

## About RESTYLANE® SILK

Before beginning your treatments, please review this important information.

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### GLOSSARY

(Note: words in the glossary are in bold throughout this document)

- *Anesthetic* – a substance that reduces sensitivity to pain.
- *Cannula* – a thin metal tube with a blunt tip. It may be used as an alternative to needles in lip injections.
- *Hyaluronic acid (HA)* – a polysaccharide (sugar) that is naturally in the body. It keeps skin moisturized and soft. HA fillers, including *Restylane Silk*, are a modified form of the HA that is naturally in your body.
- *Hyaluronidase* – an enzyme used to breakdown HA.
- *Lidocaine* – a synthetic compound used as a local anesthetic to decrease pain.
- *NSAID* – Nonsteroidal anti-inflammatory drug, such as ibuprofen
- *Perioral Lines* – the wrinkles in the skin around the mouth and lips.
- *Touch-up* – an additional injection of a small amount *Restylane Silk* usually given two weeks after treatment, if necessary to achieve the desired result.

## PRODUCT DESCRIPTION

### **What is *Restylane Silk*?**

*Restylane Silk* is a smooth, clear injectable gel composed of **hyaluronic acid (HA)**. HA is a naturally occurring sugar found in the human body. HA fillers, including *Restylane Silk*, contains HA that has been modified to last longer in the body than the naturally occurring HA. *Restylane Silk* contains 0.3 % **lidocaine** to reduce pain during injection.

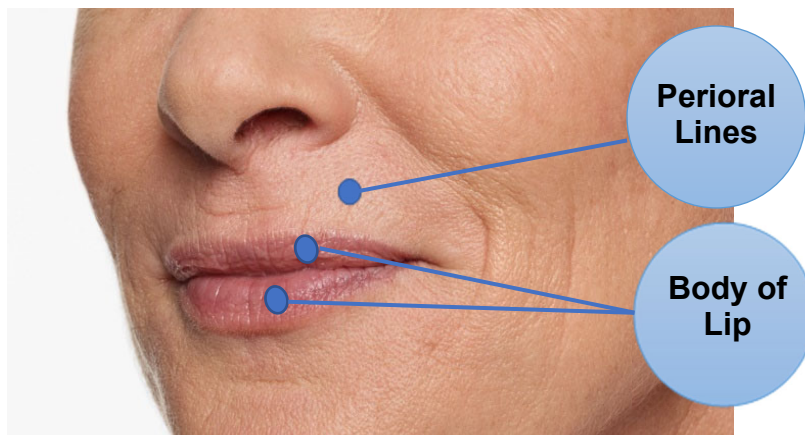
## INDICATION/INTENDED USE

### **What is it used for?**

*Restylane Silk* is injected into the lips and the lines around the mouth to temporarily add fullness to the lips and help smooth the lines around the mouth in patients over the age of 21.

### **How does it work?**

*Restylane Silk* is injected with an ultrafine needle or a small, blunt-tipped **cannula** into your lips to add fullness. It can also be injected with an ultrafine needle into the skin to help smooth the wrinkles around your mouth (**perioral lines**). The picture below shows the treatment areas for *Restylane Silk*.



## CONTRAINDICATIONS

### Who should not use *Restylane Silk*?

Your doctor will ask about your medical history to determine if *Restylane Silk* is right for you. Patients with any of these conditions should not use *Restylane Silk*:

- Highly allergic (for example: a history of severe allergic reaction or multiple severe allergies). Use may result in an allergic reaction.
- Allergic to gram positive bacteria
- If you have previous experience with allergic reactions to HA fillers. Use may result in an allergic reaction.
- Bleeding disorders. Treatment may cause bleeding to occur.
- Allergic to **anesthetics**, such as **lidocaine**. Use may result in an allergic reaction.

## PRECAUTIONS

### What precautions should my doctor discuss with me?

The following are important treatment considerations for you to discuss with your doctor and understand in order to help avoid unsatisfactory results and complications:

- The use of *Restylane Silk* where skin sores, pimples, rashes, hives, cysts, or infections are present should be postponed until healing is complete. Use of *Restylane Silk* where these are present could delay healing or make your skin problems worse.
- Tell your doctor if you are using St. John's Wort, blood thinners, high doses of Vitamin E supplements, aspirin, and other **NSAIDs**, such as ibuprofen, because these may increase bruising or bleeding at the injection site.
- Tell your doctor if you are planning other skin therapies such as laser, mechanical or chemical peeling, and hair removal after treatment. The use of *Restylane Silk* with these skin therapies may lead to other side effects such as inflammation.
- After treatment with *Restylane Silk*, you should minimize exposure to the sun or UV lamps, and avoid being in the heat and cold until any redness or swelling has disappeared. Exposure to any of these may cause temporary redness, swelling, and/or itching at the injection site.
- Tell your doctor if you are pregnant, thinking about becoming pregnant, or breastfeeding. The safety and effectiveness of *Restylane Silk* has not been established in pregnant women or nursing mothers.
- Tell your doctor if you are on a therapy to decrease the body's immune response. Treatment may result in an increased risk of infection.
- Tell your doctor if you have a history of thick, hard scars (excessive scarring). The safety and effectiveness of *Restylane Silk* in patients with a history of thick, hard scars has not been studied and may result in additional scarring.

- Tell your doctor if you have a dental block or use topical **lidocaine** at the same time as the filler treatment. High doses of **lidocaine** could cause a toxic reaction.
- The safety of *Restylane Silk* has not been established in people who are under the age of 22 years or over 65 years.
- *Restylane Silk* should only be used to be injected into the lips and wrinkles around the lips (**perioral lines**). It should not be used in other parts of the face and body.

## RISKS

**Warning:** One of the risks with using this product is unintentional injection into a blood vessel. The chances of this happening are very small, but if it does happen, the complications can be serious, and may be permanent. These complications, which have been reported for facial injections, can include vision abnormalities, blindness, stroke, temporary scabs, or permanent scarring of the skin. If you have changes in your vision, signs of a stroke (including sudden difficulty speaking, numbness or weakness in your face, arms, or legs, difficulty walking, face drooping, severe headache, dizziness, or confusion), white appearance of the skin, or unusual pain during or shortly after treatment, you should notify your health care practitioner immediately. Tell your doctor if you have had any prior surgery or procedures in the area you intend to be treated with *Restylane Silk*.

### What are the side effects?

Common side effects include swelling (other than the desired lip augmentation, i.e. unwanted swelling), tenderness, redness, bruising, itching and pain. When these events were reported by subjects in clinical studies, the majority were tolerable and most resolved within two weeks. Other, less common side effects may also occur.

### What side effects were reported by patients in the Clinical Studies?

As mentioned above, side effects related to the injection procedure usually occur, and the study patients were asked to report these in diaries daily for two weeks. The results are presented in the tables below.

*Table 1. Side effects after treatment using a needle for injection, as reported in patient diaries<sup>a</sup>*

Side effect	Experienced by
Swelling	98 out of 100 people (98%)
Tenderness	91 out of 100 people (91%)
Bruising	81 out of 100 people (81%)
Pain	77 out of 100 people (77%)
Redness	70 out of 100 people (70%)
Itching	29 out of 100 people (29%)

<sup>a</sup>Based on 177 subjects who provided information about side effects after their initial treatment

Table 2. Side effects after treatment using a cannula for injection, as reported in patient diaries<sup>a</sup>

Side effect	Experienced by
Swelling	All (100%)
Tenderness	95 out of 100 people (95%)
Redness	80 out of 100 people (80%)
Pain	73 out of 100 people (73%)
Bruising	60 out of 100 people (60%)
Itching	28 out of 100 people (28%)

<sup>a</sup>Based on 60 subjects who provided information about side effects after their initial treatment

### What side effects were reported by the Clinical Study Investigators?

Side effects that were reported by the doctors as related to the treatment included bruising, swelling, pain and lip bumps. Most of the symptoms started right after treatment and were gone within three weeks. In some patients however, lip swelling started more than three weeks (up to 20 weeks) after treatment. In the clinical study evaluating needle injection of *Restylane Silk*, some patients (5 out of 100 people) were diagnosed with lip bumps. These lasted longer than the other side effects; in one of the patients this was still ongoing at study end. There were no serious adverse events related to needle injection or **cannula** injection of *Restylane Silk* in the two clinical studies, and no concerns with regards to difference in skin color were raised.

### What are other possible adverse events?

Examples of other possible adverse events are listed below.

- As with all skin-injection procedures, the injection of *Restylane Silk* carries a risk of infection and formation of scar tissue. Rarely, people have developed infections that must be treated with antibiotics or other treatment. Infection may be hard to treat, but will generally go away when the gel is absorbed.
- Red or swollen small bumps (inflammatory papules) may occur. You may need antibiotics to treat them.
- If you have previously had facial cold sores, an injection can cause them to come back.
- Rarely, vision abnormalities including blindness have been reported when cosmetic facial fillers such as *Restylane Silk* are used in areas around the eyes, nose, and glabella.

**What side effects have been reported voluntary of *Restylane Silk* use in and outside of the United States?**

The most commonly reported serious adverse events were restricted blood flow leading to the death of skin (ischemia/necrosis), infection and abscess formation and allergic reactions (hypersensitivity reactions). Other serious events included common related symptoms such as swelling, pain/tenderness, skin redness (erythema) and bruising.

- Restricted blood flow occurred within immediately or up to 3 days after injection. Treatment included **hyaluronidase**, aspirin, nitroglycerin, corticosteroids, and antibiotics. In addition, warm compresses, massage and arnica were used.
- Infection and abscess formation occurred 2 to 52 days after injection. Treatment included **hyaluronidase**, corticosteroids and antibiotics. In addition, warm compresses, drainage, aspiration and ice were used.
- Allergic reactions occurred immediately or up to 10 days after injection. Treatment included **hyaluronidase**, antihistamine, antibiotics and corticosteroids.
- Swelling and edema occurred immediately or up to 80 days after injection. Treatment included **hyaluronidase**, antibiotics, **NSAID**, corticosteroids. In addition, aspiration and ice were used.
- Pain/tenderness occurred immediately to 14 days after injection. Treatment included corticosteroids and **NSAID**.
- Skin redness occurred immediately or up to 21 days after injection. Treatment included **NSAID**. In addition, ice was used.
- Bruising occurred one day after treatment. Treatment included **NSAID**. In addition, ice was used and the area was massaged.

Additionally, there have been reports of:

- hardening (mass/induration)
- lack of effect,
- small bumps (papules/nodules)
- skin discoloration/darkening skin tone (hyperpigmentation)
- rapid swelling (angioedema)
- injection site reactions such as burning sensation, discomfort, dryness, exfoliation, irritation, and warmth
- injury or compression to blood vessels (vascular events)
- inflammation
- tingling sensation (paresthesia) and reduced sense of touch (hypoesthesia)
- itching (pruritus)
- vision abnormalities
- symptoms of reactivation of herpes infection
- rash (dermatitis)

- implanted gel moving from site of injection (device displacement)
- blisters
- uneven appearance of the skin (asymmetry/deformity)
- scarring
- hives (urticaria)
- leakage from implant site
- small area of inflammation in tissue (granuloma/foreign body reaction)
- dilated small blood vessels (telangiectasia)
- acne
- muscular weakness
- dry lips, dry skin, skin wrinkling, and peeling of skin
- fever (pyrexia), anxiety, feeling tired (fatigue), headache and insomnia.

Delayed-onset inflammation near the site of dermal filler injections is one of the known adverse events associated with dermal fillers. Cases of delayed-onset inflammation have been reported to occur at the dermal filler treatment site following viral or bacterial illnesses or infections, vaccinations, or dental procedures. Typically, the reported inflammation was responsive to treatment or resolved on its own.

## BENEFITS

### **What will it accomplish?**

*Restylane Silk* will temporarily add volume to the lips and help smooth the lines and wrinkles around the mouth.

## BEFORE RECEIVING TREATMENT INFORMATION

### **What should patients expect before receiving treatment?**

Patients can expect their doctor to ask them questions about their medical history and treatment goals. The doctor will decide if the patient is a good candidate for *Restylane Silk*. The doctor may discuss options for pain management and explain what to expect after treatment.

## PROCEDURE DESCRIPTION

### **What should patients expect during treatment?**

*Restylane Silk* will be injected in small amounts until the desired result has been achieved. The average patient who has all of the severe wrinkles around the mouth or lips corrected will use less than half a tablespoon of *Restylane Silk*. Larger amounts of injection into the lips may increase your chances of experiencing side effects. Your doctor will determine the appropriate amount of product needed. Your doctor may gently massage the area of injection to make sure the product is evenly distributed for a smooth appearance. If you are injected with *Restylane Silk* into your lips, your doctor should be able to feel the product when touching your lips. Ice (in a suitable cloth, avoiding any direct contact with the skin) may be applied for a brief period following treatment to minimize swelling.

### **Do the injections hurt?**

Injections may cause some temporary discomfort during and after treatment. *Restylane Silk* contains **lidocaine** to help reduce injection site pain. Your doctor may choose to use additional numbing medicine to further reduce your discomfort.

## POST-TREATMENT INFORMATION

### **What should patients do after receiving treatment?**

- A clean cloth dipped in cold water (cold compresses) wrung out, and applied to the injected area may be used immediately after treatment to reduce swelling.
- Avoid touching the treated area within six hours following treatment so you do not accidentally injure your skin while the area is numb. After that, the area can be gently washed with soap and water.
- Avoid taking aspirin, **NSAID**, St. John's Wort, blood thinners, and high doses of Vitamin E supplements for one week after treatment. These agents may increase bruising and bleeding at the injection site.
- Minimize strenuous exercise and exposure to excessive heat, sun, or UV lamps for the first 24 hours after treatment. Exposure to any of these may cause temporary redness, swelling, and/or itching at the injection site. Until there is no redness or swelling, avoid exposure of the treated area to intense cold or heat such as sun lamps or sun bathing.

### **Will I need more than one treatment to achieve the desired result?**

You should discuss your treatment goals and plan with your doctor. If you are not satisfied with the treatment effect, you may need a **touch-up** treatment to achieve the desired result.



### Will the results of treatment last forever?

No. While individual results may vary, in the clinical study setting, results lasted up to 6 months in 58 out of 100 people treated with *Restylane Silk*. After this, re-treatment may be needed to maintain your desired results.

## CLINICAL STUDIES

Two clinical studies have been conducted with *Restylane Silk* in the US, one with needle injections and one with **cannula** injections. In the first study using needles for lip augmentation and treatment of **perioral lines**, there were 177 subjects treated whereof 172 were women. All subjects had light and dark skin. Subjects with very dark skin were not studied. Ninety-eight percent (98%) of subjects reported improvement in their lip fullness 14 days after injection and 76% of the subjects still had lip improvement 6 months after their injection. Please see the table below for details.

Time after injection	Subjects with improvement in lip fullness
2 weeks	98 out of 100 people (98%)
4 weeks	95 out of 100 people (95%)
8 weeks	90 out of 100 people (90%)
12 weeks	88 out of 100 people (88%)
16 weeks	79 out of 100 people (79%)
20 weeks	76 out of 100 people (76%)
24 weeks	76 out of 100 people (76%)

Improvement in the wrinkles around the lips (**perioral lines**) was also seen by the treating doctor for those subjects who were seeking treatment for improvement in wrinkles. Please see the table below for more information.

Time after injection	Subjects with improvement in wrinkles around the lips
2 weeks	78 out of 100 people (78%)
4 weeks	73 out of 100 people (73%)
8 weeks	72 out of 100 people (72%)
12 weeks	73 out of 100 people (73%)
16 weeks	67 out of 100 people (67%)
20 weeks	64 out of 100 people (64%)
24 weeks	64 out of 100 people (64%)

In the second study, where *Restylane Silk* was injected using a **cannula**, 60 patients were treated for lip augmentation only. In total, 237 patients (228 women and 9 men) participated in the two studies. Safety of treatment was evaluated, including any differences with regards to patient skin color and age. The incidence of injection site reactions in subjects 22-35 years of age was similar to subjects 35-65 years of age. Information on side effects that occurred in the clinical studies is provided in the "Risk" section above. In the clinical study using needle injection, some subjects received a second treatment 6 months after the initial treatment, and there was no increase in the number of adverse events in these subjects.

Doctors evaluated lip fullness at specified time points after treatment with *Restylane Silk*, and this was compared to how full the lips looked before treatment. Results from the first study with needle injections showed that 76 out of 100 people had improved lip fullness at 8 weeks after treatment. The improved lip fullness remained at 6 months for 58 out of 100 people. When patients were treated to smooth out wrinkles around the mouth and lips in addition to the lip treatment, doctors saw an improvement compared to before treatment.

The clinical study participants were also asked to evaluate their own improvement. In both clinical studies, the majority of patients experienced an improvement throughout the study period. The first study lasted for 24 weeks, and 87 out of 100 people considered themselves still improved at that time. The second study lasted for 12 weeks, and 84 out of 100 people considered themselves still improved at that time.

## ALTERNATIVE PROCEDURES

### **What other treatments are available to me?**

Alternative treatments of the lips that are available to you include surgical implants or injections of your own fat. You may discuss these treatment options with your doctor.

## WHEN TO CALL YOUR DOCTOR

### **When should I call my doctor?**

You should call your doctor immediately if you have:

- Changes in your vision
- Signs of a stroke (including sudden difficulty speaking, numbness or weakness in your face, arms, or legs, difficulty walking, face drooping, severe headache, dizziness, or confusion)
- White appearance of the skin
- Unusual pain during or shortly after treatment

Be sure to call your doctor if you have:

- Persistent injection site reactions beyond 14 days, as most side effects such as bruising, swelling, pain, tenderness, redness, and itching will usually go away within one to two weeks.
- Blisters or skin sores that recur, which may signal the presence of a herpes infection
- Any signs of infection such as fever, redness that spreads to surrounding areas, drainage, increasing tenderness or increasing pain that does not go away
- Significant pain away from the injection site
- Any side effect that occurs weeks or months after treatment
- Any other symptoms that cause you concern.

## ADDITIONAL INFORMATION

### **User Assistance Information**

Your questions about *Restylane Silk* can be personally answered by contacting the Galderma Laboratories, L.P. toll-free call center between 8:00 a.m. and 5:00 p.m. Central Daylight Time, Monday through Friday.

1-855-425-8722

Galderma (logo)

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