied in glass syringes together with use or re-use 30 G needles. The product is a single-use item. The addition of water helps to maintain the overall volume of the product, resulting in a longer duration.

Mode of action
RESTYLANE® is a filler that acts by adding volume to the tissue thereby supporting the overlying (dermal) tissue to reduce the skin contours or enhance the lips to the desired level of correction. The hyaluronic acid molecules’ hydrophilic nature combined with three-dimensional structure allows the molecule to bind water many times its own weight. The addition of water helps to maintain the overall volume of the product, resulting in a longer duration.

Indication and usage
RESTYLANE® is intended to be used for facial tissue augmentation. It is recommended that the product be used for the correction of wrinkles and for lip enhancement. It should be injected into the middle part of the dermis layer. With extensive contour deformities the best results are obtained if the defect can be manually stretched to the point where it is eliminated. The degree and duration of the correction depend on the character of the defect treated, the tissue status at the implant site, the depth of the implant in the tissue and the injection technique. Markedly indented defects may be difficult to correct. Other products in the RESTYLANE® range of products can be used depending on individual patient need and severity of defect. In some cases it may be beneficial to combine different products from the RESTYLANE® range of products.

Warnings
RESTYLANE® is only intended for use as an intradermal implant. Do not inject subcutaneously. RESTYLANE® should not be used or re-used with other products. Do not inject intravascularly. There is a potential risk with the procedure that if injected into the blood stream, patients may rarely lead to vascular occlusion with transient impairment of vision, transient blindness or loss of vision.

Do not use in patients with bleeding disorders or patients who have undergone therapy with thrombolytics, anticoagulants, or inhibitors of platelet aggregation in the preceding 2 weeks.

Precautions
Normal precautions associated with intradermal injections must be observed. Like any such procedure, the implantation of RESTYLANE® is associated with an inherent risk of infection. RESTYLANE® should not be used in cases with active skin diseases, infection or related conditions. Patients who are using substances that may affect platelet function, such as aspirin and non-steroidal anti-inflammatory drugs may use this injection, experience increased bruising or bleeding at injection sites. Do not re-use RESTYLANE® together with any other injectable implant, except for other products for the RESTYLANE® range of products. RESTYLANE® should not be injected into an area where a permanent implantable material is present.

Do not use on patients who are using substances that may affect platelet function, such as aspirin and non-steroidal anti-inflammatory drugs may use this injection, experience increased bruising or bleeding at injection sites.

Ifaser treatment, chemical peeling or any other procedure based on acne dermabrasion is considered after treatment with RESTYLANE® there is a theoretical risk of sensitizing the reactionary tissue at the implant site. This also applies when a technician or patient have had this treatment completely after such a procedure.

RESTYLANE® has not been tested in pregnant or breastfeeding or women or children.

Anticipated side-effects
After the injection of RESTYLANE® some common injection-related reactions might occur. These reactions include erythema, swelling, pain, itching, bruising or tenderness at the implant site. Typically resolution is spontaneous within a few days after injection into the skin and within a week after injection into the lips. Additionally temporary palpable lumps has been noted after the use of RESTYLANE® in some patients.

Adverse events
Infrastructural reactions have been reported in rare cases. These reactions have consisted of redness, oedema, tenderness and induration at the implant site. These reactions may commence either sharp short after injection or after a delay of 1-4 weeks and have generally been described as mild to moderate and self-limiting, with an average duration of 2 weeks. In pronounced cases a short course of oral corticosteroids may prove effective. Patients who have experienced this type of reaction should not be re-treated with RESTYLANE® or any other product within the RESTYLANE® range of products. The following very rare cases have been reported with RESTYLANE® products:

• In rare cases patients may develop a localized inflammatory reaction requiring medical and/or surgical intervention.

• Persistent discoloration may occur due to injection of haemoderivatives. Reassurance is essential.

• In cases of trauma, visual disturbances following intra-tissue injection into the upper half of the face has been reported.

Adverse events must be reported to the local Q-Med representative or RESTYLANE® distributor.

Interactions
Treatment with RESTYLANE® in combination with drugs and other devices or concurrent dermal therapies has not been evaluated in controlled clinical studies.

Assembly of needle to syringe
For safe use of RESTYLANE® it is important that the needle is properly assembled to the syringe. Improper assembly may result in separation of the needle and syringe during injection. See pictures 1 and 2. Be sure that:

1. Group the narrow part of the needle should be free of burrs. The needle should be free of shavings until you feel they become smooth.

2. Group the wider part of the needle should be finely. Press and turn the needle should not be free of (a quarter turn). The quarter turn in necessary to lock the needle onto the syringe.

Dosage and administration
Before the treatment, the patient’s suitability for the treatment and the need for pain relief should be assessed. The patient should be given reassurance and any local anaesthesia is recommended when treating wrinkles. For lip augmentation, anaesthesia through a nerve block can be used. The patient should be informed about the indications, expected results, contraindications, precautions, warnings and potential adverse events. The treatment should be performed in a sterile and aseptic environment. The needle of the syringe should be cleaned with a suitable antibiotic solution. RESTYLANE® is administered using a thin gauge needle (30 G) by injecting the material into the dermis. Before injecting, press the needle carefully until a small droplet of fluid is visible at the top of the needle. If RESTYLANE® is injected too deeply or intramuscularly, the duration of the implant will be shorter because of a higher hyaluronic acid turnover rate. A too superficial injection may give blanching effects and bumps on the treatment site. If blanching is observed, the overlying skin turns of a white colour due to erythema and swelling. This is stopped at once and the area massaged until it returns to a normal colour.

The injection technique with regard to the depth of injection and the administration of a series of punctal injections or a combination of the two. The cortex of the needle should be visible but not the colour of the skin. Inject RESTYLANE® while pulling the needle slowly backwards. Injection should stop just past the needle is pulled out from the skin to prevent material from leaking out from the injection site. In the treatment of lips, an enhanced vermilion border as well as fullness and pouting can be obtained.

Defects should be fully corrected, but not overcorrected, at each treatment session. The correction site should be managed to conform to the contour of the surrounding tissues. If the skin of the patient is very loose, it is recommended that RESTYLANE® be injected on two or more separate occasions for each treatment site a minimum of 2 or 3 per treatment session is recommended. If the treated area is visible directly after the injection,WAITING can be applied on the site for a short period. After the first treatment, additional complications of RESTYLANE® may be necessary to achieve the desired level of correction. Periodic follow-up injections help sustain the desired degree of correction. A follow-up treatment before the full effect of correction is completely directed may be beneficial.

Note: The current injection technique is important for the final result of the treatment. RESTYLANE® is only intended to be administered by authorized personnel in accordance with local legislation. Please consult your local Q-Med representative or RESTYLANE® distributor for more details about techniques and training opportunities.

The syringe, the needle and any unused material must be discarded immediately after the treatment session.

Performance
In a controlled multi-center study with RESTYLANE® for the correction of nasolabial folds 70% of the subjects maintained a clinically significant improvement 6 months after treatment.

How supplied
RESTYLANE® is supplied in a glass syringe with a luer-lok fitting. One or more premium irradiated sterilized needles, 30 G (2-1/2”), are packed together with each syringe. A patient record label is in a part of the syringe label. Remains is tip by flapping the mark flap with three steel arrows. This label is to be attached to patient record to ensure traceability of the product. The contents of the syringe have been sterilized using moist heat. The number of units per package and the volume contained in each syringe is as stated on the outer package.

Do not use if package is damaged.

STERILE NEEDLE
• Follow material local or institutional guidelines for use and disposal of medical device and equipment. Observe normal medical attention if injury occurs.

• To prevent avoid needle breaks, do not attempt to straighten a bent needle. Discard it and complete the procedure with a replacement needle.

• Do not reloaded needles. Recognizing by hand is a hazardous practice and should be avoided.

• Discard unfinished needles in approved sharps collectors.

Shelf life and storage
As indicated on package. Store up to 21° C. Protect from freezing and sunlight.

Manufactured by
Q-Med AB, 31-701 73 Ljusnarsdalen, Sweden
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www.qmed.com, e-mail: info@qmed.com

Symbols
CE-marked according to MDD 93/42/EEC (S.M.) is the Notified Body number for RESTYLANE®
CE-marked according to MDD 93/42/EEC (S.M) is the Notified Body number for the needle(s).

References
• Information is also available at your local Q-Med representative or RESTYLANE® distributor or on www.restylane.com.

RESTYLANE® is a trademark owned by Q-Med AB.

90-6991 4-02, Oct 2007

Chapter 8

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### RESTYLANE TOUCH INSTRUCTIONS FOR USE

**Composition**

Hyaluronic acid, stabilized
Phosphates buffered saline, pH 7
20 mg/ml
qt.

**Description**

RESTYLANE® Touch is a clear and transparent gel supplied in a glass syringe together with a 30 G needle. The product is for single use only. RESTYLANE Touch is a unique form of stabilized non-animal, hyaluronic acid. Hyaluronic acid is a natural polysaccharide which occurs as an important structural element in the skin and in subcutaneous and connective tissues as well as in the synovial tissue and fluid. Hyaluronic acid belongs to a group of very few substances which are identical in all living organisms.

**Mode of action**

RESTYLANE Touch is a filler that aids by adding volume to the tissue thereby supporting the overlying (dermal) tissue to resist the skin contours to the desired level of correction. The hyaluronic acid molecules’ hydrolipidic nature combined with its three-dimensional structure allows the molecules to bind water many times its own weight. The addition of water helps to maintain the overall volume of the product resulting in the molecules to bind water many times its own weight. The addition of water helps to maintain the overall volume of the product resulting in the molecules to bind water many times its own weight. The addition of water helps to maintain the overall volume of the product resulting in the molecules to bind water many times its own weight.

**Indication**

RESTYLANE Touch is intended to be used for facial tissue augmentation. It is recommended to use the product for the correction of the superficial lines, for example periorbital lines, perioral lines, forehead lines and smile lines.

**Warning**

RESTYLANE Touch is only intended for use as an intradermal implant. Do not use RESTYLANE Touch for injection into muscle or subcutaneous or submucosal layers. Do not use RESTYLANE Touch on or near the eyes, lips, or other sensitive areas. Do not use RESTYLANE Touch on or near the eyes, lips, or other sensitive areas. Do not use RESTYLANE Touch on or near the eyes, lips, or other sensitive areas. Do not use RESTYLANE Touch on or near the eyes, lips, or other sensitive areas. Do not use RESTYLANE Touch on or near the eyes, lips, or other sensitive areas.

**Precautions**

Normal precautions associated with intradermal injections must be observed. Like any other procedure, the implantation of RESTYLANE Touch is associated with an inherent risk of infection. RESTYLANE Touch should not be used in or near anatomic sites where there is active skin disease, inflammation or related conditions.

**Usage**

RESTYLANE Touch is administered after the skin has healed completely after such a procedure.

**Precautionary advice**

- The injection technique with regard to the depth of injection and the administered quantity may vary. The linear threading technique can be used to carefully lift up the skin superficially, but some physicians prefer to use a series of punctual injections or a combination of the two. Inject RESTYLANE Touch while pulling the needle slowly backwards. Injection should stop just before the needle is pulled out from the skin to prevent material from leaking out from the injection site. Debulking should be carefully corrected but not overcorrected on each treatment session. The correction site should be managed to conform to the contour of the surrounding tissues. If the site of the patient is very loose, it is recommended that RESTYLANE Touch be injected on two or more separate occasions. For each treatment site a maximum dosage of 1 ml is recommended. If the treated area is swollen directly after the injection, massage the skin can be applied on the site for a short period.

**Adverse events**

Inflammatory reactions have been reported in rare cases. These reactions have consisted of redness, swelling, tenderness and induration at the implant site. These reactions may occur shortly after injection or after a delay of 2-4 weeks and have generally been described as mild to moderate and self-limiting, with an average duration of 2 weeks. In pronounced cases a short course of oral corticosteroids may prove effective. Patients who have experienced this type of reaction should not be retreated with RESTYLANE Touch or any other product within the RESTYLANE range of products.

The following very rare cases have been reported with RESTYLANE products:

- Blistery pseudo-granulation formation
- Numbness possibly due to subcutaneous injection technique requiring medical and/or surgical intervention
- Persistent discoloration, possibly due to deposit of haemosiderin as a consequence of injection site bleeding. These reactions have mostly occurred after repeated injections.

Post-inflammatory pigmentation changes due to deposits of melanin have been observed in clinical studies in people with dark skin (Fitzpatrick Type IV-V).

**Contraindications**

Isolated cases of facial oedema and urticaria have also been reported but it is uncertain whether these cases are related to treatment or caused by underlying disease or concomitant medication.

One case of transient visual disturbance following intra-vascular injection into the upper half of the face has been reported.

Adverse events must be reported to the local Q-Med representative or RESTYLANE distributor.

**Interactions**

Treatment with RESTYLANE Touch in combination with other devices or concurrent dermal therapies has not been evaluated in controlled clinical studies.

**Assembly of needle to syringe**

For safe use of RESTYLANE Touch it is important that the needle is properly assembled to the syringe. Improper assembly may result in separation of the needle and syringe during injection.

**See pictures 1 and 2.**

- 1. Grasp the release part of the needle should be firmly. Turn the needle clockwise until you feel counter pressure.
- 2. Grasp the wider part of the needle should firmly. Press and turn the needle shaft (90° or a quarter turn). The quarter turn is necessary to lock the needle onto the syringe.

**Dosage and administration**

- Before the treatment, the patient’s stability for the treatment and the needle pain relief should be assessed. For optimal patient comfort, topical or local anaesthesia is recommended when treating this superficial layer.
- The patient should be informed about the indications, expected results, complications, precautions, warnings, and potential adverse events. The treatment site should be cleaned with a suitable antiseptic solution.
- RESTYLANE Touch is administered using a thin gauge needle (30 G) by inserting the needle into the superficial layer of the skin. Before injecting, press the side vent until a small droplet is visible at the tip of the needle. If RESTYLANE Touch is injected too deeply or intramuscularly, the duration of the implant will be shortened because of a higher haematic acid turnover. A too superficial injection may give blanching effects and bumps on the treatment site. If blanching is observed, a slower skin return to its normal colour, the injection should be stopped as once and the area massaged until it returns to a normal colour.

**References**

Product documentation is available at your local Q-Med representative or RESTYLANE distributor or on www.restylane.com.

**CE-marked according to MDD 93/42/EEC; 004 is the Notified Body number for RESTYLANE Touch.**

**STELLAIRE**

1. **STERILE INJECTION**

- Follow national, local or institutional guidelines for use and disposal of medical devices.
- Observe standard medical caution if injury occurs.

- Do not reshield used needles. Recapping by hand is a hazardous practice.

- Discard unshielded needles in approved sharps containers.

**Shelf life and storage**

As indicated on package. Store up to 25°C. Protect from freezing and sunlight.

Manufactured by

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www.qmed.com, e-mail: info@qmed.com

**Symbols**

- CE-marked according to MDD 93/42/EEC; 004 is the Notified Body number for RESTYLANE Touch.

- CE-marked according to MDD 93/42/EEC; 001 is the Notified Body number for RESTYLANE Touch.

- CE-marked according to MDD 93/42/EEC; 001 is the Notified Body number for RESTYLANE Touch.

- CE-marked according to MDD 93/42/EEC; 001 is the Notified Body number for RESTYLANE Touch.

- CE-marked according to MDD 93/42/EEC; 001 is the Notified Body number for RESTYLANE Touch.

**RESTYLANE Touch is a medicinal product approved by Q-Med AB.**
RESTYLANE PERLANE INSTRUCTIONS FOR USE

Composition:
Hyaluronic acid, stabilized 20 mg/mL
Phosphates and sodium, pH 7 ±1

Description
RESTYLANE Perlane® is a clear, transparent and viscous gel supplied in a glass syringe together with one or more 37 G needles. The product is for single use only. RESTYLANE Perlane is a unique form of stabilized non-animal, hyaluronic acid. Hyaluronic acid is a natural polysaccharide which occurs as an important structural element in the skin and in subcutaneous and connective tissues as well as in the synovial fluid and fluid. Hyaluronic acid belongs to a group of very few substances which are identical in all living organisms.

Mode of action
RESTYLANE Perlane is a filler that acts by adding volume to the tissue, thereby augmenting the overlying (dermal) issue to shape the contours of the face, correcting folds or enhancing the lips to the desired level of contour. The hyaluronic acid molecules hydrosoluble aggregate contained with its three-dimensional structure so that the molecules to bind water many times its own weight. The addition of water helps to maintain the overall volume of the product resulting in a longer duration. RESTYLANE Perlane is neurally integrated into the tissue and will in time undergo, cosmetically degradation. The viscoelastic pattern of degradation increases the water binding capacity of the gel thus allowing RESTYLANE Perlane to maintain the overall volume during the degradation process.

Indication and usage
RESTYLANE Perlane is intended to be used for facial tissue augmentation. It is recommended that the product be used for shaping the contours of the face, the correction of folds and for lip enhancement. It should be injected into the deep layer of the dermis and/or the superficial layer of the subcutaneous connective tissue to achieve the best results if the defect can be accurately recovered to the point where it is eliminated. The degree and duration of the correction depend on the character of the defect treated the tissue area at the injection site, the depth of the implant in the tissue and the injection technique. Meticulously injected defects may be difficult to correct. Other products in the RESTYLANE range of products can be used dependent on individual patient need and severity of defect. in such cases may benefit to combine different products from the RESTYLANE range of products.

Warnings
RESTYLANE Perlane is intended only for use in an interventional and/or subcutaneous injection. Do not resuspend RESTYLANE Perlane. Do not mix with other products.

Do not inject intravascularly. There is a potential risk with the procedure that the needle becomes inappropriate needle vessels. This may result in the injection of the product. Do not use in patients with bleeding disorders or patients who have undergone surgery with anticoagulants, antiplatelets or platelets before the procedure in the previous 3 weeks.

Precautions
Normal precautions associated with intradermal and/or subcutaneous injections must be observed. Like any other procedure, the implantation of RESTYLANE Perlane is associated with an inherent risk of infection. RESTYLANE Perlane should not be used in any patient with a known history of drug allergy.

Patients should be informed that the main side effects are erythema, bruising, swelling, induration of the treatment area, and a transient increase in pigmentation. The duration of these effects varies from patient to patient and is usually no longer than 6 weeks. No allergic reaction to the products has been observed. Despite this, patients should be warned against discontinuing any treatment before completion if not satisfied with the results. Restylane Perlane is supplied in a single-use syringe without the needle. The needle should be inserted into the skin and the required volume of product should be injected slowly. The needle should be inserted in a depth of 1 – 2 mm below the surface of the skin. The needle should be removed slowly. The needle should be inserted in a depth of 1 – 2 mm below the surface of the skin. The needle should be removed slowly. The needle should be inserted in a depth of 1 – 2 mm below the surface of the skin. The needle should be removed slowly. The needle should be inserted in a depth of 1 – 2 mm below the surface of the skin. The needle should be removed slowly. The needle should be inserted in a depth of 1 – 2 mm below the surface of the skin. The needle should be removed slowly. The needle should be inserted in a depth of 1 – 2 mm below the surface of the skin. The needle should be removed slowly.

Adverse events
Inflammatory reactions have been reported in rare cases. These reactions have consisted of redness, swelling, tenderness and induration at the implant site. These reactions may occur either shortly after injection or after a delay of 24 – 48 hours and have generally been described as mild to moderate and subsiding in an average duration of 2 weeks. In pronounced cases a course of oral corticosteroids may prove effective. Patients who have experienced this type of reaction should not be re-injected with RESTYLANE Perlane or any other product within the RESTYLANE range of products.

The following very rare cases have been reported with RESTYLANE Perlane:

- Suppuration/Granuloma formation – rare cases possibly due to subclinical bacterial infection requiring medical and/or surgical intervention
- Paramyxomatous plaque – rare cases possibly due to deposits of heamatoma as a consequence of injection site bleeding. These reactions have mostly occurred after repeated injections.

Post-injection pigmentary changes due to deposits of melanin have been observed in clinical studies in people with dark skin (Pigmentary Type IV). Isolated cases of facial oedema and urticaria have also been reported but there is uncertainty whether these cases are related to treatment or caused by underlying disease or consequent medication.

One case of transient visual disturbance following intra-arterial injection into the upper half of the face has been reported.

Adverse events must be reported to the local Q-Med representatives or RESTYLANE distributor.

Interactions
Treatment with RESTYLANE Perlane in combination with drugs or other devices or concurrent dermal therapies has not been evaluated in controlled clinical studies.

Assembly of needle to syringe
For all use of RESTYLANE Perlane it is important that the needle is properly assembled to the syringe. Improper assembly may result in contamination of the needle and syringe during injection. See pictures 1 and 2.

1. Group the narrow part of the needle should firmly Press and turn the needle shield 90° (a quarter turn). The quarter turn is necessary to lock the needle onto the syringe.

Usage and administration
Before the treatment, the patient’s suitability for the treatment and the need for pain relief should be assessed. For optimal patient comfort, topical and/or local anaesthesia is recommended when shaping the contours of the face and correcting folds. For lip augmentation, anaesthesia through a numb block can be used. The patient should be informed about the indications, expected results, contraindications, precautions, warnings and potential adverse events. The treatment site should be cleaned with a suitable antiseptic solution. RESTYLANE Perlane is administered using a thin gauge needle (up to 37 G) by injecting the material into the deep layer of the dermis and/or the superficial layer of the subcutaneous. Before injecting, press the needle firmly until a small drip is visible at the tip of the needle. If RESTYLANE Perlane is injected too deeply or too intravenously, the duration of the implant will be shorter because of a higher hyaluronic acid turnover rate. A too superficial injection may give bloating, blanches and bumps on the treatment site. If bloating is observed, the overlying skin turns a whitish colour, the injection should be stopped once and the area massaged until it returns to a normal colour. The injection technique with regard to the depth of injection and the administered quantity may vary RESTYLANE Perlane should only be injected by practitioners who have experience of deep dermal and subcutaneous injections in the facial area. The linear threading technique can be used and some physicians prefer a series of punctual injections or a combination of the two. RESTYLANE Perlane while pulling the needle slowly backwards. Injection should stop just before the needle is pulled out from the skin to prevent material from leaking out from the injection site. The treatment of lips, fullness and pouting of the lips can be obtained. Defects should be fully corrected, but not overcorrected, at each treatment session. The correction site should be managed to conform to the contour of the surrounding tissue. If the skin of the patient is very loose, it is recommended that RESTYLANE Perlane be injected on two or more separate occasions. For each treatment site a maximum dosage of 2 ml per treatment session is recommended. If the treated area is swollen directly after the injection, icing ice can be applied on the site for a short period. After the first treatment additional implantations of RESTYLANE Perlane may be necessary to achieve the desired level of correction. Periodic follow-up injections help sustain the desired degree of correction. A follow-up treatment before the full esthetic correction is completely diminished may be beneficial.

Note! The correct injection technique is important for the final result of the treatment. RESTYLANE Perlane is only intended to be administered by authorized personnel in accordance with local legislation. Please consult your local Q-Med representative or RESTYLANE distributor for more details about technique and training opportunities.

The syringe, the needle and any unused material must be discarded immediately after the treatment session.

Performance
In a controlled multicenter study with RESTYLANE Perlane for the correction of nasolabial folds 75% of the subjects maintained a clinically significant improvement 6 months after treatment.

How supplied
RESTYLANE Perlane is supplied in a glass syringe with a low-latch fitting. One or more pre-removed needles. 37 G ± 1°. The needle is packed together with each syringe. A patient record label is part of the syringe label. Remove by pulling the flap marked with three small arrows. This label is to be attached to patient records to ensure traceability of the product. The needle has been designed using medical grade. The number of units per package and the volume contained in each syringe is stated on the outer package.

Do not use if package is damaged.

STERILE NEEDLE
- Follow national, local or institutional guidelines for use and disposal of medical devices. Obtain the rests of medical rejection.
- To help avoid needle traumatic, do not attempt to strip a blunt needle. Dispose and complete the procedure with a replacement needle.
- Do not re-used needles. Recapping by hand is a hazardous practice and should be avoided.
- Discard unsheilded needles in approved sharps collectors.

Shelf life and storage
Accompanied on package. Store up to 25° C. Protect from freezing and sunlight.

Manufactured by:
Q-Med AB, Sweden Estate: 21, 18-792 28 Upplands, Sweden Phone: +46(8) 474 90 00 Fax: +46(8) 474 90 01 Website: www.qmed.com

Symbols on packaging
Do not use if package is damaged.

CE-marked according to MDD 93/42/EEC. 0384 is the Notified Body number for RESTYLANE Perlane.

BE-marked according to MDD 93/42/EEC. 0588 is the Notified Body number for the needle(s).

References
Product documentation is available at www.qmed.com, or at www.restylane.com.

RESTYLANE® and PERLANE are trademarks owned by Q-Med AB.
Restylane Vital™ INSTRUCTIONS FOR USE

Composition

Hyaluronic acid, stabilized

Phosphate buffered saline, pH 7

20 mg/ml

4+.

Description

Restylane Vital is a clear, transparent and viscous gel supplied in a glass syringe together with 30 G needles. The product is for single use only. Restylane Vital is a unique form of stabilized non-animal hyaluronic acid. Hyaluronic acid is a naturally polysaccharide which occurs as an important structural element in the skin and in subcutaneous and connective tissues as well as in the synovial fluid and fluid. Hyaluronic acid belongs to a group of very few substances which are identical in all living organisms.

Mode of action

Restylane Vital is essentially integrated into the skin where it helps to restore skin hydration, improve skin structure and the elasticity of the skin. This is accomplished by the water associated with the stabilized hyaluronic acid in the gel. The unique characteristics of the gel help maintain the effect for a long period of time.

Indication and usage

Restylane Vital is intended to restore skin hydration, improve skin structure and the elasticity of the skin. It should be injected in the dermal layer of the skin, preferably deeper. The duration of the result depends on the character of the area treated, the tissue stress at the injection site, the depth of the injection in the tissue and the injection technique.

Colder Restylane® products are recommended for the correction of folds and lines for facial contouring and to create volume.

Performance

In a clinical study with Restylane Vital, patients experienced significant improvement in dermal elasticity and skin morphology 6 months after initial treatment.

Warning

Restylane Vital is only intended for intradermal injections. Do not re-use Restylane Vital. Do not mix with other products. Do not inject excessively. There is a potential risk with the procedure that the material could be inadvertently injected into blood vessels. This may lead to vascular obstruction with tissue impairment of vision, transient ischemia or even necrosis. Do not use in patients with bleeding disorders or patients who have undergone therapy with immunotherapeutics, anticoagulants, or inhibitors of platelet aggregation in the preceding 2 weeks.

Precautions

Normal precautions associated with intradermal injections must be observed. Like any such procedure, the injection of Restylane Vital is associated with inherent risk. Restylane Vital should not be used in or near anatomic areas where there is active skin disease, inflammation or related conditions.

Patients who are using substances that may affect platelet function, such as aspirin and non-steroidal anti-inflammatory drugs, i.e., with any injection, experience increased bruising or bleeding at injection sites. Do not inject Restylane Vital into an area where another injectable implant is present, except for other products from the Restylane range of products.

Restylane Vital should not be injected into an area where a non-injectable implant has been placed. Restylane Vital should not be used for patients with unreasonatable expectations.

The patient should be informed that he or she should not expose the treated area to intense heat (e.g. solarium and sunbathing) or extreme cold or an ice pack until the initial swelling and bruising have resolved. If laser treatment, chemical peeling or any other procedure based on active thermal response is considered after treatment with Restylane Vital there is a theoretical risk of eliciting an inflammatory response at the injection site. This also applies if Restylane Vital is administered before the skin has healed completely after such a procedure.

Restylane Vital has not been tested in pregant or breastfeeding women or in children.

Anticipated side effects

After the injection of Restylane Vital, some common injection-related reactions might occur. These reactions include erythema, swelling, pain, itching, bruising or tenderness at the injection site. Typically resolution is spontaneous within a few days after injection. In addition, temporary palpable lumpsiness has been noted in some patients. If injected in too large volumes or too superficially, the product may cause intradermal lumps.

Adverse events

In rare cases intradermal lumps have been reported to revert for several months or periods over one year after the use of Restylane Vital.

Inflammatory reactions have been reported in rare cases. These reactions have consisted of redness, swelling, tenderness and induration at the injection site. These reactions may commence either shortly after injection or after a delay of 2–4 weeks and have generally been described as mild to moderate and self-limiting with an average duration of 2 weeks. Infections should be excluded or treated if necessary. In pronounced cases a short course of oral antibiotics may prove effective. For patients who have experienced clinically significant adverse reactions, a decision for remanagement with Restylane Vital or any other product within the Restylane range of products should take into consideration the cause and significance of previous reactions. For example, remanagement is not recommended following rare cases of granulomas or unexplained significant inflammatory reactions.

The following very rare cases have been reported with Restylane Vital:

- Biopsy proven granuloma formation
- Nerves, possibly due to suboptimal injection technique requiring medical and/or surgical intervention
- Persistent discoloration, possibly due to deposit of hemoglobin as a consequence of injection site bleeding. These reactions have mostly occurred after repeated injections.

Post inflammatory pigmentation changes due to deposit of melanin have been observed in clinical studies in people with dark skin ( Fitzpatrick Type IV/VI).

Isolated cases of facial edema and urticaria have also been reported but it is uncertain whether these cases are related to treatment or caused by underlying disease or concomitant medication.

One case of transient visual disturbance following retro-aural injection into the upper half of the face has been reported.

Adverse events must be reported to the local Q-Med representative or Restylane distributor.

Basic hygienic approach should be applied during the injection procedure.

The treatment site should be cleaned with a suitable antiseptic solution. Restylane Vital is administered using a single-use needle [20 G] by injecting the material into the dermal layer of the skin, preferably deeper. Before you puncture the skin, make sure that a small droplet is visible at the tip of the needle. If Restylane Vital is injected too deeply or in an imprecise manner, the duration of the effect might be shorter because of a higher hyaluronic acid turnover rate. A too large volume or a too superficial injection may give bumps on the treatment site. If blanching is observed, i.e., the overlying skin turns a white colour, the injection should be stopped at once and the area massaged until it returns to normal colour.

The injection technique and the administered quantity may vary. The short linear threading technique can be used to correctly lift up the skin, but the microcannula technique or a combination of the two can also be used. Valid for both techniques are that very small amounts, micro-deposits, should be injected at each site. Treated areas can be gently massaged immediately after the injection if any irregularities are noted. A treatment plan for Restylane Vital is recommended with three treatments 4 weeks apart. Generally it is recommended to repeat the treatment plan every 6 months, but results and patient preferences may vary.

Restylane Vital is only intended to be administered by authorized personnel in accordance with local legislation. Please consult your local Q-Med representative or Restylane distributor for more details about techniques and training opportunities.

The syringes, the needle and any unused material must be disposed immediately after the treatment session.

How supplied

Restylane Vital is supplied in a glass syringe with a luer-lock fitting. Gamma irradiation sterilized needles, 30 G x ½", are packed together with such syringes. A patient record label is a part of the syringe label. Remove it by pulling the flapt marked with three small arrows. This label is to be attached to patient records and sent to the dealer.

The contents of the syringes have been sterilized using moist heat. The number of syringes, the dosage and the volume contained in each syringe is as stated on the outer package.

Do not use if packages is damaged.

Shelf life and storage

As indicated on the package. Store up to 25°C. Protect from freezing and sunlight.

Manufactured by

Q-Med AB, Jernvägen 21, SE-752 28 Uppsala, Sweden

Phone: +46(0)18 474 90 00 Fax: +46(0)18 474 90 01

www.q-med.com, e-mail info@q-med.com

Symbols

Do not use if package is damaged.

CE-marked according to PPD 93/42/EEC (0344 is the Notified Body number for Restylane Vital).

CE-marked according to PPD 93/42/EEC (0344 is the Notified Body number for the needle).

References

Product documentation is available at your local Q-Med representative or Restylane distributor, or on www.restylane.com.

Restylane and Restylane Vital are trademarks owned by Q-Med AB.
Restylane Vital™ Light – Instructions for Use

**Composition**
Hyaluronic acid, stabilized
Phosphate buffered saline, pH 7.4

**Description**
Restylane Vital Light is a clear, transparent and viscous gel supplied in a glass syringe together with 30 G needles. The product is for single use only. Restylane Vital Light is a unique form of stabilized non-animal hyaluronic acid. Hyaluronic acid is a natural polysaccharide which occurs as an important structural element in the skin and in subcutaneous and connective tissues as well as in the synovial fluid. Hyaluronic acid belongs to a group of very few substances which are identical in all living organisms.

**Mode of action**
Restylane Vital Light is naturally integrated into the skin where it helps to restore skin hydration, improve skin structure and the elasticity of the skin. This is accomplished by the water associated with the stabilized hyaluronic acid in the gel. The unique characteristics of the gel help maintain the effect for a long period of time.

**Indication and usage**
Restylane Vital Light is intended to restore skin hydration, improve skin structure and the elasticity of the skin. It should be injected in the dermal layer of the skin. The duration of the result depends on the character of the area treated, the tissue areas at the injection site, the depth of the injection in the tissue and the injection technique.

Other Restylane® products are recommended for the correction of folds and lines for facial contouring and to create volume.

**Performance**
In a clinical study with Restylane Vital™, patients experienced significant improvements in dermal elasticity and skin morphology 6 months after initial treatment.

**Warning**
Restylane Vital Light is only intended for intradermal injections. Do not remove Restylane Vital Light. Do not use with other products. Do not inject intravenously. There is a potential risk with the product that the material could be inadvertently injected into blood vessels. This may result in vascular occlusion with transient impairment of vision, transient ischemia or even necrosis.

Do not use in patients with bleeding disorders or patients who have undergone therapy with chemoembolies, anticoagulants, or inhibitors of platelet aggregation in the preceding 3 weeks.

**Precautions**
Normal precautions associated with intradermal injections must be observed. Like any such procedure, the injection of Restylane Vital Light is associated with an inherent risk of infection. Restylane Vital Light should not be used in or near anastomotic sites where there is active skin disease, inflammation or relapsed conditions.

Patients who are using substances that may affect platelet function, such as aspirin and non-steroidal anti-inflammatory drugs, or any injection, experienced increased bruising or bleeding at injection sites.

Do not inject Restylane Vital Light into an area where another injectable implant is present, except for other products from the Restylane range of products. Restylane Vital Light should not be injected into an area where a non-resorbable implant has been placed. Restylane Vital Light should not be used for patients with uncontrolled expectations.

The patient should be informed that for or she she should not expose the treated area to intense heat (e.g. solarium and sunbathing) or extreme cold at least until the initial swelling and redness have resolved.

**Flower treatment, chemical peeling or any other procedure based on active dermal responses is considered after treatment with Restylane Vital Light there is a theoretical risk of eliciting an inflammatory response at the injection site.**

This also applies if Restylane Vital Light is administered before the skin has healed completely after such a procedure.

Restylane Vital Light has not been tested in pregnant or breastfeeding women or in children.

**Anticipated side effects**
After the injection of Restylane Vital Light, some common injection-related reactions may occur. These reactions include erythema, swelling, pain, itching, bruising or tenderness at the injection site. Typically resolution is spontaneous within a few days after injection. If injected in too large volumes or too superficially, the product may cause intraluminal lumps.

**Adverse events**
Inflammatory reactions have been reported in rare cases for other products within the Restylane range of products. These reactions include redness, swelling, tenderness and induration at the injection site. These reactions may commence either shortly after injection or after a delay of 2-4 weeks and have generally been described as mild to moderate and self-limiting, with an average duration of 2 weeks. Infections should be excluded in all cases if necessary. In pronounced cases a short course of oral corticosteroids may prove effective.

For patients who have experienced clinically significant reactions a decision for re-treatment with Restylane Vital Light or any other product within the Restylane range of products should be taken into consideration. The cause and significance of previous reactions. For example, re-treatment is not recommended following rare cases of granulomas or unsupervised significance inflammatory reactions.

In rare cases intraluminal lumps have been reported to remain for several months or periods or one year after the use of Restylane Vital Light.

The following very rare cases have been reported with Restylane products:
- biopsy proven granulomas formation
- necrosis, possibly due to subcutaneous injection technique requiring medical and/or surgical intervention
- persistent discoloration, possibly due to deposit of hemosidens as a consequence of injection site bleeding. These reactions have mostly occurred after repeated injections.

Post-inflammatory pigmentation changes due to deposit of melanin have been observed in clinical studies in people with dark skin (Farrer-Langford Type IV-V).

Isolated cases of facial edema and urticaria have also been reported but it is uncertain whether these cases are related to treatment or caused by underlying disease or concomitant medication.

One case of transient visual disturbance following intra-arterial injection into the upper half of the face has been reported. Adverse events must be reported to the local C-Med representative or Restylane distributor.

**Interactions**
Treatment with Restylane Vital Light is combination with drugs and other devices or concomitant dermal therapies has not been evaluated in controlled clinical studies.

**Assembly of needle to syringe**
For safe use of Restylane Vital Light it is important that the needle is properly assembled to the syringe. Improper assembly may result in separation of the needle and syringe during injection.

**See pictures 1 and 2.**
1. Grasp the narrow part of the needle sheath loosely. Turn the sheath should clockwise until you feel counter pressure.
2. Grasp the wider part of the needle firmly. Press and turn the needle should 90° (a quarter turn). The quarter turn is necessary to lock the needle onto the syringe.

**Dosage and administration**
Before the treatment, the patient’s suitability for the treatment and the need for pain relief should be assessed. The patient should be informed about the indication, expected result, complications, precautions, warnings and potential adverse events.

Basic hygienic approach should be applied during the injection procedure. The treatment site should be cleaned with a suitable antiseptic solution. Restylane Vital Light is administered using a thin gauge needle (25 G) by injecting the material into mid dermis of the skin. Before injecting areas the risk carefully until a sharp in the tip of the needle.

If Restylane Vital Light is injected too deep or intramuscularly the duration of the effect might be shorter because of a higher hyaluronic acid turnover rate. A too large volume or a too superficial injection may give lumps on the treatment site. If bleeding is observed, i.e. the overlying skin turns a whitish colour the injection should be stopped at once and the area managed until it returns to a normal colour.

The injection technique and the administered quantity may vary. The short linear threading technique can be used to carefully RA the skin, but the microprocedural technique or a combination of the two can also be used. Valid for both techniques are that very small amounts, micro-drops, should be injected at each site. Treated areas can be gently massaged immediately after the injection if any irregularities are noted.

A treatment plan for Restylane Vital Light with three treatments 2-4 weeks apart is recommended. Generally the treatment plan is repeated every 4-6 months, but results and patient preferences may vary.

**Note!** The correct injection technique is important for the aesthetic effect of the treatment. Restylane Vital Light is only intended to be administered by trained authorized personnel in accordance with local legislation. Please consult your local C-Med representative or Restylane distributor for more details about techniques and training opportunities.

**The syringes, the needle and any unused material must be discarded immediately after the treatment session.**

**How supplied**
Restylane Vital Light is supplied in a glass syringe with a bar-lock fitting. Gamma-irradiated sterilized needles, 30 G x 1/2”, are packed together with each syringe. A patient record label is a part of the syringe label. Remove it by pulling the cap marked with three small arrows. This label should be attached to the patient record to ensure irradation of the material. The contents of the syringes have been sterilised using moist heat. The number of units per package and the volume contained in each syringe is as stated on the outer package.

Do not use if package is damaged.

**Shelf life and storage**
As indicated on the package. Store up to 25°C. Protect from freezing until use.

**Manufactured by**
Q-Med AB, Seminärberg 21, SE-752 28 Uppsala, Sweden
Phone: +46(0)8 474 91 00, Fax: +46(0)8 474 91 31
www.q-med.com, e-mail: info@q-med.com

**Symbols**
Do not use if package is damaged.

CE-marked according to PPD 93/42/EEC 0944 is the Notified Body number for Restylane Vital Light.

CE-marked according to PPD 93/42/EEC 0066 is the Notified Body number for the needle(s).

**References**
Product documentation is available at your local C-Med representative or Restylane distributor.

Restylane and Restylane Vital are trademarks owned by Q-Med AB.
Restylane Vital™ Light – Injector – Instructions for Use

Composition:
Hyaluronic acid
Phosphate buffered saline, pH 7.0 ± 0.2

Description:
Restylane Vital Light is a clear, transparent and viscous gel supplied in a prefilled premixed container with a 3 ml syringe. The product is designed so that Restylane Vital Light is a single-use form of stabilized non-animal hyaluronic acid and Hyaluronic acid is a natural polysaccharide which occurs as an important structural element in the skin and in connective tissue to maintain the flexibility and suppleness of skin. It is a dermal filler that is used to improve facial contours and fill in wrinkles. However, the use of Restylane Vital Light is intended for intradermal injections only and is not to be used in skin tissues. Restylane Vital Light is a dermal filler that is used to improve facial contours and fill in wrinkles. However, the use of Restylane Vital Light is intended for intradermal injections only and is not to be used in skin tissues.

Warning:
Restylane Vital Light is intended for intradermal injection only. Do not use on areas where there is active skin disease, inflammation or recent injections of other substances. Restylane Vital Light should not be used in skin tissues. Restylane Vital Light is a dermal filler that is used to improve facial contours and fill in wrinkles. However, the use of Restylane Vital Light is intended for intradermal injections only and is not to be used in skin tissues.

Precautions:
Restylane Vital Light is associated with an inherent risk of infection. Observations of the previously treated site, the surrounding area and the patient’s general health should be made before the injection. All patients should be warned of the possibility of local reactions to the injection site, including injection site reactions, such as pain, swelling, redness, bruising, tenderness, itching, skin irritation, and the possibility of systemic reactions, including systemic reactions such as fever, chills, and malaise, which may occur after the injection of Restylane Vital Light. 

Packaging:
Restylane Vital Light is supplied in a sterile, single-use prefilled premixed container. The container is made of medical grade polyethylene and contains the following:

- Restylane Vital Light (3 ml)
- Injector

Shelf life and storage:
Store at 2-8°C (36-46°F) until used. Do not freeze or autoclave. Store at 2-8°C (36-46°F) until used. Do not freeze or autoclave. Store at 2-8°C (36-46°F) until used. Do not freeze or autoclave. Store at 2-8°C (36-46°F) until used. Do not freeze or autoclave.

Preparation of the injector:
1. Hold the product reservoir and remove the grey protective cap.
2. Prepare the skin for treatment.

Injection technique:
1. Hold the product reservoir and remove the grey protective cap.
2. Prepare the skin for treatment.

Advantages:
Intraoperative measurements must be recorded to ensure that the material could be inadvertently injected into blood vessels. This may not lead to serious complications with an injection site. Restylane Vital Light is intended for intradermal injection only. Do not use on areas where there is active skin disease, inflammation or recent injections of other substances. Restylane Vital Light should not be used in skin tissues. Restylane Vital Light is a dermal filler that is used to improve facial contours and fill in wrinkles. However, the use of Restylane Vital Light is intended for intradermal injections only and is not to be used in skin tissues.

Design and administration:
Before the treatment, the patient’s suitability for the treatment and the need for post-treatment should be assessed. The patient should be informed about the indication, expected results, contraindications, precautions, monitoring, and potential complications of the treatment. The patient should be informed about the indication, expected results, contraindications, precautions, monitoring, and potential complications of the treatment.

1. Hold the product reservoir and remove the grey protective cap.
2. Prepare the skin for treatment.

2. Assemble the needle (Figure 2a) and (b):
   a) Hold the product reservoir and remove the grey protective cap.
   b) Hold the product reservoir and remove the grey protective cap.

3. The patient should be informed that he or she should not expose the injection site to intense light before the injection or during the procedure. The patient should be informed that he or she should not expose the injection site to intense light before the injection or during the procedure. The patient should be informed that he or she should not expose the injection site to intense light before the injection or during the procedure. The patient should be informed that he or she should not expose the injection site to intense light before the injection or during the procedure. The patient should be informed that he or she should not expose the injection site to intense light before the injection or during the procedure. The patient should be informed that he or she should not expose the injection site to intense light before the injection or during the procedure. The patient should be informed that he or she should not expose the injection site to intense light before the injection or during the procedure. The patient should be informed that he or she should not expose the injection site to intense light before the injection or during the procedure.

4. Treatments (Figure 4):
   a) Hold the product reservoir and remove the grey protective cap.
   b) Hold the product reservoir and remove the grey protective cap.
   c) Hold the product reservoir and remove the grey protective cap.

5. Reuse:
   a) Hold the product reservoir and remove the grey protective cap.
   b) Hold the product reservoir and remove the grey protective cap.
   c) Hold the product reservoir and remove the grey protective cap.

6. Shelf life and storage:
   a) Hold the product reservoir and remove the grey protective cap.
   b) Hold the product reservoir and remove the grey protective cap.
   c) Hold the product reservoir and remove the grey protective cap.

7. Manufactured by:
   a) Q-Med AB, Box 10, 581 35, Uppsala, Sweden

8. Product documentation is available at your local Q-Med representa-
RESLYTANE LIPP INSTRUCTIONS FOR USE

Composition: Hyaluronic acid, stabilized 20 mg/ml Phosphate buffered saline, pH 7 ± 0.2

Description: RESLYTANE® Lipp is a clear, transparent and viscous gel supplied in a glass syringe together with an orifice 27 G needle. The product is for single use only. RESLYTANE® Lipp is a unique form of stabilized non-animal, hyaluronic acid Hyaluronic acid is a natural polysaccharide which occurs as an important structural element in the skin and in subcutaneous and connective tissues as well as in the synovial fluid and fluid. Hyaluronic acid belongs to a group of very few substances which are identical in all living organisms.

Mode of action
RESLYTANE® Lipp is a filler that acts by adding volume to the tissue, thereby supporting the overlying (dermal) tissue to enhance the lips to the desired level of correction. The hyaluronic acid/molecular hydrogel nature combined with its three dimensional structure allows the molecule to bind water many times its own weight. The addition of water helps to maintain the overall volume of the product resulting in a longer duration. RESLYTANE® Lipp is naturally integrated into the tissue and will in time undergo biodegradation. The biodegradation process increases the water binding capacity of the gel thus allowing RESLYTANE® Lipp to maintain the overall volume during the degradation process.

Indication and usage
RESLYTANE® Lipp is intended to be used for lip enhancement. It should be injected into the deep layer of the dermis and/or the superficial layer of the subcutis. The degree and duration of the correction depends on the tissue area at the implant site, the depth of the implant in the tissue and the injectant technique. It is often advisable to combine RESLYTANE® Lipp with other products from the RESLYTANE® range of products.

Warning
RESLYTANE® Lipp is only intended for use in the deep layer of the dermis and/or superficial layer of subcutis. Do not resorb RESLYTANE® Lipp. Do not mix with other products. Do not inject intra-arterially. There is a potential risk with the material that the procedure could be inadvertently injected into blood vessels. This may result in vascular occlusion with transient impairment of vision, transient or even permanent.

Do not use in patients with bleeding disorders or patients who have undergone any procedure with thrombolytic agents or inhibitors of platelet aggregation in the preceding 2 weeks.

Precautions
Non-surgical procedures associated with injecting into the dermis and/or superficial layer of subcutis must be observed. Like any such procedure, the implantation of RESLYTANE® Lipp is associated with an inherent risk of infection. RESLYTANE® Lipp should not be used in or near anatomic sites where there is active skin disease, infection or resolved conditions. Patients who are using substances that may affect inflammatory such as aspirin and non-steroidal anti-inflammatory drugs may be at risk for injection, experience increased bruising or bleeding at injection sites. Do not use RESLYTANE® Lipp together with any injectable implant, except for other products from the RESLYTANE® range of products. RESLYTANE® Lipp should not be injected into an area where a permanent implant has already been placed. RESLYTANE® Lipp should not be used for patients with uncontrolled infections.

The patient should be informed that he or she should not expose the treated area to intense heat (e.g. solarium and sunbathing) or extreme cold or heat until the initial swelling and redness have resolved. If laser treatment, chemical peeling or any other procedure based on chemical or physical reactions is performed after treatment with RESLYTANE® Lipp there is a theoretical risk of existing inflammatory reaction in the injected area. RESLYTANE® Lipp should not be used for patients who have been treated with resurfacing procedures within 6 months and until a full healing process has been completed.

RESLYTANE® Lipp has not been tested in pregnant or breastfeeding women or in children.

Anticipated side effects
After the injection of RESLYTANE® Lipp some common injection-related reactions might occur. These reactions include swelling, pain, itching, bruising or tenderness at the implant site. Typically resolution is spontaneous within a week after injection into the lips. Additionally temporary palpable lumps has been noted after the use of RESLYTANE® Lipp. In some patients. Gentle massage can reduce the risk for such a result.

Adverse events
Inflammatory reactions have been reported in rare cases. These reactions have consisted of redness, swelling, tenderness and induration at the implant site. These reactions may occur either shortly after injection or after a delay of 2-4 weeks and have generally been described as mild to moderate and self-limiting, with an average duration of 2 weeks. In pronounced cases a short course of oral corticosteroids may prove effective. Patients who have experienced this type of reaction should not be re-injected with RESLYTANE® Lipp or any other product within the RESLYTANE® range of products.

The following very rare cases have been reported with RESLYTANE® products:
- biopsy proven granuloma formation
- necrosis, possible due to suboptimal injection technique requiring medical and/or surgical intervention
- persistent discoloration, possible due to deposit of hemosiderin, as a consequence of injection site bleeding. These reactions have rarely occurred after repeated injections.

Post-inflammatory pigmentation changes due to deposits of melanin have been observed in clinical studies in people with dark skin (Frasapart type H+V).

Isolated cases of facial oedema and urticaria have also been reported but it is uncertain whether these cases are related to treatment or caused by underlying disease or concomitant medication.

One case of transient visual disturbance following intra-dermal injection into the upper half of the face has been reported.

Adverse events must be reported to the local Q-Med representative or RESLYTANE distributor.

Interactions
Treattment with RESLYTANE® Lipp in combination with drugs and other devices or concomitant dental therapies has not been evaluated in controlled clinical studies.

Assembly of needle to syringe
For use only RESLYTANE® Lipp is important that the needle is properly assembled to the syringe. This may result in separation of the needle and syringe during injection. See pictures 1 and 2.

1. Group the narrow part of the needle should tightly Turn the needle clockwise until you feel counter pressure.

2. Grasp the outer part of the needle should firmly Press and turn the needle should 90° (a quarter turn). The quarter turn is necessary to lock the needle onto the syringe.

Doseage and administration
Before the treatment, the patient’s suitability for the treatment and the need for pain relief should be assessed. For optimal patient comfort anesthetise through nerve block is recommended. The patient should be informed about the indications, expected result, contraindications, precautions, warnings and potential adverse effects. The treatment site should be cleaned with a suitable antiseptic solution. RESLYTANE® Lipp is administered using a thin gauge needle (up to 27 G) by injecting the material into the deep layer of the dermis and/or the superficial layer of the subcutis. Before injecting area the not carefully and a small dorsal is visible at the tip of the needle. If RESLYTANE® Lipp is injected too deeply or intramuscularly, the duration of the implant will be shorter because of a higher hyaluronic acid turnover rate. A too superficial injection may give blanching effects and lumps in the treated area. If blanching is observed, the oedematous skin turn a whitish colour, the injection should be stopped at once and the area massaged until it returns to a normal colour.

The injection technique with regard to the depth of injection and the administered quantity may vary. RESLYTANE® Lipp should only be injected by trained practitioners. To accommodate the lip the linear threading techniques can be used. When adding volume to either the upper or the lower lip, both the linear threading and the serial puncture technique can be used. Treatment should always be calibrated and personalized for each patient.

Insert RESLYTANE® Lipp while pushing the needle slowly backwards. Injection should stop just before the needle is pulled out from the skin to prevent material from leaking out from the injection site. To avoid unnecessary bleeding and swelling it is advised to inject slowly and to leave the needle in the tissue for a few extra seconds. Always consider the harmony of the face and try to keep a good balance. Look at the nose, lips and chin, and let these features guide the treatment. Do not overcorrect. The lips should be gently massaged in order to obtain a favorable result.

For each treatment site a maximum dosage of 2 ml per treatment session is recommended. If the treated area is swollen directly after the injection, melting ice can be applied on the ice for a short period. After the first treatment, additional implantations of RESLYTANE® Lipp may be necessary to achieve the desired level of correction. Periodical follow-up injections help sustain the desired degree of correction. A follow-up treatment before the full aesthetic correction is completely diminished may be beneficial.

Note! The correct injection technique is important for the final result of the treatment. RESLYTANE® Lipp is only intended to be administered by authorized personnel in accordance with local legislation. Please consult your local Q-Med representative or RESLYTANE distributor for more details about techniques and training opportunities.

The syrings, the needle and any unused material must be discarded immediately after the treatment.

How supplied:
RESLYTANE® Lipp is supplied in a glass syringe with a barrel fitting. 1 or more gossamer sterilized needles. 27 G (¼") is packed together with each syringe. A patient record label is a part of the syringe. A patient record label. Remove it by pulling the flat marked with three small arrows. This label is to be attached to patient records to ensure traceability of the product. The contents of the syringe has been sterilised using moist heat. The number of units per package and this volume contained in each syringe is as stated in the outer package.

Do not use if package is damaged.

STERILE NEEDLE
Follow local or/and institutional guidelines for use and disposal of medical sharp devices. Obtain prompt medical attention if injury occurs.

To avoid needle breakages, do not attempt to straighten a needle that is bent. Dispose of the procedure with a replacement needle.

Do not re-use needles. Replacing by hand is a hazardous practice and should be avoided.

Discard unsealed needles in approved sharps collectors.

Shell-life and storage
As an indoor product. Store up to 25°C. Protect from freezing and sunlight.

Manufactured by Q-Med AB, Södertälje, Sweden Phone +46 8 479 00 50 Fax +46 8 479 40 91 www.qmed.com e-mail info@qmed.com

Symbols on packaging

<table>
<thead>
<tr>
<th>Symbol</th>
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References
A product documentation is available in your local Q-Med representative or RESLYTANE distributor or on www.Qmed.com.

* RESLYTANE® is a trademark owned by Q-Med AB.

90-38176-02, Sep. 2007

Chapter 8

25
Restylane SubQ™ – INSTRUCTIONS FOR USE

Composition
Hyaluronic acid and stabilized 20 mg/mL

Pharmacological and physiological effect

Restylane SubQ is a clear, transparent and viscous gel supplied in a glass syringe. Restylane SubQ is intended to be used for facial tissue augmentation. It is supplied in a glass syringe. Restylane SubQ™ is only intended for subcutaneous and/or supraperiostal administration depending on the treatment site. Restylane SubQ™ is intended to be administered by authorized personnel in accordance with local legislation. It is a sterile product with local mobility and lumpiness. If any disturbing mobility or lumpiness should occur, correction can be attempted by aspiration of some of the implanted gel.

Indications
Restylane is intended to be used for facial tissue augmentation. It is supplied in a glass syringe. Restylane SubQ is intended for subcutaneous and/or supraperiostal administration depending on the treatment site. Restylane SubQ™ is only intended to be administered by authorized personnel in accordance with local legislation.

Precautions

Nasal passages associated with subcutaneous and/or supra-periosteal injections must be observed. Like any such procedure, the administration of Restylane SubQ is associated with an inherent risk of infection. Contact your local Q-Med representative or Restylane distributor for more information about injection techniques and training opportunities.

Mode of action

Restylane SubQ acts by adding volume to the tissue, thereby supporting the overlying (dermal) tissue to shape the contours of the face, to define the contours of areas. This is accomplished by hyaluronic acid particles combined with a three-dimensional structure allowing the molecules to bind water many times its own weight. The addition of water helps to maintain the overall volume of the product resulting in a larger duration. Restylane SubQ is naturally integrated into the tissue and will in time undergo continuous degradation. The viscoelastic pattern of degradation increases the water binding capacity of the gel, thus allowing Restylane SubQ to maintain the overall volume during the degradation process.

Anticipated side effects

During injection of Restylane SubQ, some minor injection-related reactions may occur. These may include erythema, swelling, tenderness, pain, bruising or itching in the implant site. Typically resolution is spontaneous within one to two weeks.

Adverse events

If a clinical study local mobility and lumpiness of Restylane SubQ was observed in a few patients. The most likely explanation to local mobility is the use of too large volume injections and/or a sub-optimal injection technique; including superficial placement of Restylane SubQ. Based on clinical experience, adequate soft tissue cover and soft tissue support are important parameters to minimize the risk of local mobility and lumpiness. If any disturbing mobility or lumpiness should occur, correction can be attempted by aspiration of some of the implanted gel.

The incidence of adverse events from post-marketing surveillance is less than 1%. These adverse events include erythema, swelling, injection, inflammation and granulomas. Inflammatory symptoms have been reported to occur more than one month after injection and may resolve at the injection sites. Injection should be excluded or treated if necessary. A short course of oral corticosteroids may prove effective for implant site infiltration.

For patients who have experienced clinically significant reactions, a decision for remanufacture should take into consideration the cause and significance of previous reactions. For example, remanufacture is not recommended following rare cases of granulomas or associated significant inflammatory reactions.

In pronounced cases a short course of oral corticosteroids may prove effective for implant site infiltration. If any disturbing mobility or lumpiness should occur, correction can be attempted by aspiration of some of the implanted gel.

Infections should be excluded or treated if necessary. In pronounced cases a short course of oral corticosteroids may prove effective for implant site infiltration. If any disturbing mobility or lumpiness should occur, correction can be attempted by aspiration of some of the implanted gel.

3. Different injection and administration techniques can be used. Contact your local Q-Med representative or Restylane distributor for more information about injection techniques and training opportunities. Restylane SubQ should not be used by patients with unstable emotions.

4. Restylane SubQ should be administered by injecting the material into the subcutaneous tissue or supra-periostal tissue. A superficial injection may give rise to lumpiness.

5. Restylane SubQ™ is intended for subcutaneous facial tissue augmentation. It is intended to be used for facial tissue augmentation. It is supplied in a glass syringe. Restylane SubQ™ is only intended to be administered by authorized personnel in accordance with local legislation. It is a sterile product with local mobility and lumpiness. If any disturbing mobility or lumpiness should occur, correction can be attempted by aspiration of some of the implanted gel.

6. Before injecting, the air is removed from the syringe up to the point where a drop is visible at the tip of the cannula/needle.

7. If a needle is used, aspiration prior to injection is recommended.

8. Do not inject Restylane SubQ™ into the eye. If any reaction is encountered the cannula/needle should be partially withdrawn and the injection repeated.

9. Inject Restylane SubQ™ while pulling the cannula/needle slowly backwards.

10. Do not inject the material into the eye. If any reaction is encountered the cannula/needle should be partially withdrawn and the injection repeated.

How supplied

Restylane SubQ™ is supplied in a glass syringe with a needle. Each syringe is terminally sterilized by filtration and packed in a paper carton. A patient record label is part of the syringe label (see Figure 4.6). Remove it by pulling the flip strip on three small arrows. This label is to be attached to patient records to ensure transparence of the product. The number of units per package and the volume contained in each syringe is stated on the outer package. Do not use if package is damaged.

Shelf life and storage

As indicated on package: Store up to 25° C. Protect from freezing and sunlight.

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Symbols on packaging

Restylane™ Product documentation is available at your local Q-Med representative or Restylane distributor or on www.restylane.com.

References
For safe use of any Restylane® product it is important that the needle is properly assembled.

1. Grasp the narrow part of the needle shield loosely. Turn the needle shield clockwise until you feel counter pressure.

2. Grasp the wider part of the needle shield firmly. Press and turn the needle shield 90° (a quarter turn). The quarter turn is necessary to lock the needle onto the syringe.
Treatment results

Skin rejuvenation

Indication: Face
Product used: Restylane Vital and Restylane Vital Light

Indication: Neck
Product used: Restylane Vital

Indication: Décolletage
Product used: Restylane Vital

Indication: Hands
Product used: Restylane Vital Light

Tissue augmentation, men

Indication: Lip enhancement, nasolabial folds, worry lines, periorbital lines
Product used: Restylane Perlane, Restylane and Restylane Touch

Indication: Nose-eyebrow augmentation, tear trough deformity, forehead lines, nasolabial folds, upper lip contour
Product used: Restylane Touch, Restylane, Restylane Perlane
Tissue augmentation, women

**Before**

**After**

- **Indication:** Nasolabial folds, mouth corners, lip line
  **Product used:** Restylane, Restylane Perlane

- **Indication:** Nasolabial folds, lip lines, mouth corners, eyebrow, glabella, scar
  **Product used:** Restylane

- **Indication:** Glabella, cheek fold, oral commissures, nasolabial folds, chin
  **Product used:** Restylane, Restylane Perlane

- **Indication:** Lips, nasolabial folds, horizontal rythid at the root of the nose, glabella, oral commissures
  **Product used:** Restylane, Restylane Lipp and Restylane Perlane

- **Indication:** Cheek augmentation, tear trough deformity, lip augmentation, cupids bow
  **Product used:** Restylane, Restylane Lipp, Restylane SubQ

- **Indication:** Cheek augmentation, tear trough deformity, lip augmentation, philtrum, nasolabial folds, glabella
  **Product used:** Restylane, Restylane Perlane, Restylane SubQ
What is Restylane®?
Restylane is a gel that is injected into the skin in order to add volume to lips and lift up wrinkles and folds. Restylane consists of stabilized non animal hyaluronic acid (HA), which mimics natural HA already present in the human body. Restylane works by creating volume in the skin. Some dermal fillers are derived from animal substances. The hyaluronic acid in Restylane is of non-animal origin.

How was Restylane developed?
After many years of research, Dr Bengt Ågerup, the founder of Q-Med AB in Uppsala, Sweden, succeeded in developing the NASHA™ technology to produce minimally stabilized non animal hyaluronic acid (HA) gels, to replace the loss of volume in the skin. The first product, Restylane, was launched in 1996. Before this, only collagen made from cow hide and hyaluronic acid made from rooster combs had been available.

How do Restylane products contain?
All Restylane products consist of stabilized hyaluronic acid 20 mg/ml and phosphate buffered saline, pH 7 q.s. They are clear, transparent, viscous gels supplied in glass syringes. The hyaluronic acid is produced biotechnologically by bacterial fermentation.

What are Restylane products produced?
The hyaluronic acid in Restylane, is produced biotechnologically by bacterial fermentation. A specific type of bacteria is used because of its ability to produce a high yield of hyaluronic acid. The hyaluronic acid is extracted and purified and is then subjected to slight chemical modification (stabilization) to increase its longevity in the tissue and to form a gel. The gel is put into syringes and sterilized by moist heat. The syringes are put in blister packs together with a needle. The blister packs are subsequently put in a carton in which the instructions for use are packed.

What is the difference between the Restylane products?
The difference between the Restylane products is the size of the gel particles as well as intended use and recommended technique to achieve optimal results.

Is there a difference in structure between the products?
All the products are gels and have the same structure, however the properties of the gel differ depending on which specific Restylane product is in question.

What is the molecular weight of the Restylane products?
From a scientific point of view, it is not common practice to calculate the molecular weight of a gel. Nevertheless, it may be appropriate to do this in order to demonstrate the very large difference between non-stabilized hyaluronic acid products and stabilized hyaluronic acid in Restylane. In the NASHA™ gel particles, the hyaluronic acid molecules are connected to each other in a network, i.e. every individual gel particle can be regarded as a single molecule. The molecular weight of a NASHA™ gel particle can then be estimated to be about $10^{7}$ which is much larger than the molecular weight of non-stabilized hyaluronic acid in various products, which varies from one to ten million ($10^{6} – 10^{7}$).

Why are Restylane products moist heat-sterilized?
Restylane products are moist heat-sterilized for maximum safety. Restylane has a sterility assurance level (SAL) of $10^{-6}$. This method is superior to aseptic manufacturing and results in a product where the probability of finding a syringe containing a micro-organism is less than one in one million units.

Restylane is biodegradable. What does this mean?
Restylane is biodegraded in the body by free radical processes and the action of enzymes.

How is a treatment performed?
During treatment, Restylane gel is injected into the skin in tiny amounts with a very fine needle. The gel produces volume under the wrinkle, which is lifted up and smoothed out. When enhancing lips or facial contours, Restylane adds volume and shape to the treated area.

How long will the treatment session take?
Treatment with Restylane is a very quick and easy process. As no pre-test is needed, the treatment can be carried out immediately. A treatment generally takes 30 minutes. The time differs somewhat, depending on the correction you wish to achieve.

Which areas of the face can be treated with Restylane?
Restylane can be used for smoothing out folds and wrinkles, lip enhancements and shaping facial contours. The most common areas are the glabellar lines (between the eyebrows), the nasolabial folds (from the root of the nose to the angle of the mouth) and the lips, although other sites can also be treated.

Does the treatment cause pain?
Most people find the injections relatively painless. If needed, a topical anesthetic, ice, subcutaneous anesthesia or a nerve block can be applied to the area being treated prior to the procedure. When enhancing the lips, a local anesthetic injection is often given. When contouring the cheeks or chin, a nerve block is recommended.

Do Restylane products expand after injection?
Because the tissue pressure is sometimes disturbed and takes on a higher value, e.g. in connection with oedema, or a lower value, during low water intake, a small, yet significant, change (swelling or shrinkage) may occur.

Is there a need for overcorrection?
No.

How soon will I see the results?
The results can be seen immediately. Except for with Restylane Vital, this requires a treatment program and the best results will appear after the third treatment.

How will I look like after the treatment?
Immediately after the treatment you can expect slight redness, swelling, tenderness, bruising or an itching sensation in the treated area. This is a normal result of the injection. The discomfort is temporary and generally disappears in a few days. After a lip treatment, the lips may become swollen and look somewhat uneven. This can persist for a few days (up to a week). If the discomfort continues, please contact your physician.
What should a patient bear in mind after a treatment with Restylane?

During the first 48 hours after a treatment, there should be no massage or rubbing of the treated area unless you as the treating physician instruct otherwise. If you have had a lip enhancement, avoid puckering your lips for the first two days after the treatment. Until the initial swelling and redness have resolved, do not expose the treated area to intense heat (e.g. in a solarium or by sunbathing) or extreme cold.

Can Restylane be removed?

No. However, Restylane biodegrades naturally with time. If you feel uncertain about the desired result, you can choose to have the treatment done in steps on different occasions. In extreme cases hyaluronidase has been described in the literature as a method to make the Restylane product dissipate. Also, palpable bolus injections of Restylane can be aspirated using an empty syringe. Too superficial deposits can also be aspirated or evacuated using as small incision in the skin and then applying subsequent pressure.

Can Restylane replace surgical procedures?

Restylane can in certain cases be used in conjunction with surgery to fill out wrinkles that cannot be removed by surgery.

How long does the effect of a Restylane treatment last?

The length of time the effect of a Restylane treatment lasts is very individual and depends on many factors, such as the structure of the skin, lifestyle, age, the degree of perfection demanded and the injection technique of the practitioner. Experience indicates that touch-up and follow-up treatments will add to the duration. Most people choose to have a new treatment within a year after the treatment of wrinkles and folds and within 6 months after a lip enhancement.

Does Restylane get stiffer in cold weather? What happens in the sun?

You should not expose the treated area to intense heat (e.g. in a solarium or by sunbathing) or extreme cold for the first few days after the treatment in order to avoid the risk of inflammation as the area has been disturbed. After the initial few days, you can recommend the patient to return to their normal lifestyle.

What is the shelf life of Restylane products?

The shelf life is set at 36 months after the production date for most of the Restylane products. Restylane SubQ and Restylane Lipp have a shelf life of 18 months.

If the product is about to expire, will the durability be shorter once injected?

No, degradation of the product does not start until it is injected.

At which temperature should Restylane be stored?

Restylane products should be stored at up to 25 degree C. Prevent from freezing and keep out of sunlight.

What is the CE number of the Restylane range of products? What does this actually mean?

The CE number is the same for all Restylane products, CE 0344. This is the number of the Notified Body. A Notified Body is an institution that issues the CE certificate. The CE certificate means that the product complies with the requirements in the EU directive and can be sold within the EU.

At what depth in the tissue should Restylane products be injected?

It is recommended that: Restylane Touch should be injected in the superficial dermal layer, Restylane should be injected in the mid part of the dermis. Restylane Perlane should be injected in the deep layer of the dermis and/or the surface layer of the subcutis. Restylane Vital should be injected in the dermal layer, preferably deeper, while Restylane Vital Light should be injected in mid-dermis. Restylane Lipp should be injected into the deep layer of the dermis and/or into the superficial layer of the subcutis. Regarding Restylane SubQ the depth of injection may vary from injection into the subcutaneous fatty tissue to supraperiostal administration depending on the treatment site.

What happens if a Restylane product is not injected at the recommended tissue depth?

Each Restylane product is tailored to match the tissue matrix density at the different dermal layers. To ensure satisfactory results, it is important that each product is injected at the right tissue depth. For example, if a Restylane product intended to be only injected in dermis (eg Restylane) is injected too deeply, the gel can move in the tissue because the gel particles are too small.

Why do the lips sometimes become swollen immediately after treatment and how long does the swelling normally last?

The cause of this is not yet understood. However, the swelling is usually gone within a week after injection.

Which Restylane products are recommended for the treatment of the lips?

Restylane Lipp is recommended for the enhancement of lips. However, both Restylane and Restylane Perlane have also been used to produce fuller lips and a pouting look.

How long does the effect of a Restylane treatment of lips last?

It has been shown in clinical trials that Restylane is effective for up to six months. Clinical experience indicates that touch-up and follow-up treatments add to the duration.

Can Restylane products be combined with other types of implant?

Restylane products should not be used together with any other injectable implant. The Restylane products should not be injected into or nearby an area where a permanent implant has been placed.

Can Restylane products be injected in a so-called "sandwich" procedure?

Yes, a combination of our products can be used in this procedure. For example, in a deep fold, Restylane Perlane can be injected first and Restylane or Restylane Touch can then be added at a more superficial level.

What needle size should I use?

For each Restylane product the appropriate needle size is recommended in the corresponding IFU. Each needle size is matched to facilitate the injection of that specific product. Too small a needle can disrupt the gel.

Is different extrusion force needed to inject the different Restylane products?

Yes, but in practice this difference is only of clinical importance.
when working with Restylane Vital and Restylane Vital Light. Restylane Vital Light has a lower extrusion force, so care must be
taken not to over-inject.

Is there any risk for migration and/or displacement of Restylane
products from the site of injection?
There are no specific scientific studies related to migration of
Restylane products. However, when larger volumes of Restylane
products than those recommended in the instructions for use are
used the risk of displacement may no longer be negligible.

Are there any side effects or adverse reactions?
After the injection of Restylane, some common injection-related
reactions might occur. These reactions include erythema, swelling,
pain, itching, bruising or tenderness at the implant site. Typically
resolution is spontaneous within a few days after injection into the
skin and within a week after injection into the lips. Additionally,
temporary palpable lumpiness has been noted after the use of
Restylane in some patients. Inflammatory reactions have been
reported in rare cases. These reactions have consisted of redness,
swelling, tenderness and induration at the implant site. These
reactions may commence either shortly after injection or after a
delay of 2-4 weeks and have generally been described as mild to
moderate and self-limiting, with an average duration of 2 weeks. In
pronounced cases a short course of oral corticosteroids may prove
effective. The infection should be excluded or treated if necessary. Patients who have experienced this type of reaction should not be
retreated with a Restylane product.

The following very rare cases have been reported with Restylane
products:
• biopsy proven granuloma formation
• necrosis, possibly due to suboptimal injection technique
  requiring medical and/or surgical intervention
• persistent discoloration, possibly due to deposit of hemosiderin
  as a consequence of injection site bleeding. These reactions have
  mostly occurred after repeated injections.
• post inflammatory pigmentation changes due to deposit of
  melanin have been observed in clinical studies in people with
dark skin (Fitzpatrick Type IV-VI).
• isolated cases of facial oedema and urticaria have also been
  reported but it is uncertain whether these cases are related to
  treatment or caused by underlying disease or concomitant
  medication.
• one case of transient visual disturbance following intra-arterial
  injection into the upper half of the face has been reported.

Can the products be used for patients who have undergone
laser treatment or chemical peeling?
Yes, although we recommend that these patients should wait until
the treated area has totally healed and the skin has normalized
(normally four to six weeks).

What happens if you use laser or chemical peeling on top of an
area treated with a Restylane product?
If laser treatment, chemical peeling or any other procedure based
on active dermal response is considered after treatment with
Restylane, there is a theoretical risk of eliciting an inflammatory
reaction at the implant site. This also applies if a Restylane product
is administered before the skin has healed completely after a
procedure of this kind.

Can Restylane products be used for patients during pregnancy
or breast-feeding?
Treatment with Restylane products during pregnancy or breast-
feeding has not been tested. During pregnancy there are multiple
significant metabolic, hormonal and immunologic changes
that produce cutaneous manifestations. Any therapy should be
reconsidered in the light of the pregnancy.

Are there any known interactions with antibiotics?
Treatment with Restylane products in combination with other
drugs and devices has not been tested. Theoretically, there is no
basis for any interaction with commonly used antibiotics.

Can patients with different kinds of allergy be more sensitive
to Restylane products?
So far, we have seen no connection between patients with allergies
and patients who report a reaction to Restylane products.

If a patient has had problems with recurrent facial herpes
simplex, can Restylane treatment contribute to another herpes
simplex eruption?
There is a risk that the injection process itself, i.e. the insertion of
a needle into the skin, could contribute to another herpes simplex
eruption.

Should you consider any prophylactic treatment for patients
with a medical history of recurring facial herpes?
You should take a decision about the need for prophylactic antiviral
treatment in consultation with your patient.

Can a person suffering from an autoimmune disease be treated
with Restylane products?
Autoimmune diseases are in general no contraindication for
treatment. However, it is Q-Med’s policy to recommend patients
with an underlying disease to discuss and ask the treating physician
of the disease if he or she think it’s OK to inject Restylane. Thus,
a doctor performing the injection should not primarily make such
decision.

Are there any articles about injections with Restylane and
patients with autoimmune diseases?
Until February 2008 no article is found when performing a
MEDLINE search combining search words autoimmune diseases
and Restylane.

Can a patient on Roaccutan (Isotretionin) treatment be injected
with Restylane?
Roaccutan (Isotretionin) treatment may cause dryness and even
irritation of the skin. Therefore it is recommend that the patient
discuss and ask the doctor who has prescribed Roaccutan if he or
she think it’s OK to inject Restylane. Thus, the doctor performing
the injection should not make such a decision, unless he or she is
the prescriber of the patient’s Roaccutan. In general, it is advisable
to wait some time after the Roaccutan treatment is finished before
Restylane treatment is started.

Will a vaccination for hepatitis A and B cause any interaction/
elicit any reaction to Restylane?
There is no known interaction between vaccines and Restylane.
However, it is advisable to discuss this matter during consultation.
What is the minimum age that a patient has to be before they can be treated with Restylane?
The studies that were performed to gain approval from the European and US authorities were conducted on adults, so there is no documented data on treatment of non-adults. Therefore, we recommend that the minimum age should be in accordance with the local legislation in each country concerning lawful adult age.

Is there a top age for Restylane to have effect?
The oldest patient receiving Restylane treatment in the study performed to gain approval from the US authority was 78 years old. Anecdotal reports and clinical experience indicates that there are no upper age limit for treatment effect.

A patient has received 4 treatments with Restylane and after the 4th treatment she developed a blue-grey discoloration in the treated area. Is there any explanation for this?
The etiology of discoloration developing over time includes 1) hemosiderin deposition after some bleeding in the tissue and 2) postinflammatory hypo- or hyper-pigmentation because of repeated tissue trauma. An immediate blue discoloration (e.g. Tyndall effect due to light is reflected differently) is presumably caused by superficial deposition. However, in order to understand each individual case, detailed information and photographs is needed. Also, a punch biopsy would give the answer.

A patient has been treated 3 times (once every year for 3 years) with Restylane in the lips. But the 4th time, she felt the product has not had a long-lasting effect and both patient and doctor are very surprised. What is the explanation of this?
This happens but fortunately it’s a rare thing. Also very experienced physicians will report from time to time that the effect of a lip treatment will disappear within days. The explanation for this is unknown. It’s hard to believe it is technique related and it’s absolutely not due to the product which is always very carefully checked before leaving the production unit in Uppsala.

A patient was treated with Restylane and Restylane Perlane, but no visual difference was seen after treatment. Do we recommend to inject the patient again or is it not worth it?
This is something that many physicians can give witness to, sometimes you just don’t get any effect after injecting Restylane. We know that this can sometimes happen, however there is no clear explanation as to why it happens at this time. If the patient so wishes it’s perfectly OK to give a new treatment and maybe sometimes it should even be recommended to offer this, otherwise the patient will go away with a negative impression of Restylane.

Is the duration of Restylane used for lip enhancement different in smokers compared to non-smokers?
We have no data on how smokers are responding to Restylane. What is known is that the skin is damaged by smoking. One hypothesis might be that if someone is smoking the lips will be more active and maybe the duration will be shorter because of this.

What is the difference between Restylane Vital and Restylane Vital Light?
Restylane Vital and Restylane Vital Light are 2 different products for rejuvenation of the skin. Both products are based on stabilized hyaluronic acid, ensuring a long-term effect. Restylane Vital efficiently rejuvenates mature and photodamaged skin where it gives a profound, long-lasting effect. The product contains 20 mg/ml stabilized hyaluronic acid and should be administered in a treatment cycle of three sessions 4 weeks apart, to be repeated after 6 months.

Restylane Vital Light is a smoother, softer and more fluid gel designed to rejuvenate thin and delicate skin, such as neck, décolletage and back of hands. Restylane Vital Light is also ideal when treating younger skin which requires a lighter treatment with a refreshing effect. The product contains 12 mg/ml stabilized hyaluronic acid and should be administered in a treatment cycle of three sessions 2-4 weeks apart, to be repeated after 4-6 months.

Why is Restylane Vital Light of a lower concentration than the rest of the Restylane range?
The lower gel concentration of Restylane Vital Light makes the product more fluid and easier to inject in areas with thin skin such as the neck. Restylane Vital Light distributes evenly upon injection, and does not cause bumps if injected correctly.

Is Restylane Vital Light a mesotherapy treatment?
No, neither Restylane Vital nor Restylane Vital Light are mesotherapy treatments. Correct injection technique is essential when using the Restylane Vital products, too superficial injection will cause bumps. Use the multipuncture or short linear threading technique to inject small deposits of gel about 1 cm apart. For safe and easy injection of Restylane Vital Light the Restylane Injector can be used.

Can I combine Restylane Vital and Restylane Vital Light on the same patient?
Yes, use the product suitable for the skin area that is treated. For photodamaged facial skin Restylane Vital is ideal, but for neck and décolletage Restylane Vital Light should be used.
References


6. Carruthers J, Carruthers A. A prospective, randomized, parallel-group study analyzing the effect of BTX-A (Botox) and nonanimal sourced hyaluronic acid (NASHA™, Restylane) in combination compared with NASHA™ (Restylane) alone in severe glabellar rhytides in adult female subjects: Treatment of severe glabellar rhytides with a hyaluronic acid derivative compared with the derivative and BTX-A. Dermatol Surg 2003; 29: 802-809.


