Patient brochure

Restylane-L®
Injectable Gel with 0.3% **Lidocaine**

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Glossary

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

- **Anesthetic** – a substance that reduces sensitivity to pain.
- **Hyaluronic acid (HA)** – a polysaccharide (sugar) that is naturally in the body. It keeps skin moisturized and soft. **HA** fillers, including *Restylane-L*, are a modified form of the **HA** that is naturally in your body.
- **Hyaluronidase** – a medicine used to breakdown **HA** in the area of injection.
- **Lidocaine** – a medication used to numb a specific area to decrease pain.
- **BDDE** – the ingredient used to crosslink the **HA**.
- **Crosslinked** – a process in which **HA** chains are connected together to form a network.

About *Restylane-L*

Q What is *Restylane-L*?
A *Restylane-L*® is a crystal clear injectable gel composed of **hyaluronic acid**, a natural substance that already exists in the body. *Restylane-L* is crosslinked with BDDE, an ingredient that helps form a network of HA to provide a gel filler that lasts longer. *Restylane-L* is non-animal based and free from animal protein. Allergy pretesting is not necessary. *Restylane-L* contains 0.3% **lidocaine**. The **lidocaine** in *Restylane-L* has been added to reduce the discomfort associated with the treatment.

Q How does *Restylane-L* work?
A *Restylane-L* is injected into the skin with an ultrafine needle to plump the skin to smooth away wrinkles and folds such as the lines from your nose to the corners of your mouth (nasolabial folds) or into your lips for patients over the age of 21 for lip enhancement.

Q Why add Lidocaine to *Restylane*?
A Lidocaine was added to *Restylane-L* to reduce the pain and discomfort during and after injection. In a clinical study, 60 patients received *Restylane*® on one side of the face and *Restylane-L*® on the other side of the face. *Restylane-L* had an effect on reducing pain. At the time of injection, patients rated their pain about 45 on a scale of 0 to 100 for the side of the face treated with *Restylane*. In comparison, patients rated their pain about 15 on the same scale for the side of the face treated with *Restylane-L*. Patients reported less pain on the side of the face treated with *Restylane-L* up to 60 minutes after treatment.

Q How long does *Restylane-L* last?
A *Restylane-L* effects generally last about six months and gradually disappears from the body.

Q Has *Restylane-L* been studied?
A A clinical study was conducted with *Restylane-L* to evaluate the pain reducing effect up to 60 minutes after injection. This study enrolled 60 patients with moderate to severe nasolabial fold wrinkles. The study included 58 female patients and 2 male; 34 were White, 21 were Hispanic or Latino, 3 were African American, 1 was Asian, and 1 was “Other”.
In this study 71.7% of patients experienced less pain after injection of *Restylane-L* than with *Restylane* alone. Please see the below table for additional information.

Timepoint	Number of patients with pain reduction	
	No.	%
After Injection	43/60	71.7
15 Minutes	28/60	46.7
30 Minutes	17/60	28.3
45 Minutes	10/60	16.7
60 Minutes	4/60	6.7

In addition to evaluating the pain reducing effects, the study assessed patient satisfaction with *Restylane-L* treatment. All 60 subjects were asked to rate the level of improvement seen in their nasolabial folds after injection with *Restylane-L*. At day fourteen after injection 100% saw some improvement (Improved, Much Improved, and Very Much Improved). See below table for additional details.

Category	*Restylane-L*	
	Number of Patients	%
Very Much Improved (4)	17	28.3
Much Improved (3)	29	48.3
Improved (2)	14	23.3
No Change (1)	-	0.0
Worse (0)	-	0.0

Safety

Q Who should not use *Restylane-L* (Contraindications)?

A Safety has not been established and should not be used in people who are:

- Pregnant
- Breast feeding
- Trying to become pregnant
- Under the age of 22 for lip enhancement
- Under the age of 18 or over the age of 65
- Highly allergic (for example: gram positive bacteria)
- Prone to bleeding disorders

Q What are some warnings to consider?

A The use of *Restylane-L* at sites with skin sores, pimples, rashes, hives, cysts, or infections should be postponed until healing is complete. Use of *Restylane-L* in these instances could delay healing or make your skin problems worse.

You may experience skin discoloration (bruising), swelling, redness, tenderness, pain, itching, or small lumps in the area where you are injected. If any of these events occur, the majority usually last one to two weeks. If any symptom lasts longer than two weeks, call the doctor who administered the *Restylane-L* injection.

Red or swollen small bumps (inflammatory papules) may rarely occur. You may need antibiotics to treat them. In clinical studies swelling was higher in younger patients (28%) compared to older patients (18%) and bruising was higher in older patients (28%) compared to younger patients (14%). The majority of these events were mild.

If you are injected with *Restylane-L* into your lips, your physician should be able to feel the product when touching your lips.

Q What are some potential risks you may encounter?

A As with all procedures like this, the injection of *Restylane-L* carries a risk of infection and formation of scar tissue.

The safety and effectiveness of *Restylane-L* has not been established in pregnant or nursing mothers, and in patients under 18 or over 65 years of age. *Restylane-L* use while nursing could harm you or the nursing child. *Restylane-L* should not be used for lip enhancement in patients under the age of 22.

The use of *Restylane-L* in African-American patients can result in darkening of skin color (hyperpigmentation), which may take several weeks to correct.

If you have previously had facial cold sores, an injection can cause them to come back.

The safety of *Restylane-L* used with other skin therapies such as laser, mechanical or chemical peeling, and hair removal has not been established. The use of *Restylane-L* with these skin therapies may lead to other side effects such as inflammation.

You should avoid exposing the area(s) treated with *Restylane-L* to excessive sun or UV lamps, and extreme heat and cold until any redness or swelling has disappeared.

Clinical volunteers keeping diaries reported the following short-lived events:
Restylane-L was evaluated in a clinical study of 60 patients. The below table shows what patients reported each day after injection of *Restylane-L* in the diary they kept. The most common events were: pain, swelling, redness, tenderness, bruising, itching and other. The reporting of these events decreased over time and by day 14 most events had resolved.

Percentage of Patients Reporting Adverse Events After Treatment with *Restylane-L*

	Total (%)	Number of days			
		1	2–7	8–13	14
Bruising	58.3%	8.6%	80.0%	11.4%	0.0%
Redness	50.0%	33.3%	56.7%	6.7%	3.3%
Swelling	66.7%	10.0%	72.5%	17.5%	0.0%
Pain	45.0%	48.1%	40.7%	3.7%	7.4%
Tenderness	68.3%	31.7%	48.8%	12.2%	7.3%
Itching	13.3%	87.5%	12.5%	0.0%	0.0%
Other	6.7%	0.0%	50.0%	0.0%	50.0%

Q What are some benefits from clinical evaluation?

A In one study in which 135 patients received *Restylane* injections in their lips, two weeks after the injection 96% of the patients said their lips were improved compared to before the injection. At least 74% of the patients still saw an improvement in their lips at 6 months after the injection

Post-Marketing Surveillance:

Q Have there been adverse events reported through post-market surveillance?
A The adverse events received from post-marketing surveillance (voluntary reporting and published literature) for *Restylane* with and without **lidocaine** in the U.S. and other countries most commonly included: reports of transient swelling (edema) and inflammatory reactions with – immediate onset or delayed onset, up to several weeks after treatment.

The following events were also reported in decreasing order of frequency:

- lumps or bumps (mass formation), hardening (induration),
- short duration of effect,
- skin redness (erythema),
- pain or tenderness,
- bruising (hematoma),
- small bumps (papules or nodules),
- presumptive bacterial infections and pus (abscess formation),
- skin discoloration (hyperpigmentation),
- injection site reactions including burning sensation, warmth, irritation,
- restricted blood flow leading to the death of skin (ischemia and necrosis),
- allergic reaction (hypersensitivity), rapid swelling (angioedema),
- eye disorders such as dry eye, eye irritation, eye pain, eye swelling, increased flow of tears (increased lacrimation), eyelid drooping (eyelid ptosis) and
- visual disturbance including blurred vision, reduced vision, and blindness,
- reduced sense of touch (hypoaesthesia), tingling sensation (paraesthesia), tremor, and facial nerve paralysis,
- itching (pruritus),
- leakage of product from implant site (extrusion of device),
- scarring,
- small area of inflammation in tissue (granuloma),
- device dislocation,
- symptoms of reactivation of herpes infection,
- rash,
- blisters/vesicles,
- spider veins/broken capillaries (telangiectasia),
- abnormal connection between two body parts (fistula),
- leakage from implant site (effusion/discharge),
- acne,
- skin inflammation (dermatitis),
- hives (urticaria),
- muscle disorders such as muscle twitching and muscle weakness,
- encapsulation of gel in the tissue,
- fungal infection of the skin (dermaphytosis) and
- other dermatological events including dry skin, skin wrinkling, peeling of skin and localized hair loss (alopecia), and
- non-dermatological events including headache, discomfort (malaise), fever, dizziness, sinus infection, shortness of breath (dyspnea), feeling tired (fatigue), influenza like illness, insomnia, nausea and anxiety.

The treatments of these events included ice, massage, warm compress, nitroglycerine paste, drugs to reduce inflammation (corticosteroids), antibiotics, medicine that prevents the clotting of blood (anticoagulants), drugs to relieve allergy symptoms (antihistamines), drugs to relieve pain (analgesics), antiviral agents, medicine to relieve the body of excess fluid (diuretic agents), surgical procedure (incision and drainage) or a medicine used to help breakdown **hyaluronic acid** in the body (**hyaluronidase**).

The most commonly reported serious adverse events were infection/pocket of pus (abscess), restricted blood flow leading to the death of skin (ischemia/necrosis), scarring, vision loss, allergic reactions (hypersensitivity), scarring, and areas of inflammation in tissue (granuloma) including cases of hardening (mass/induration). Other serious events included common related symptoms such as; swelling, pain/tenderness, skin redness (erythema), reduced sense of touch (hypoaesthesia), tingling sensation (paraesthesia), inflammation, bruising and skin discoloration.

Serious infections/pocket of pus (abscess) were reported with a time to onset ranging from one day to 6 months following the injection. The infections usually resolved after two days up to a few months and most of the patients had recovered or were recovering at the time of last contact. The treatments included antibiotics, drugs to relieve pain (analgesics), drugs to reduce inflammation (corticosteroids) and **hyaluronidase** (a medicine to help break down the *Restylane-L* so that it is more easily absorbed).

Serious small area of inflammation in tissue (granuloma), including hardening, were reported with a time to onset ranging from a month up to a year or longer. The outcomes were mostly recovered or recovering at the time of last contact. Treatment included drugs to relieve pain (analgesics), drugs to relieve allergy symptoms (antihistamines,) antibiotics, drugs to reduce inflammation (corticosteroids) and surgical removal (excisions). Incisions to examine tissue (biopsies) have been taken in some cases, but the majority of cases are non-biopsy confirmed.

Serious allergic reactions (hypersensitivity) were reported in most cases with a time to onset ranging from immediately to few weeks post injection. Most of the events were recovered or recovering at the time of last contact. The treatments included drugs to relieve pain (analgesics), drugs to relieve allergy symptoms (antihistamines), antibiotics, and drugs to reduce inflammation (corticosteroids).

Blockage of a blood vessel (vascular occlusion) resulting in restricted blood flow and vision disturbances including blindness have been reported following injection of any soft tissue filler in the face especially in the nose, between the eyebrows (glabella), around the eyes (periorbital areas), smile lines (nasolabial folds) and cheek, with a time to onset ranging from immediate to a few weeks following injection. This may appear as whitening of the skin (blanching), discoloration, death of skin (necrosis) or ulceration at the implant site or in the area supplied by the blood vessels affected; or rarely as restriction in blood supply to tissues (ischemic events) in other organs due to blocked blood vessels (embolisation).

Isolated rare cases of restriction in blood supply to tissues (ischemic events) affecting the eye leading to visual loss, and the brain resulting in stroke (cerebral infarction), following facial aesthetic treatments have been reported. Reported treatments include medicine to prevent blood clotting (anticoagulant), medicine to treat allergic reactions (epinephrine), aspirin, a medicine to help break down **hyaluronic acid** in the body (**hyaluronidase**), drugs to reduce inflammation (corticosteroid treatment), drugs to relieve pain (analgesics), antibiotics, local wound care, drainage, hyperbaric oxygen and surgery. Outcome of the events ranged from resolved to ongoing at the time of last contact.

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.

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

About the Procedure

Q What are the serious side effects?
A Rarely, the doctor may accidentally inject the product into a blood vessel, which can cause injury to the blood supply and damage to the skin or lips. In rare cases injection into a blood vessel could also result in vision changes (including blindness) and stroke.

Rarely, a few 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.

Q What should patients do prior to treatment?

A *Restylane-L* requires no pretesting, but you should take a few precautions before being treated. Avoid using St. John's Wort, high doses of Vitamin E supplements, aspirin, and other non-steroidal anti-inflammatory medications, such as ibuprofen prior to treatment, because these may increase bruising or bleeding at the injection site. Please speak to your doctor about when to stop these medications before your procedure. Also, if you have previously suffered from facial cold sores, discuss this with your physician. He or she may consider prescribing a medication to minimize recurrences.

Q What is the dose of *Restylane-L*?
A The amount used depends on your face and what you would like to have treated. The average patient who has all of the severe wrinkles around the mouth or lips corrected will use less than half a tablespoon.

Please speak to your doctor to determine the correct amount of product needed.

Q Do the injections hurt?

A *Restylane-L* is injected directly into the skin with an ultrafine needle. To help maximize your comfort, you should discuss the use of numbing medicines with your doctor before treatment.

Q How much does *Restylane-L* treatment cost?
A *Restylane-L* is a customized procedure based on your specific needs, so the cost will vary from patient to patient. In general, the cost of *Restylane-L* is similar to the cost of similar procedures. Please ask your doctor to give you an estimate of the cost.

Q Are there post-treatment instructions to follow after a *Restylane-L* treatment? A Please observe the following after treatment with *Restylane-L*:

- A 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.

- Until there is no redness or swelling, avoid exposure of the treated area to intense heat such as sun lamps or sun bathing.

- If you have previously suffered from facial cold sores, there is a risk that the needle punctures could contribute to another occurrence. Speak to your physician about medicine to prevent this from happening again.

- Avoid taking aspirin, non-steroidal anti-inflammatory medications, St. John's Wort, and high doses of Vitamin E supplements for one week after treatment. These agents may increase bruising and bleeding at the injection site.

Troubleshooting

Q When should I call my doctor?
A Most side effects like bruising, swelling, pain, tenderness, redness, and itching will usually go away within one to two weeks. Call your doctor if you have persistent problems beyond 14 days.

Blisters or skin sores that recur may signal the presence of a herpes infection that must be treated.

You can develop an infection that should be treated with antibiotics. If you experience any signs of infection such as fever, redness that spreads to surrounding areas, drainage, increasing tenderness, or increasing pain that does not go away you should call your doctor.

Seek immediate medical attention if you develop symptoms such as unusual pain, vision changes, a white appearance of skin near the injection site, or any 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) during or shortly after the procedure (http://www.nlm.nih.gov/medlineplus/stroke.html).

Restylane-L®

User Assistance Information
Your questions about *Restylane-L* 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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