

About Restylane® Defyne

Before beginning your treatments, please review this important information.

1. GLOSSARY

Anesthetic – a medication (or “treatment”) that reduces pain

Chin retrusion – recessed chin or lack of chin projection

Dermal filler – a material that is injected underneath the skin to smooth a wrinkle or restore volume to an area of skin

Hyaluronic acid – a naturally occurring sugar, found in the body that gives the skin moisture, volume and elasticity

Hyaluronidase – an enzyme that breaks down hyaluronic acid

Lidocaine – a commonly used local anesthetic to numb the skin, see “anesthetic”

Nasolabial folds – the medical term for the creases that run from the sides of your nose to the corners of your mouth. Commonly known as “laugh lines”

Pigmentation disorder – a disorder that results in a change in skin color

Topical – a cream or ointment applied to the top of the skin, affecting only the area to which it is applied

Touch-up – an additional injection of dermal filler that is usually given a short time after the initial injection. Some patients may require a touch-up treatment to achieve the desired result

BDDE – the ingredient used to crosslink the hyaluronic acid

Crosslinked – a process in which hyaluronic acid chains are connected together to form a network

2. PRODUCT DESCRIPTION

What is Restylane® Defyne?

Restylane® Defyne is a **dermal filler** injected under the (facial) skin. Once in place, it helps smooth away your “laugh lines” – the wrinkles and folds that may form at the sides of your nose and run down toward the corners of your mouth. *Restylane® Defyne* may also be used to improve the profile, shape and size of your chin.

Restylane® Defyne is made out of **hyaluronic acid** - a naturally occurring sugar, found in the body that gives the skin moisture, volume and elasticity – and a small amount of **lidocaine**, which is a commonly used local **anesthetic** to numb the skin. The **hyaluronic acid** is **crosslinked** with **BDDE**, an ingredient that helps form a network of **hyaluronic acid** to provide a gel filler that lasts longer. **Hyaluronic acid** fillers, including *Restylane® Defyne*, contains **hyaluronic acid** that has been modified to last longer in the body than the naturally occurring **hyaluronic acid**.

3. INDICATIONS FOR USE

What is Restylane® Defyne for?

As you age, your facial skin begins to lose its elasticity and volume. As a result, your “laugh lines”, the creases that run from the sides of your nose toward the corners of your mouth, become more pronounced. *Restylane® Defyne* injectable gel is designed to temporarily help counter this by smoothing out these wrinkles and folds and restoring a natural, soft look to your face.

Restylane® Defyne may also be used for augmentation of the chin region to improve the chin profile in patients with mild to moderate **chin retrusion** over the age of 21. This means it may be used in the chin area to improve the profile, shape and size of your chin.

Restylane® Defyne has been shown to maintain this effect for up to 12 months.

Note: Facial features can differ. Speak to your doctor about the lines on your face that are appropriate for treatment with *Restylane® Defyne*.

How is Restylane® Defyne used?

Restylane® Defyne is injected into the facial skin through a small needle to smooth facial wrinkles and folds (laugh lines), resulting in a more youthful appearance of the skin. *Restylane® Defyne* may also be injected in your chin improve the profile, shape and size of your chin. For most patients, the procedure only takes 15 – 30 minutes.

4. CONTRAINDICATIONS

Are there any reasons why I should not receive Restylane® Defyne?

Before using *Restylane® Defyne*, your doctor will talk to you about your medical history, to determine if you are an appropriate candidate for treatment. You will be asked questions about possible allergies to ensure that *Restylane® Defyne* can be safely administered. Tell your doctor about all your medical conditions, including if you:

- Have severe allergies with a history of severe reactions (anaphylaxis). Use of *Restylane® Defyne* may result in an allergic reaction.
- Are allergic to the **anesthetic lidocaine** or to any of the proteins used to make the **hyaluronic acid** in *Restylane® Defyne* (bacterial proteins). Use may result in an allergic reaction.

If you are not sure about your medical history concerning these allergies, please discuss further with your doctor.

5. PRECAUTIONS

What precautions should my doctor advise me about?

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

- *Restylane® Defyne* helps improve the profile and appearance of your chin and helps treat laugh lines – the natural facial wrinkles and folds that can occur due to aging. *Restylane® Defyne* has not been tested to treat any other types of wrinkles.
- *Restylane® Defyne* may be unintentionally injected into a blood vessel during the procedure. The chances of this happening are very small, but if it does happen, the complications can be serious, and may be permanent. 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 doctor immediately.
- The use of *Restylane® Defyne* if you have skin sores, pimples, rashes, hives, cysts, or infections should be postponed until healing is complete. Use of *Restylane® Defyne* in these instances could delay healing or make your skin problems worse.
- Any time a **dermal filler** gel like *Restylane® Defyne* is injected into facial skin there is risk of infection, which could appear as small, swollen or red bumps. These are called inflammatory papules. These infections are rare, however you should talk to your doctor about further treatment if you see any of these signs or symptoms.

- *Restylane® Defyne* is for adults over the ages of 21.
- Tell your doctor if you are pregnant, planning to become pregnant, or breastfeeding. The safety of *Restylane® Defyne* has not been studied in women who are pregnant or breastfeeding. The risk of using *Restylane® Defyne* in pregnant or breastfeeding women is unknown.
- Tell your doctor about any medication you are taking. You may have a greater risk of developing an infection if you use *Restylane® Defyne* while taking any medication that reduces your body's natural defense system. These medications are called "immunosuppressants" because they stop your body's immune system from functioning normally.
- Tell your doctor about any medication you are taking. Some medication like aspirin and warfarin can thin your blood, which may increase your risk of bleeding or prolong any bleeding that occurs. These medications also increase your risk of bruising or bleeding at the injection site.
- As with any injection procedure, you may have a higher risk of bruising or bleeding at the injection site if you have a bleeding disorder.
- If you have any history of scarring, particularly thick and stiff scars, or any skin color (pigmentation) disorders, talk to your doctor about this before your procedure. Scarring and skin color changes can occur with **hyaluronic acid** fillers in general. When *Restylane® Defyne* was studied in patients with different skin tones (pale to dark), there were no reports by patients of excessive scarring (keloids) or changes in skin color.
- The use of *Restylane® Defyne* with skin therapies such as laser treatment, mechanical or chemical peels or hair removal may lead to other side effects such as redness, swelling, heat and/or pain of the skin (inflammatory reaction). Tell your doctor if you have had any of these procedures.
- If you have had cold sores in the past, there is a risk that they will return after your procedure with *Restylane® Defyne*.
- Within the first 24 hours after treatment with *Restylane® Defyne*, you should avoid or minimize hard (strenuous) exercise. You should also minimize exposure to extensive sun, UV lamps, indoor tanning beds/booths, or extreme heat and cold as any of these may cause temporary redness, swelling, and/or itching at the injection site. Exposure to UV sources may result in irritation at the site of treatment. An ice pack can be applied for relief, if needed.

If you have any additional questions about any topic in this section, please discuss further with your doctor.

6. CLINICAL STUDIES

How was Restylane® Defyne Studied?

Restylane® Defyne was tested before it was approved for use in all patients to ensure that it worked properly (effective) and was safe to use.

A study was performed in 162 patients for treatment of the wrinkles and folds that form around your nose and extend down to the corners of your mouth (laugh lines). These patients included 156 women, 6 men, and were from various ethnic groups with different skin tones (pale to dark skin). Each of these patients expressed desire to improve the appearance of their facial wrinkles and folds (laugh lines).

The study was created to compare two different **dermal filler** gel products. It was conducted by 11 different doctors in 11 different locations across the United States.

Patients who participated in the study received an initial treatment with *Restylane® Defyne* on one side of their face and another, similar **dermal filler** gel, without **anesthetic**, on the other side of their face. **Touch-up** injections were given as needed, and each patient was monitored for 12 months following the procedure to measure the effects of the treatments. For each patient, the amount of product used was based on their individual needs.

In order to objectively measure improvements in appearance over 12 months, each patient was evaluated by a doctor other than the one who had performed the treatment. Patients also evaluated themselves. To measure side effects following the procedure, each patient kept a diary for 21 days to record side effects. These were then shared with the doctors.

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Restylane® Defyne was tested in 140 patients to ensure it was safe and effective to use in treatment of the chin to improve the profile, shape and size of your chin. The patients included were 125 women and 15 men and were from various ethnic groups with skin tones ranging from pale to dark skin. Each patient included had expressed a desire to improve the appearance of their chin.

The study was conducted by 11 different doctors in 11 different locations across the United States.

Patients who participated either received an initial treatment or acted as a control without treatment for comparison of results. **Touch-up** injections were given as needed, and each patient was monitored for 12 months following the procedure to measure the effects of the treatments. For each patient, the amount of product used was based on their individual needs.

Each patient was evaluated by a doctor other than one who had performed the treatment, in order to objectively measure improvements in appearance over 12 months. Patients also evaluated themselves. To measure side effects following the procedure, each patient kept a diary for 28 days to record side effects. These were then shared with the doctors.

After 12 months, all subjects could receive an optional treatment with *Restylane® Defyne*, independent on whether they received initial treatment or acted as control. Subjects that received treatment were monitored for another 12 weeks for the effect and safety of initial or repeat treatments.

7. BENEFITS

What will *Restylane® Defyne* do for me?

Restylane® Defyne temporarily reduces signs of aging on your face by smoothing the wrinkles and folds that form around your nose and extend down to the corners of your mouth (laugh lines). This natural, smooth look should last for up to 12 months.

Restylane® Defyne was studied in many patients like yourself to determine if it was effective in treating laugh lines and to ensure that it is safe for use.

The study doctors reported:

- 77% of patients had at least a 1-point improvement in wrinkle appearance 6 months after treatment.
- 70% of patients had at least a 1-point improvement in wrinkle appearance 1 year after treatment.

The patients reported:

- 78% rated an improvement in the appearance of their wrinkles 6 months after treatment.
- 64% rated an improvement in the appearance of their wrinkles 1 year after treatment.

For further information regarding the results of the clinical study, see Section 6.

Restylane® Defyne temporarily improves the profile, shape and size of your chin and the results has been shown to maintain its effect for up to 12 months.

Restylane® Defyne was evaluated in many patients like yourself to determine if it was effective in correcting the profile, shape and size of the chin and to ensure that it is safe for use.

The study doctors reported:

- 86.1% of patients had at least a 1-point improvement in the profile appearance of the chin 3 months after treatment.
- 73.7% of patients had at least a 1-point improvement in the profile appearance of the chin 1 year after treatment.

The patients reported:

- 99% rated an improvement in the appearance of their chin 3 months after treatment.
- 84.8% rated an improvement in the appearance of their chin 1 year after treatment.

8. RISKS

What side effects were seen in the clinical studies?

In the study of *Restylane® Defyne* for correction of wrinkles and folds that form around your nose and extend down to the corners of your mouth (laugh lines), most patients reported the following side effects at the site where they received the injection:

- Swelling
- Lumps/Bump Formation
- Redness
- Pain/Tenderness
- Bruising
- Itching

Most patients said their side effects were mild, short-lived and did not require them to call their doctor. These patients said that their side effects disappeared within 1-2 weeks.

Patients also reported that the **anesthetic lidocaine**, which is part of the *Restylane® Defyne* injection and used to numb the injection site, significantly reduced pain during and after their procedure.

Table 1 below provides additional information about the side effects that patients reported in this study.

Table 1. Most common side effects of Restylane® Defyne recorded by patients who participated in the study, reported in their 21-day diary

Side Effect	Number of patients
Swelling	119 out of 162 patients
Lump/Bump Formation	105 out of 162 patients
Redness	101 out of 162 patients
Pain/Tenderness	100 out of 162 patients
Bruising	95 out of 162 patients
Itching	40 out of 162 patients

In the study of *Restylane® Defyne* in treatment of the chin to improve the profile, shape and size of the chin, most patients reported the following side effects at the site where they received the injection:

- Tenderness
- Pain
- Swelling
- Lumps/Bump Formation
- Bruising
- Redness
- Itching

Most patients said their side effects were mild (71.6%, 83/116) and disappeared within 1-2 weeks. Moderate side effects were experienced by 25.9% of subjects and severe side effects experienced by 2.6% of subjects. Most subjects experienced side effects less than 14 days. Side effects lasting 14-27 days were experienced by 20.7% of subjects and 8.6% of subjects experienced side effects lasting 28 days or more.

Table 2 below provides additional information about the side effects that patients reported in this study after the initial treatment.

Table 2. Most common side effects of Restylane® Defyne recorded by patients who participated in the study, reported in their 28-day diary

Side Effect	Number of patients
Tenderness	90 out of 125 patients
Pain	72 out of 125 patients
Swelling	78 out of 125 patients
Lump/Bump Formation	80 out of 125 patients
Bruising	68 out of 125 patients
Redness	57 out of 125 patients
Itching	36 out of 125 patients

It is important to understand that any procedure carries a risk of side effects. After an injection of **dermal filler** gel, you may experience skin reactions due to the injection and/or from the **dermal filler** gel.

When *Restylane® Defyne* was studied, side effects that occurred at the injection site included swelling, small bumps, redness, pain, tenderness, bruising, and itching. These were mainly mild to moderate reactions that disappeared within 1-2 weeks. If any symptoms last longer than 2 weeks, you should call your doctor.

What side effects have been voluntarily reported following use of Restylane® Defyne with and without lidocaine use in and outside of the United States?

The most common reported side effects included reports of temporary swelling (edema) 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)
- small bumps (papules/nodules)
- skin redness (erythema)
- pain/tenderness
- short duration of effect
- bruising (hematoma)
- presumptive bacterial infections/pocket of pus (abscess formation)
- inflammation
- skin discoloration
- injection site reactions including burning sensation and warmth
- restricted blood flow (ischemia/necrosis)
- allergic reaction (hypersensitivity)/rapid swelling (angioedema)
- small area of inflammation in tissue (granuloma)
- itching (pruritus)
- reduced sense of touch (hypoesthesia), tingling sensation (paraesthesia)
- eye disorders such as eye swelling, blurred vision, eye discomfort, and visual disturbance
- rash
- device displacement
- blisters/vesicles
- symptoms of reactivation of herpes infection
- deformity/overcorrection
- leakage from implant site (discharge)
- scarring
- hives (urticaria)
- dilated small blood vessels (telangiectasia)
- skin inflammation (dermatitis)
- acne
- extrusion of device
- muscle disorders such as muscle twitching
- non-dermatological events including chills, headache, discomfort (malaise), nausea and fever (pyrexia) and
- other dermatological events including pain of skin

When required, treatments for these events included ice, massage, warm compress, local drugs that widen blood vessels, drugs to reduce inflammation (corticosteroids), antibiotics, drugs to relieve allergy symptoms (antihistamines), drugs to relieve pain (analgesics), drug to relieve the body of excess fluid (diuretic agents), surgical procedure (incision, drainage or excision), surgery or an enzyme used to help break down **hyaluronic acid (hyaluronidase)**.

Reports of serious adverse events for *Restylane® Defyne* with and without **lidocaine** are rare. The most commonly reported serious adverse events were infection/pocket of pus (abscess), lumps and bumps (mass) and hardening (induration), injury due to restricted blood flow (ischemia/necrosis) and eye disorders. Other concurrent serious adverse events included: swelling, pain/tenderness, skin redness (erythema) and skin discoloration.

Serious infection/pocket of pus (abscess) were mostly reported with a time to onset ranging from one day up to 4 months following the injection. Most of the patients were recovering at the time of last contact. The treatments may include: antibiotics, drugs to relieve pain (analgesics), drugs to reduce inflammation (corticosteroids) and an enzyme used to help break down **hyaluronic acid (hyaluronidase)**.

Serious lumps and bumps (mass)/hardening/(induration) including small area of inflammation in tissue (granuloma/foreign body reaction) was mostly reported with a time to onset ranging from a month to 4 months or longer. The outcome was mainly recovered or recovering at the time of last contact. The treatments may include: drugs to relieve pain (analgesics), drugs to relieve allergy symptoms (antihistamine), antibiotics, drugs to reduce inflammation (corticosteroids), surgical procedures (excisions and biopsy).

Blockage of a blood vessel (vascular occlusion) resulting in restricted blood flow (ischemia/necrosis) and vision changes, have been reported following facial aesthetic treatments with injectable soft tissue fillers with a time to onset ranging from immediate to a few weeks following injection. Blockage of a blood vessel may occur due to an accidental injection into the blood vessel or as a result of local compression of the blood vessel by the implant. This may appear as discoloration and other local tissue injury at the implant site, or area supplied by the blood vessels. If injected in a blood vessel (embolization), this may rarely affect other organs, and rare cases of restriction in blood supply to tissues (ischemic events) after affecting the eye and brain have led to vision loss and stroke (cerebral infarction), respectively.

You should tell your doctor immediately if you experience any of these side effects or if you notice anything unusual at the site of treatment. Treatments may include medicine to prevent blood clotting (anticoagulant), medicine to treat allergic reactions (epinephrine), aspirin, enzyme used to help breakdown **hyaluronic acid (hyaluronidase)**, drugs to reduce inflammation (corticosteroids), drugs to relieve pain (analgesics), local drugs that widen blood vessels (vasodilating agents) including nitropaste, antibiotics, surgery (including drainage), and hyperbaric oxygen.

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.

9. BEFORE PROCEDURE INFORMATION

What happens in the office before the injection?

Note that each doctor may have a unique process for treating patients.

The following is an example of what your doctor may do before the injection procedure.

- Talk to you about your medical history, including questions about prior procedures, surgeries, illnesses and medications you have taken.
- Talk to you about your desired results for your procedure.
- Examine your face and discuss whether *Restylane® Defyne* is the right treatment for you.
- Review what you should expect during and after the procedure.
- Let you know of any possible side effects that you may experience, and what to do if you experience these.
- Take photos of the area of your face that will be treated.

Your doctor may also have additional ways of evaluating patients and preparing them for a procedure.

10. PROCEDURE DESCRIPTION

What happens during the procedure?

Your doctor may do the following during your procedure:

- Your skin will be cleansed prior to treatment.
- Use a cream or ointment called a **topical anesthetic** to numb the area where you will receive your injection.
- Your doctor will begin the procedure by giving you the first injection, then pausing to allow the **anesthetic** that is part of *Restylane® Defyne* to continue to numb the area around your injection. The **anesthetic** part of *Restylane® Defyne* has been shown to significantly reduce the pain and discomfort that may occur with a **dermal filler** gel injection.
- Your doctor will continue the injection of *Restylane® Defyne* until the area being treated shows the desired results.
- After the injection is completed, your doctor may gently massage the area that was treated to ensure the **dermal filler** gel is distributed evenly and looks natural.

11. AFTER PROCEDURE INFORMATION

What should I expect following the procedure?

Your doctor will also tell you what to expect following 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.

In the clinical studies the most common side effects were temporary reactions at the treatment site such as pain, tenderness, swelling, bruising, redness, itching, and lumps/bumps. These side effects generally lasted 1 to 2 weeks. See Section 8 for additional information on side effects seen in the clinical studies.

12. ALTERNATIVE PROCEDURES

What other treatments are available to me?

There are other **dermal filler** gels in the United States that are available to you for treatment of wrinkles and folds. Additionally, there are alternative treatments such as botulinum toxins, laser therapy and chemical peels for the treatment of lines and wrinkles. There are other **dermal filler** gels in the United States that are available as well as other procedures for improvement of the profile, shape and size of your chin such as fat grafting, implants, and jaw advancement surgery. Each alternative has its own advantages and disadvantages. You can discuss these treatments with your doctor to determine which one is right for you.

13. WHEN TO CALL YOUR DOCTOR

When should I call my doctor?

If you experience any of the following symptoms, you should call your doctor immediately:

- Unusual pain
- Vision changes
- A white appearance in the skin near the injection site
- Any sign 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>)

You should call your doctor if you have any of the following side effects that last for more than 14 days:

- Bruising
- Swelling
- Pain
- Tenderness
- Redness
- Itching

These side effects typically go away within two weeks.

If you experience fever, redness that spreads to areas around the injection site, drainage, or increasing tenderness or pain that does not go away, you may be at risk for developing an infection. You should call your doctor so that you can be treated with antibiotics.

If you develop blisters or recurring skin sores, this may be cold sores. You should call your doctor so that you can be treated.

Be sure to call your doctor if you have:

- Significant pain away from the injection site
- Any side effect that occurs weeks or months after treatment
- Any other symptoms that cause you concern.

14. ADDITIONAL INFORMATION

What if I experience a problem?

If you believe that you have experienced a serious problem related to *Restylane® Defyne* you should call your doctor. Your questions about *Restylane® Defyne* 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 to through Friday.

1-855-425-8722

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Revised: September 2023

Part Number: 90-74302-01

GALDERMA