DIRECTIONS FOR USE - USA

Restylane® Refyne

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed physician or properly licensed practitioner.

BEFORE USING PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.

1. DEVICE DESCRIPTION

Restylane® Refyne is a sterile, biodegradable, viscoelastic, non-pyrogenic, clear, colorless, and homogeneous soft hyaluronic acid gel with a moderate lifting capacity. The product has a sodium hyaluronate concentration of 20 mg/mL in phosphate buffered saline at pH 7 and contains 3 mg/mL lidocaine hydrochloride.

2. INTENDED USE/INDICATIONS

Restylane Refyne is indicated for injection into the mid-to-deep dermis for correction of moderate to severe facial wrinkles and folds (such as nasolabial folds) in patients over the age of 21.

3. CONTRAINDICATIONS

- Restylane Refyne is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.
- Restylane Refyne may contain trace amounts of gram-positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.
- Restylane Refyne contains lidocaine and is contraindicated for patients with a history of allergies to such material.

4. WARNINGS

- Introduction of Restylane Refyne into the vasculature may lead to embolization, occlusion of the vessels, ischemia, or infarction. Take extra care when injecting soft tissue fillers, for example inject the product slowly and apply the least amount of pressure necessary. Rare but serious adverse events associated with the intravascular injection of soft tissue fillers in the face have been reported and include temporary or permanent vision impairment, blindness, cerebral ischemia or cerebral hemorrhage, leading to stroke, skin necrosis, and damage to underlying facial structures. Immediately stop the injection if a patient exhibits any of the following symptoms, including changes in vision, signs of a stroke, blanching of the skin, or unusual pain during or shortly after the procedure. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care practitioner specialist should an intravascular injection occur.
- Restylane Refyne must not be implanted into blood vessels and should not be used in vascular rich areas. Localized superficial necrosis and scarring may occur after injection in or near

vessels. It is thought to result from the injury, obstruction, or compromise of blood vessels. Special caution should be taken if the patient has undergone a prior surgical procedure in the planned treatment area.
- Product use at sites in which an active skin disease is present, such as inflammation (skin eruption such as cysts, pimples, rashes or hives), infection, or tumors, in or near the intended treatment site should be deferred until the underlying process has been controlled.

For additional information please see the Post-Marketing Surveillance in Adverse Events.

5. PRECAUTIONS

- Restylane Refyne is packaged for single-patient and single-session use only. Do not resterilize. Do not use if package is open or damaged.
- The safety and effectiveness for the treatment of anatomic regions other than the facial wrinkles and folds have not been established in controlled clinical studies.
- As with all transcutaneous procedures, dermal filler implantation carries a risk of infection. Standard precautions associated with injectable materials should be followed.
- Restylane Refyne is to be used as supplied. Modification or use of the product outside the Directions for Use may adversely impact the sterility, homogeneity, and performance of the product.
- The safety for use during pregnancy, in breastfeeding females, or in patients under 22 years has not been established.
- Injection of Restylane Refyne in patients with pre-existing tendency towards edema formation may be associated with prominent discoloration and excessive swelling due to fluid build-up.
- Injection of Restylane Refyne too superficially or in facial areas with limited soft tissue support, thin skin or limited soft tissue cover, may result in contour irregularities and palpable lumps.
- Restylane Refyne should be used with caution in patients on immunosuppressive therapy.
- Restylane Refyne should be used with caution in patients with bleeding disorders.
- Do not inject the product in close proximity to a site that has been treated with a permanent implant as this could potentially aggravate latent adverse events or interfere with the aesthetic outcome of the treatment. Limited data is available on injecting into an area where an implant other than hyaluronic acid has been placed.
- Patients who are using substances that can prolong bleeding (such as aspirin, nonsteroidal anti-inflammatory drugs, and warfarin) may, as with any injection, experience increased bruising or bleeding at treatment sites.
- Patients should minimize exposure of the treated area to excessive sun, UV lamp exposure and extreme temperatures at least until any initial swelling and redness has resolved.
- If laser treatment, chemical peeling or any other procedure based on active dermal response is considered after treatment with Restylane Refyne, there is a possible risk of eliciting an inflammatory reaction at the implant site. This also applies if Restylane Refyne is administered before the skin has healed completely after such a procedure.
- Injections of Restylane Refyne into patients with a history of previous herpetic eruption may be associated with reactivation of the herpes.
- Inflammatory pigmentation changes and scarring might occur following dermal filler injections. Patients with abnormal wound healing or dark skin (Fitzpatrick Type IV-VI) may be more prone to develop hypertrophic scarring and keloid formation.

- After use, treatment syringes and needles may be potential biohazards. Handle and dispose of these items in accordance with accepted medical practice and applicable local, state, and federal requirements.
- Individual variation and treatment area may affect the bio-degradation of Restylane Refyne and product might be detected in the tissue even after the clinical effect has disappeared.
- Restylane Refyne injectable gel is a clear, colorless gel without particulates. In the event that the content of a syringe shows signs of separation and/or appears cloudy, do not use the syringe; notify Galderma Laboratories, L.P. at 1-855-425-8722
- In order to minimize the risks of potential complications, this product should only be used by health care practitioners who have appropriate training, experience and who are knowledgeable about the anatomy at and around the site of injection.
- Health care practitioners are encouraged to discuss all potential risks of soft tissue injection with their patients prior to treatment and ensure that patients are aware of signs and symptoms of potential complications.
- Failure to comply with the needle attachment instructions could result in needle disengagement and/or product leakage at the Luer lock and needle hub connection.
- Restylane Refyne contains lidocaine. If additional dental block or topical lidocaine or other local anesthetics or agents structurally related to amide-type local anesthetics are used concurrently with the product the following considerations should be observed:
    - Use with caution in patients with epilepsy, impaired cardiac conduction, severely impaired hepatic function or severe renal dysfunction
    - High doses of lidocaine (more than 4.5 mg/kg of bodyweight) can cause acute toxic reactions manifesting as symptoms affecting the central nervous system and cardiac conduction
    - Systemic toxic effects could be additive

6. ADVERSE EVENTS

A. Clinical Evaluation of Restylane Refyne

One hundred seventy (170) subjects were enrolled in a randomized, double-blinded (subject and evaluator), active controlled, split-face comparison clinical trial to evaluate the safety and effectiveness of Restylane Refyne vs. a non-lidocaine-containing comparator. Touch-up treatments occurred approximately 3 weeks after initial injection, as needed, to achieve volume correction. After 48 weeks, subjects could opt for retreatment with Restylane Refyne to both sides of the face, with a subsequent touch-up as needed 3 weeks afterwards. One hundred twelve subjects (112, 65.9%) opted for retreatment.

Preprinted diary forms were used by subjects for subject-reported assessments of specific signs and symptoms experienced during each of the first 21 days after initial, touch-up, and repeat treatments. Subjects rated each treatment site response as "Mild" "Moderate" "Severe" or "None." Of the 170 subjects who received treatment, 98.8% (168 subjects) completed the diary forms. Of the 112 subjects who opted for retreatment, 97.3% (109) subjects completed the diary forms after retreatment.

After initial treatment, subjects rated pre-defined treatment site responses (redness, swelling, bruising, lump/bump formation, pain/tenderness, and itching) as predominantly mild or moderate in intensity (Table 1), typically with a duration of 1 to 2 weeks (Table 2). Based on data from 109 subjects, no increase in frequency or in intensity of signs/symptoms was observed following the retreatment injection or retreatment touch-up injection.

The trend in adverse events remained the same across subject skin types. Among the 73 subjects of Fitzpatrick Skin Types IV, V, and VI (18 of which were of Skin Type V or VI) in the study, no cases of keloid formation or of hyperpigmentation were reported.

Treatment site responses reported in subject diaries that lasted longer than 3 weeks were considered adverse events (AEs). AEs were also reported by the Treating Investigator at all follow-up visits where applicable.

Among the 170 treated subjects, 7.1% (12/170) experienced device- and injection-related AEs following initial and touch-up treatment, as well as retreatment and touch-up treatment. These subjects reported a total of 9 events related to control treatment and 10 events related to Restylane Refyne. The most common of treatment site responses was injection site erythema, which was reported for 4 subjects. Other treatment site responses (swelling, mass, hematoma, pruritus, and anesthesia) were reported for 1 subject each. Other related adverse events included presyncope (2 subjects), headache (1 subject), syncope (1 subject), and ecchymosis (1 subject).

Two subjects reported 2 serious adverse events (SAEs) that were considered to be unrelated to the device. The events were worsened knee osteoarthritis and a case of cholecystitis.

Treatment site responses after initial treatments are summarized by severity in Table 1 and by duration in Table 2.

Table 1 - Treatment Site Responses by Maximum Severity Occurring In Subjects After Initial Treatment

	Restylane Refyne (N=170) n (%)				Control (N=170) n (%)			
	Mild	**Moderate**	**Severe**	**Total**	**Mild**	**Moderate**	**Severe**	**Total**
Post-Initial Injection[a] (N= 168 for Restylane Refyne and N= 168 for the control)								
Redness	60 (35.7)	24 (14.3)	9 (5.4)	93 (55.4)	62 (36.9)	22 (13.1)	14 (8.3)	98 (58.3)
Swelling	66 (39.3)	30 (17.9)	5 (3.0)	101 (60.1)	52 (31.0)	44 (26.2)	6 (3.6)	102 (60.7)
Bruising	49 (29.2)	29 (17.3)	18 (10.7)	96 (57.1)	51 (30.4)	31 (18.5)	14 (8.3)	96 (57.1)
Lump/Bump Formation	39 (23.2)	26 (15.5)	10 (6.0)	75 (44.6)	45 (26.8)	27 (16.1)	11 (6.5)	83 (49.4)
Pain/Tenderness	58 (34.5)	11 (6.5)	3 (1.8)	72 (42.9)	65 (38.7)	19 (11.3)	2 (1.2)	86 (51.2)
Itching	21 (12.5)	3 (1.8)	1 (0.6)	25 (14.9)	28 (16.7)	1 (0.6)	0	29 (17.3)

Percentages are based on total number of subjects who reported local tolerability assessments in a subject diary.
[a] Number of subjects who completed subject diaries.

Table 2 - Duration of Treatment Site Responses Occurring In Subjects After Initial Treatment

Injection site response	Restylane Refyne (N=170) n (%)				Control (N=170) n (%)			
Duration[a]	1-3 Days	4-7 Days	8-14 Days	>14 Days	1-3 Days	4-7 Days	8-14 Days	>14 Days
Post-Initial Injection[b] (N= 168 for Restylane Refyne and N= 168 for the control)								
Redness	71 (42.3)	13 (7.7)	5 (3.0)	4 (2.4)	73 (43.5)	18 (10.7)	5 (3.0)	2 (1.2)
Swelling	58 (34.5)	23 (13.7)	14 (8.3)	6 (3.6)	55 (32.7)	24 (14.3)	17 (10.1)	6 (3.6)
Bruising	31 (18.5)	30 (17.9)	27 (16.1)	8 (4.8)	28 (16.7)	35 (20.8)	29 (17.3)	4 (2.4)
Lump/bump Formation	33 (19.6)	19 (11.3)	9 (5.4)	14 (8.3)	34 (20.2)	21 (12.5)	16 (9.5)	12 (7.1)
Pain/tenderness	53 (31.5)	11 (6.5)	8 (4.8)	0	63 (37.5)	19 (11.3)	4 (2.4)	0
Itching	22 (13.1)	2 (1.2)	1 (0.6)	0	26 (15.5)	3 (1.8)	0	0

Percentages are based on total number of subjects who reported local tolerability assessments in a subject diary.

[a] Number of days was defined as the sum of days when a sign/symptom was scored 'Mild' or higher.

[b] Number of subjects who completed subject diaries.

B. Other Safety Data

Post-Market Surveillance

The adverse event reports received from post-marketing surveillance (from voluntary reporting and published literature) for the use of *Restylane Refyne* with and without lidocaine in the U.S. and other countries most commonly included reports of transient swelling/edema and with immediate onset or delayed onset, up to several weeks after treatment.

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

- mass formation/induration
- erythema
- pain/tenderness
- papules/nodules
- bruising/hematoma
- short duration of effect
- discoloration/hyperpigmentation
- ischemia and necrosis including pallor due to unintentional intravascular injection or embolization
- presumptive bacterial infections and abscess formation
- injection site reactions including burning sensation, discomfort, dryness, exfoliation, irritation and warmth
- hypersensitivity/angioedema

- inflammation
- device dislocation
- pruritus
- deformity/overcorrection
- neurological symptoms including hypoesthesia and paraesthesia
- eye disorders such as eye swelling, blurred vision, ocular discomfort, and visual impairment
- granuloma/foreign body reaction
- blisters/vesicles
- rash
- atrophy/scarring
- acne
- urticaria
- discharge
- symptoms of reactivation of herpes infection
- dermatitis
- muscle disorders such as muscle twitching and muscle spasm
- capillary disorder such as telangiectasia
- non dermatological events chills, dizziness and dyspnoea and headache
- other dermatological events including dry skin, chapped lips and epidermolysis

When required, treatments for these events included ice, massage, warm compress, nitroglycerine paste, corticosteroids, antibiotics, antihistamines, analgesics, antiviral agents, diuretic agents, aspiration/incision, drainage, surgery or enzymatic degradation (with hyaluronidase) of the product.

Reports of serious adverse events for *Restylane Refyne* with and without lidocaine are rare. The most commonly reported serious adverse events were ischemia/necrosis, eye disorders, infection/abscess, and hypersensitivity. Other concurrent serious events included: swelling, bruising/bleeding, discolouration, erythema and pain/tenderness.

Serious infection/abscesses 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, analgesics, corticosteroids and hyaluronidase.

The onset of serious hypersensitivity/allergic reactions generally vary from immediately to a few weeks post injection. Most of the events were recovering or recovered at the time of last contact. The treatments may include analgesics, antihistamine, antibiotics, and corticosteroids.

Vascular occlusion resulting in ischemia/necrosis and visual disturbances, including blindness, 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. Vascular occlusion may occur due to an inadvertent intravascular injection or as a result of local vascular compression by the implant. This may manifest as ischemia or necrosis at the implant site or in the area supplied by the blood vessels affected; or rarely as ischemic events in other organs due to embolization. Isolated, rare ischemic events affecting the eye and brain have led to vision

loss and cerebral infarction, respectively. Treatments may include anticoagulants, epinephrine, aspirin, hyaluronidase, corticosteroid treatment, analgesics, local vasodilating agents such as PDE-5 inhibitor and nitropaste, antibiotics, drainage, surgery, and hyperbaric oxygen. Outcomes ranged from resolved to ongoing at the time of last contact. In many of the events requiring medical intervention the patient was injected into the highly vascularized areas of the glabella, nose, and periorbital area, which are outside the device indications for use.

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.

7. CLINICAL STUDIES

A. Pivotal Study for Restylane Refyne

Pivotal Study Design

A multi-center, double-blinded (subject and evaluator), randomized, active-controlled, clinical study with a split-face design was conducted to evaluate the safety and effectiveness of Restylane Refyne versus a comparator, a non-lidocaine HA dermal filler, in the treatment of moderate to severe nasolabial folds. Subjects were randomized to treatment with Restylane Refyne on either the right or left side of the face in a 1:1 ratio. The non-lidocaine containing comparator was injected into the other side of the face. Up to 2 initial treatments approximately 3 weeks apart (initial treatment and up to 1 touch-up treatment) and 48 weeks later up to 2 retreatments approximately 3 weeks apart (1 optional retreatment and up to 1 touch-up treatment) were allowed.

Treated subjects returned for routine safety visits with the Treating Investigator at 3, 12, 24, 36, and 48 weeks after the initial injection(s). All subjects returned for effectiveness follow-up visits with the evaluating investigators at 3, 12, 24, 36, and 48 weeks after the initial injection(s). The evaluating investigator assessed subjects' nasolabial folds on the validated 5-point Wrinkle Severity Rating Scale (WSRS). The subjects self-assessed the wrinkle severity on a 5-point scale and also used an 11-point Numeric Pain Intensity Scale (NPIS).

Study Endpoints

The primary effectiveness variable was the change in WSRS from Baseline to 24 weeks after treatment as assessed by the Blinded Evaluating Investigator compared to the control.

Secondary effectiveness endpoints included the difference in WSRS change from baseline to each visit up to Week 48 after treatment, WSRS response rate, defined as the percentage of subjects with at least a 1-grade improvement in WSRS from Baseline up to Week 48 after treatment, pain assessment after each injection (compared between treatments), the difference in subject self-assessment of wrinkle severity (SSA) response rate at weeks 3, 12, 24, 36, and 48 after treatment, and the change from baseline in SSA score at weeks 3, 12, 24, 36, and 48 after treatment.

Subject Demographics

A total of 171 subjects were randomized per protocol, 1 of whom discontinued prior to treatment. Of the remaining 170 subjects, 21 subjects prematurely discontinued the study, primarily due to subject request (67%, 14/21) or due to loss to follow-up (19%, 4/21).

At baseline, all subjects had moderate (55%, 93/170) or severe (45%, 77/170) WSRS scores for their nasolabial folds. The majority of subjects self-assessed their wrinkle severity as either moderate (45%) or severe (45%). Subject demographics and pre-treatment characteristics are presented in Table 3.

Table 3 - Demographics and Pre-treatment Characteristics (N= 170) - All Subjects

Characteristic		(N = 170) % (n)
Gender	Female	94% (160)
	Male	6% (10)
Age (years)	Median	54.5
	Range (min, max)	(26-77)
Race	Caucasian	68% (116)
	Hispanic	22% (38)
	Black	9% (15)
	Other	1% (1)
Fitzpatrick Skin Type	I	4% (6)
	II	23% (39)
	III	31% (52)
	IV	33% (55)
	V	5% (9)
	VI	5% (9)

Primary Effectiveness Results

The primary endpoint of the study was met. The mean change from baseline to month 6 on the Wrinkle Severity Rating Scale (WSRS) was 1.1 for subjects treated with Restylane Refyne and 1.2 for subjects treated with the control. The effect of Restylane Refyne was demonstrated to be non-inferior to the control, with both products showing a clinically meaningful improvement in

wrinkle severity. For the primary effectiveness variable of change from Baseline in WSRS at Week 24 post-treatment, both study products caused a mean reduction of similar magnitude. The two products' point estimates differed by -0.07 units (confidence interval -0.15 to 0.01). In addition, similar numbers of subjects experienced a 1-grade, 2-grade, or 3-grade improvement with both study products.

Throughout the follow-up period, Restylane Refyne continued to provide a clinically significant improvement in wrinkle severity (≥ 1-point mean improvement on the WSRS), with a majority of folds treated with Restylane Refyne demonstrating improvement through 1 year (Table 4).

At 6 months, improvements in nasolabial folds (≥ 1-point mean improvement on the WSRS) treated with Restylane Refyne were observed in 78.8% (134/170) of subjects. At 1 year, 62.3% (101/162) of folds treated with Restylane Refyne maintained improvement.

On Subject Self-Assessment at 6 months, 78.8% (134/170) of subjects reported improvement in fold severity for the folds treated with Restylane Refyne. At 1 year, 66.7% (108/162) of subjects reported improvement in folds treated with Restylane Refyne.

Table 4 – Effectiveness Results through 1 Year

	Restylane Refyne % (n/N ITT)
Week 12	90.6 (154/170)
Week 24	78.8% (134/170)
Week 36	78.0% (128/164)
Week 48	62.3% (101/162)

Restylane Refyne presented a statistically (P= <0.001) more favorable pain profile than the non-lidocaine containing control. At the time of injection, subjects rated their pain as 2.9 on a scale of 0 (no pain) to 10 (worst possible pain) for the side of the face treated with Restylane Refyne. In comparison, subjects rated their pain as 5.6 on the same scale for the side of the face treated with the control. At the time of the initial injection until the 60-minute time point, subjects recorded more pain with the comparator than with Restylane Refyne.

Subject Self-Assessments

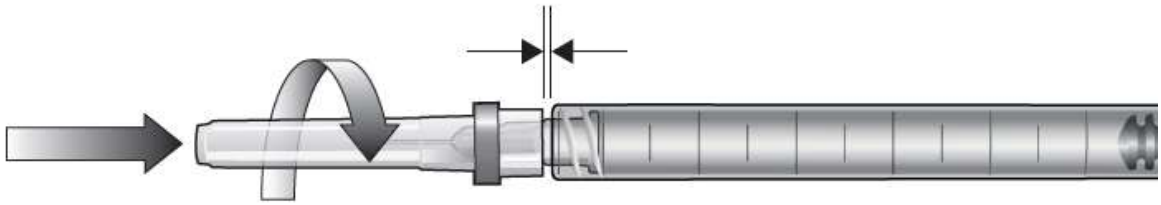
Subjects performed self-assessments of wrinkle severity. Most subjects (78.8% at Week 24 and 66.7% at Week 48) had at least a 1-grade improvement in SSA scores with Restylane Refyne.

8. INSTRUCTIONS FOR USE

A. To Attach Needle to Syringe

Using surgical gloves, remove the cap from the needle and unscrew the tip cap from the syringe. Hold firmly around the syringe barrel and grasp the needle shield with the other hand. Screw the needle tight onto the syringe by simultaneously pushing and rotating firmly until the needle is completely locked. To ensure proper assembly, minimize the gap between the needle shield and the syringe. See the figure below.

Remove the needle shield just before injection by pulling it straight out. Do not rotate.
Note: Improper assembly may cause leakage or needle disconnection.



B. Health Care Professional Instructions

1. Restylane Refyne is a cross-linked formulation resulting in a soft injectable gel that can be injected using a 30 G needle, for contouring and volumizing of facial wrinkles and folds.

2. Prior to treatment, the patient's medical history should be obtained, and the patient should be fully apprised of the indications, contraindications, warnings, precautions, treatment responses, adverse reactions, and method of administration. Patients also should be advised that supplemental "touch-up" implantations may be required to achieve and maintain maximum correction. Pre-treatment photographs are recommended.

3. Although the study showed that lidocaine in Restylane Refyne had an effect on pain, supplementary anesthesia may be used for additional pain management during and after injection.

4. After ensuring that the patient has thoroughly washed the treatment area with soap and water, the area should be prepped with alcohol or other antiseptic.

5. To avoid breakage of the needle, do not attempt to bend or otherwise manipulate it before or during treatment. If needle gets bent, discard it and complete the procedure with a replacement needle. Do not re-shield used needles. Recapping by hand is a hazardous practice and should be avoided. Discard unshielded needles in approved sharps collectors.

6. Before injection press the plunger rod carefully until a small droplet is visible at the tip of the needle.

7. If the needle is blocked, do not increase the pressure on the plunger rod. Instead, stop the injection and replace the needle. If resistance is encountered the needle should be partially withdrawn and repositioned or fully withdrawn and checked for function and replaced if needed.

8. After insertion of the needle, and just before injection, the plunger rod should be withdrawn slightly to aspirate and verify the needle is not in a blood vessel.

9. After the first small amount of material has been injected into the patient, wait a few seconds to allow the lidocaine to take effect before proceeding with the rest of the injection.

10. The injection technique, the depth of injection and volume administered may vary based on the subject's treatment needs. A retrograde linear threading technique, serial puncture injections, or a combination of the 2 have been used to achieve optimal results. Injecting the product too superficially may result in visible lumps and/or bluish discoloration. It is recommended to change needle for each new treatment site.

11. Inject Restylane Refyne by applying even pressure on the plunger rod while slowly pulling the needle backward. It is important that the injection be stopped just before the needle is pulled out of the skin to prevent material from leaking out or ending up too superficially in the skin.

12. Injection volume to achieve optimal correction of moderate to severe nasolabial folds is generally about 1.5 mL per treatment site. Injection volume to achieve optimal correction for retreatment is generally about 1.0 mL per treatment site.

13. Correct to 100% of the desired volume effect. Do not overcorrect.

14. If immediate blanching occurs, the injection should be stopped and the area massaged until it returns to a normal color. Blanching may represent a vessel occlusion. If normal skin coloring does not return, do not continue with the injection. Treat in accordance with American Society for Dermatologic Surgery guidelines, which include hyaluronidase injection.[1]

15. When injection is completed, the treated site may be gently massaged to mold the product to the contour of the surrounding tissue and assure that it is evenly distributed. If overcorrection occurs, massage the area between your fingers or against an underlying superficial bone to obtain optimal results.

16. With patients who have localized swelling, the degree of correction is sometimes difficult to judge at the time of treatment. In these cases, it is better to invite the patient back to the office for a touch-up treatment.

17. Patients may experience treatment site responses, which typically resolve within 1 to 2 weeks. If the treated area is swollen directly after the injection, an ice pack with adequate protective cloth may be applied on the site for a short period following treatment to minimize swelling and reduce pain. Ice should be used with caution if the area is still numb from anesthetic to avoid thermal injury.

18. The health care practitioner should instruct the patient to promptly report any problems associated with the use of Restylane Refyne.

C. Patient Instructions

It is recommended that the following information be shared with patients:

- Within the first 24 hours, patients should avoid strenuous exercise and extensive sun or heat exposure. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the treatment sites
- If the treated area is swollen, an ice pack may be applied to the site for a short period
- To report an adverse reaction, phone Galderma Laboratories, L.P, 1-855-425-8722.

9. HOW SUPPLIED

Restylane Refyne injectable gel is supplied in individual treatment syringes with needles as indicated on the carton. The volume in each syringe is as stated on the syringe label and on the carton. The contents of the syringe are sterile. Do not resterilize. Do not use the product if package is open or damaged or if expiry date or lot number is missing or illegible. Immediately return the damaged product to Galderma Laboratories, L.P

10. SHELF LIFE AND STORAGE

Restylane Refyne must be used prior to the expiration date on the package. Store at a temperature of up to 25ºC/77ºF. Do not freeze. Protect from sunlight. Refrigeration is not required.

Restylane Refyne injectable gel has a clear appearance. In the event that a syringe contains material that is not clear, do not use the syringe; notify Galderma Laboratories, L.P. immediately at 1-855-425-8722.

[1] Alam, M, Gladstone H, Kramer EM, et al. ASDS guidelines of care: injectable fillers *Dermatol Surg.* 2008;34(suppl 1):S115-S148.

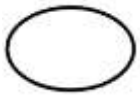
To place an order, contact. Galderma Laboratories, L.P. at 1-855-425-8722

Rx only

U.S. Patent 8,357,795; 8,450,475; 8,822,676

SYMBOL GLOSSARY

SYMBOL	STANDARD	STANDARD TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	ISO 15223-1 Ref. No. 5.1.1	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Manufacturer	Indicates the medical device manufacturer
	ISO 15223-1 Ref. No. 5.1.4	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Use-by date	Indicates the date after which the medical device is not to be used.
	ISO 15223-1 Ref. No. 5.1.5	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Batch code	Indicates the manufacturer's batch code so that the batch or lot can be identified.
	ISO 15223-1 Ref. No.5.1.6	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Catalogue number	Indicates the manufacturer's catalogue number so that the medical device can be identified.
	ISO 15223-1 Ref. No. 5.2.4	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Sterilized using irradiation	Indicates a medical device that has been sterilized using irradiation.

	ISO 15223-1 Ref. No. 5.2.11	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Single sterile barrier system	Indicates a single sterile barrier system
	ISO 15223-1 Ref. No. 5.4.2	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Do not re-use	Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure.
	ISO 15223-1 Ref. No. 5.4.4	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Caution	Indicates that caution is necessary when operating the device or control close to where the symbol is placed, or that the current situation needs operator awareness or operator action in order to avoid undesirable consequences.

SYMBOLS NOT DERIVED FROM STANDARDS

SYMBOL	REFERENCE	REFERENCE TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	21 CFR 801.15I(1)(i)F	Labeling – Medical devices; prominence of required label statements; use of symbols in labeling.	Prescription use only	Caution: Federal law restricts this device to sale by or on the order of a physician or properly licensed practitioner.
	21 CFR 801.109	Labeling – Prescription devices.		
	Medical Device Regulation (EU) 2017/745, Article 20	CE marking of conformity	CE marking	Signifies European technical conformity. 0123 is the notified body number for the needles.

	Inmetro Ordinance No. 84, February 10, 2021 and Inmetro Ordinance No. 385, September 17, 2021	Hypodermic needles for Inmetro conformity	INMETRO mark	Brazilian technical requirements for conformity of hypodermic needles for single usage. TÜV Rheinland is the name of the certification body.

Manufactured for
Galderma Laboratories, L.P.
2001 Ross Ave.
Suite 1600
Dallas, TX 75201 USA
Phone: 1-855-425-8722

Manufactured by:
Q-Med AB
Seminariegatan 21
SE-752 28 Uppsala
Sweden

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All other trademarks are the property of their respective owners.

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