MEDICA DEPOT

RESTYLANE® EYELIGHT™ Product Specifications

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Restylane® Eyelight
Injectable Gel with 0.3% Lidocaine

Caution: Federal Law restricts this device to sale by or on the order of a physician or licensed practitioner.

1. DEVICE DESCRIPTION

Restylane Eyelight is a transparent, viscous, and sterile gel of hyaluronic acid (HA) generated by *Streptococcus* species of bacteria, chemically crosslinked with BDDE (1.4-butanediol diglycidyl ether). The gel is suspended in phosphate buffered saline pH 7 at a HA concentration of 20 mg/mL with 0.3% lidocaine.

2. INDICATION

Restylane Eyelight is indicated for the improvement of infraorbital hollowing in patients over the age of 21.

3. CONTRAINDICATIONS

- *Restylane Eyelight* is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.
- *Restylane Eyelight* contains trace amounts of gram positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.
- *Restylane Eyelight* contains lidocaine and is contraindicated for patients with a history of allergies to such material or other amide type anesthetics.

4. WARNINGS

- Introduction of *Restylane Eyelight* 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.

- Defer use of *Restylane Eyelight* at specific sites in which an active inflammatory process (skin eruptions such as cysts, pimples, rashes, or hives) or infection is present until the process has been controlled.
- *Restylane Eyelight* 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, such as in the periorbital area. 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.
- Patients with bleeding disorders or patients using substances that affect platelet function, thrombolytics or anticoagulants may, as with any injection, experience increased bruising or bleeding at injection site.

5. PRECAUTIONS

- *Restylane Eyelight* is for single patient and single session use only and should be discarded immediately after use. Do not resterilize. Do not use if package is opened or damaged.
- Health care professionals 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.
- In order to minimize the risks of potential complications, this product should only be used by health care professionals who have appropriate training, experience, and who are knowledgeable about the anatomy at and around the site of injection in order to minimize the risks of potential complications (perforation or compression of vessels, nerves and other vulnerable structures).
- Based on U.S. clinical study, patients should be limited to up to 1 mL per side and treatment session in the infraorbital hollow area. If a volume of more than 1 mL per side is needed to achieve optimal correction, a follow-up treatment session is recommended. The safety of injecting greater amounts per treatment session has not been established.
- The safety and effectiveness of cannula injection of *Restylane Eyelight* have only been clinically evaluated in one brand of blunt-tip cannulas (TSK STERIGLIDE) that are 25G-27G and 1.5 inches in length.
- As with all transcutaneous procedures, *Restylane Eyelight* implantation carries a risk of infection. Standard precautions associated with injectable materials should be followed.
- The safety of *Restylane Eyelight* for use during pregnancy, in breastfeeding females or in patients under 22 years has not been established.
- Patients with abnormal wound healing or dark skin (Fitzpatrick Type IV-VI) may be more prone to develop hypertrophic scarring and keloid formation following dermal filler injections. Clinical studies in patients with Fitzpatrick Skin Types IV, V and VI in other indications with a similar gel, reported a 9% incidence of inflammatory hyperpigmentation and no reports of keloid formation.

- Injection of *Restylane Eyelight in* patients with pre-existing tendency toward edema formation may be associated with excessive swelling due to fluid build-up.
- Injection in the lower periorbital region in patients with pre-existing pigmented dark lower eyelid circles may be associated with more prominent discoloration.
- Injection of *Restylane Eyelight* too superficially and injection in facial areas with limited soft tissue support or soft tissue cover, or thin skin, such as the periorbital area, may result in contour irregularities and palpable lumps and/or bluish discolouration.
- *Restylane Eyelight* should be used with caution in patients on immunosuppressive therapy.
- Avoid injecting *Restylane Eyelight* into areas in close proximity to permanent implants, as this could potentially aggravate latent adverse events or interfere with the aesthetic outcome of the treatment. Limited data is available on injecting *Restylane Eyelight* into an area where an implant other than hyaluronic acid has been placed.
- The safety of *Restylane Eyelight* with concomitant dermal therapies such as epilation, UV irradiation, or laser, mechanical or chemical peeling procedures has not been evaluated in controlled clinical trials.
- 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 Eyelight*, there is a possible risk of eliciting an inflammatory reaction at the implant site. This also applies if *Restylane Eyelight* is administered before the skin has healed completely after such a procedure.
- Injection of *Restylane Eyelight* into patients with a history of previous herpetic eruption may be associated with reactivation of the herpes.
- The product contains lidocaine. If 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
    - Systemic toxic effects could be additive
    - Peribulbar injections carry a low risk of persistent ocular muscle dysfunction
- Individual variation and treatment area may affect the biodegradation of injectable HA fillers and product might be detected in the tissue even after the clinical effect has disappeared.
- *Restylane Eyelight* 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 and notify Galderma Laboratories, L.P. at 1-855-425-8722.
- Glass is subject to breakage under a variety of unavoidable conditions. Care should be taken with the handling of the glass syringe and with disposing of broken glass to avoid laceration or other injury.
- After use, syringes and needles/cannulas should be handled as potential biohazards. Disposal

should be in accordance with accepted medical practice and applicable local, state and federal requirements.

- *Restylane Eyelight* should not be mixed with other products before implantation of the device.

6. ADVERSE EVENTS

U.S. Pivotal study of *Restylane Eyelight* for correction of infraorbital hollows

The U.S. randomized, controlled clinical study involved 333 subjects at 16 centers for correction of infraorbital hollows. The subjects were randomized to *Restylane Eyelight* (287 subjects) or no treatment (46 subjects). Subjects randomized to treatment with *Restylane Eyelight*, were treated at study start and were offered an optional touch-up treatment after one month. At Month 12 both the no-treatment control subjects and the treatment group subjects were offered an optional *Restylane Eyelight* treatment. Subjects were injected with a needle or a cannula.

Subjects reported injection site reactions (IREs) in a 28-day paper diary following each performed treatment (initial treatment, optional touch-up and optional 12 Month treatment). Subject were to assess the presence of pre-defined expected post-treatment events, i.e., swelling, redness, tenderness, pain (including burning), bruising, itching or lumps/bumps were assessed for the treated area and to rate the level of intensity (i.e., none, tolerable, affects daily activities, or disabling) for each of the pre-defined events (**Table 1**).

Over 77,5% of the pre-defined IREs after injection with *Restylane Eyelight* (initial, touch-up and retreatment) were considered tolerable and over 63.7% lasted 7 days or less (**Table 2**).

Table 1: Pre-defined Injection Related Events (IREs) by Maximum Severity Occurring in Subjects After Injection

	Tolerable n (%)	Affects Daily Activities n (%)	Disabling n (%)	Total n (%)
Post Initial Injection [1] (N=301)				
Pain (including burning)	164 (91.1)	14 (7.9)	2 (1.1)	180 (59.8)
Tenderness	255 (94.4)	14 (5.2)	1 (0.4)	270 (89.7)
Redness	164 (88.6)	20 (10.8)	1 (0.5)	185 (61.5)
Bruising	153 (80.5)	35 (18.4)	2 (1.1)	190 (63.1)
Swelling	207 (80.9)	47 (18.4)	2 (0.8)	256 (85.0)
Lumps/Bumps	139 (86.3)	21 (13.0)	1 (0.6)	161 (53.5)
Itching	42 (97.7)	1 (2.3)	0	43 (14.3)
Post-optional Touch-up Injection [1] (N=206)				
Pain (including burning)	98 (89.1)	12 (10.9)	0	110 (53.4)
Tenderness	152 (92.1)	13 (7.9)	0	165 (80.1)
Redness	110 (90.2)	11 (9.0)	1 (0.8)	122 (59.2)
Bruising	109 (86.5)	15 (11.9)	2 (1.6)	126 (61.2)
Swelling	141 (87.6)	18 (11.2)	2 (1.2)	161 (78.2)
Lumps/Bumps	85 (89.5)	10 (10.5)	0	95 (46.1)
Itching	24 (92.3)	2 (7.7)	0	26 (12.6)
Post-Retreatment Injection [1] (N = 153)				
Pain (including burning)	77 (88.5)	10 (11.5)	0	87 (56.9)
Tenderness	111 (90.2)	12 (9.8)	0	123 (80.4)
Redness	72 (86.7)	11 (13.3)	0	83 (54.2)
Bruising	62 (77.5)	18 (22.5)	0	80 (52.3)
Swelling	97 (81.5)	20 (16.8)	2 (1.7)	119 (77.8)
Lumps/Bumps	65 (87.8)	9 (12.2)	0	74 (48.4)
Itching	22 (88.0)	3 (12.0)	0	25 (16.3)

[1] Number of subjects who completed at least one diary entry and were injected.

Note 1: Percentages for symptom severity columns are based on the total number of subjects who reported 'Tolerable' or higher for a respective symptom in their subject diary; The total column percentages are based on the number of subjects who completed at least one diary entry and were injected.

Note 2: Maximum severity of both sides of the face is presented.

Note 3: Initial treatment includes subjects randomized to *Restylane Eyelight* that received a baseline injection plus subjects randomized to No Treatment that had an optional initial treatment; Optional touch-up includes subjects randomized to *Restylane Eyelight* that received an optional touch-up at one month; Retreatment includes subjects randomized to *Restylane Eyelight* that received an optional retreatment at Month 12.

Table 2: Duration of Pre-defined Injection Related Events (IREs) [1] Occurring in Subjects After Injection

	1 Day n (%)	2 - 7 Days n (%)	8 - 13 Days n (%)	14 - 28 Days n (%)
Post-Initial Injection [2] (N=288)				
Pain (including burning)	67 (37.2)	105 (58.3)	8 (4.4)	0
Tenderness	30 (11.1)	201 (74.4)	30 (11.1)	9 (3.3)
Redness	44 (23.8)	129 (69.7)	9 (4.9)	3 (1.6)
Bruising	24 (12.6)	105 (55.3)	45 (23.7)	16 (8.4)
Swelling	30 (11.7)	196 (76.6)	25 (9.8)	5 (2.0)
Lumps/Bumps	29 (18.0)	78 (48.4)	23 (14.3)	31 (19.3)
Itching	19 (44.2)	24 (55.8)	0	0
Post-Optional Touch-up Injection [2] (N=182)				
Pain (including burning)	37 (33.6)	67 (60.9)	4 (3.6)	2 (1.8)
Tenderness	17 (10.3)	130 (78.8)	12 (7.3)	6 (3.6)
Redness	35 (28.7)	76 (62.3)	6 (4.9)	5 (4.1)
Bruising	19 (15.1)	65 (51.6)	31 (24.6)	11 (8.7)
Swelling	24 (14.9)	108 (67.1)	17 (10.6)	12 (7.5)
Lumps/Bumps	14 (14.7)	50 (52.6)	15 (15.8)	16 (16.8)
Itching	10 (38.5)	15 (57.7)	1 (3.8)	0
Post-Retreatment Injection [2] (N=131)				
Pain (including burning)	24 (27.6)	58 (66.7)	5 (5.7)	0
Tenderness	19 (15.4)	85 (69.1)	14 (11.4)	5 (4.1)
Redness	26 (31.3)	48 (57.8)	7 (8.4)	2 (2.4)
Bruising	8 (10.0)	43 (53.8)	21 (26.3)	8 (10)
Swelling	15 (12.6)	86 (72.3)	12 (10.1)	6 (5.0)
Lumps/Bumps	10 (13.5)	45 (60.8)	11 (14.9)	8 (10.8)
Itching	14 (56.0)	11 (44.8)	0	0

[1] Number of days was defined as the sum of days when a sign/symptom was scored 'Tolerable' or higher, on either side of face.
[2] Number of subjects who completed at least one diary entry and were injected when a sign/symptom was scored ‘Tolerable’ or higher.
Note 1: Percentages are based on the total number of subjects who reported 'Tolerable' or higher for a respective symptom in their subject diary.
Note 2: Initial treatment includes subjects randomized to *Restylane Eyelight* that received a baseline injection plus subjects randomized to No Treatment that had an optional initial treatment; Optional touch-up includes subjects randomized to *Restylane Eyelight* that received an optional touch-up at one month; Retreatment includes subjects randomized to *Restylane Eyelight* that received an optional retreatment at Month 12.

Adverse Events (AEs) were assessed and reported by the Treating Investigator at the follow-up visit throughout the study. 40/316 (12.7%) treated subjects experienced an AE considered related to treatment or product after initial treatment. The percentage of subjects who experienced related AEs was higher in subjects who were injected using cannula compared with subjects who were injected using needle, 20.9% (32/153) and 4.9% (8/163) respectively. Females and subjects with BMI less or equal to 25.4 experienced more related AEs (**Table 3**). The percentage of subjects who experienced related AEs was higher in subjects who were injected at multiple depths (supraperiosteal and other) compared with subjects who were injected supraperiosteally only, 29.2% and 11.3%, respectively. The percentage of subjects who experienced related AEs was higher in subjects who received local injection of anesthetics before treatment compared with subjects who received topical anesthetics, 20.9% and 9.9%, respectively.

Table 3: Related AEs per sex and BMI subgroups

Subgroup		**Subjects with related AEs after initial treatment including touch-up treatment (%)**
Sex	Female	14% (38/276)
	Male	5% (2/40)
Body Mass Index (BMI)	BMI <= 25.4 (n=154)	18% (28/154)
	BMI > 25.4 (n=161)	7% (12/161)

The most common treatment or product related AEs (occurring in at least 1% of the subjects) after initial treatment were injection-site swelling (3.8%), injection-site pain (2.5%), headache (2.2%) injection-site bruising (1.6%), injection-site mass (1.3%), and injection-site edema (1.3%). All related AEs were mild or moderate in severity. Ten (3.2%) subjects who received *Restylane Eyelight* experienced moderate events; all moderate events considered related to study product or injection procedure were resolved by the end of the study.

In the clinical study, eight subjects had related AEs with an onset after 21 days. Two subjects experienced in total 3 AEs with moderate intensity (injection-site edema and injection-site swelling on left and right side), all other were of mild intensity. All but one of these (mild injection-site swelling) were resolved during the study.

There were no treatment-related serious AEs reported in the study.

Safety assessments such as visual acuity, confrontational visual fields, and ocular motility were evaluated throughout the study. The visual acuity assessments showed that over 97% of treatment group participants had no worsening (the same or better) from baseline to any assessment timepoints. Four (2.5%) subjects injected using needle reported AEs of special interest (AESIs), and thirteen (8.5%) subjects injected using cannula. For the AESIs, 25 events of visual acuity worsening were reported by 6% (19/316) of the treated subjects during the study. For 8 subjects (9 events) the visual acuity decline was maintained at the end of the study, with a maximum decline of a 2 line decrease from start to end of study. All the visual acuity changes were considered mild in intensity, and not related to the study product or injection procedure.

One subject experienced a light sensitivity in one eye that started 5 days after retreatment and lasted for 3 days before the event resolved, without any action taken. The event was considered mild in intensity and not related to study product.

Post-Marketing Surveillance

The adverse event reports received from post-marketing surveillance (from voluntary reporting and published literature) for the use of *Restylane Eyelight* with and without lidocaine, for infraorbital hollowing 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:

- mass formation/induration,
- erythema,
- bruising/bleeding,
- pain or tenderness,
- discoloration/hyperpigmentation,
- papules or nodules
- asymmetry/deformity
- short duration of effect,
- presumptive bacterial infections and abscess formation including cellulitis and purulent discharge,
- other injection site reactions and skin reactions including burning sensation, dryness, discomfort, exfoliation, irritation and warmth,
- eye disorders such as dry eye, eye swelling, increased lacrimation, eyelid ptosis, and visual impairment including blurred vision and blindness,
- hypersensitivity,
- pruritus,
- neurological symptoms including hypoesthesia, paraesthesia,
- scarring,
- ischemia and necrosis due to unintentional intravascular injection or embolisation,
- granuloma/foreign body reaction,
- device dislocation,
- rash,
- discharge/extrusion of device,
- urticaria,
- blisters/vesicles,
- dermatitis,
- capillary disorders such as telangiectasia,
- acne,
- muscle twitching and muscle weakness,
- encapsulation,
- symptoms of reactivation of herpes infection,
- dermatophytosis,
- other dermatological events including dry skin and skin wrinkling
- non-dermatological events including malaise, headache, pyrexia, sinusitis

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 Eyelight* are rare. The most commonly reported serious adverse events were infection/abscess, swelling, mass, hypersensitivity/allergic reactions and ischemia/necrosis. Other concurrent serious events included: pain/tenderness, erythema and bruising.

Serious infections/abscesses were mostly reported with a time to onset ranging from a few days up to 2 months following the injection. The infections usually resolved after three months and most of the patients had recovered or were recovering at the time of last contact. The treatments included; antibiotics, analgesics and corticosteroids .

Serious swelling was mostly reported with a time to onset ranging from a day to a few months. Most of the patients had recovered or were recovering at the time of last contact. The treatments included; corticosteroids, antibiotics and hyaluronidase.

Serious mass was reported with a time to onset ranging from two weeks to a year. The outcome usually was recovered or recovering at the time of last contact. The treatments included: analgesics, antihistamine, antibiotics, corticosteroids and hyaluronidase.

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

Vascular occlusion resulting in ischemia/necrosis and visual disturbances including blindness have been reported following injection of any soft tissue filler in the face especially in the nose, glabella, periorbital areas, nasolabial folds, and cheek, with a time to onset ranging from immediate to a few weeks following injection. Vascular compromise may occur due to an inadvertent intravascular injection or as a result of vascular compression associated with implantation of any injectable product. This may manifest as blanching, discoloration, necrosis or ulceration at the implant site or in the area supplied by the blood vessels affected; or rarely as ischemic events in other organs due to embolisation.

Isolated rare cases of ischemic events affecting the eye leading to visual loss, and the brain resulting in cerebral infarction, following facial aesthetic treatments have been reported. Reported treatments include anticoagulant, epinephrine, aspirin, hyaluronidase, steroid treatment, analgesics, antibiotics, local wound care, drainage, surgery and hyperbaric oxygen. Outcome of the events 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 (See Warnings section).

Late-onset adverse events (greater than 2 years after injection with dermal fillers), such as delayed-onset inflammation or granulomas, in the infraorbital region following treatment with Restylane fillers is low but, have been reported. Adverse events, such as puffiness, lumps, or swelling, have resulted in negative cosmetic outcomes, but, these presentations were noted as rare as well as correctable.

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.

Adverse reactions should be reported to Galderma Laboratories, L.P. at 1-855-425-8722

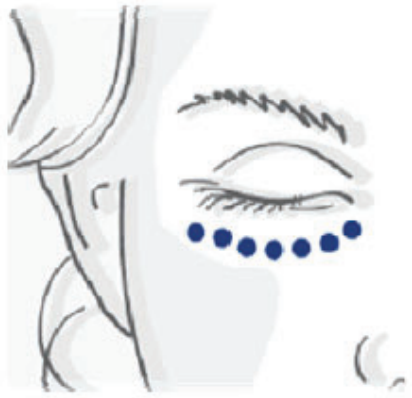
7. U.S. CLINICAL STUDIES

Pivotal study of *Restylane Eyelight* for correction of infraorbital hollows

Study Design:

A prospective, randomized, evaluator-blinded, controlled clinical study was conducted at 16 U.S. centers, to evaluate the safety and effectiveness on *Restylane Eyelight* for correction of infraorbital hollows. The study participants were randomized to *Restylane Eyelight* (287 subjects) or no treatment (46 subjects). Subjects randomized to treatment, were treated at study start and offered optional touch-up treatment after one month if optimal aesthetic improvement was not achieved. At Month 12 both the no-treatment control subjects and the treatment group subjects were offered an optional *Restylane Eyelight* treatment.

Study centers were given the option to inject the subjects with a 29 G, ½" needle, or 25 or 27G, 1½" cannula. All subject at a particular study center were injected with the same tool (needle or cannula). The maximum volume allowed of product injected was 2 mL (1 mL per side) at each treatment. *Restylane Eyelight* were to be placed into the supraperiosteal plane with a 29 G, ½" needle, or 25 or 27G, 1½" cannula. The infraorbital treatment area was defined as at the junction of the lower eyelid and midface where a volume deficit had formed. The area is bordered by the nasal sidewall medially, the temporal region of the bony orbit laterally, the bulk of the lower eyelid superiorly, and the superior aspect of the mid-face inferiorly.



The subjects were followed for safety and effectiveness, at study visits at 1, 3, 6, 9, and 12 months after baseline. Subjects that received optional treatment at Month 12 were followed for another 6 months, with visits at 1, 3, and 6 months after the optional treatment.

Study Endpoints

The primary effectiveness endpoint for the study was the Blinded Evaluators' live assessment of the subjects' Infraorbital hollows using the 4-grade photographically-based Galderma Infraorbital Hollows Scale (GIHS), performed separately for each infraorbital area. The primary objective for the study was met if the treatment group responder rate was statistically greater than the no-treatment control group at 3 months after baseline, with a responder defined as a subject with at least a 1-point improvement from baseline, on both sides of the face, concurrently.

Secondary measurements include the Blinded Evaluators' GIHS assessment at further follow-up visits, the subjects' and Treating Investigators' assessment of Global Aesthetic Improvement Scale (GAIS), the subjects' assessment of the Satisfaction with outcome module

of the FACE-Q, the subjects' assessment of the Subject Satisfaction Questionnaire, the subjects' assessment for return to social engagement (from the Subject Diaries) and the Independent Photographic Reviewer's (IPRs) assessment of improvement from random pairings of baseline and post-baseline photographs.

Safety measures included incidence, severity and duration of injection related events (IREs) and AEs, the visual assessments including visual acuity, confrontational visual fields, and ocular motility.

Subject Demographics:

Subject demographic and study start (baseline) characteristics, presented in **Table 4**, were generally similar between subjects who received *Restylane Eyelight* and the no treatment control group.

Table 4: Demographic and Baseline Characteristics (Intention-to-Treat Population)

Category	*Restylane Eyelight* (N=287)	No Treatment (N=46)	Overall (N=333)
Age at baseline (years)			
Mean (standard deviation)	44.3 (11.58)	45.5 (12.27)	44.4 (11.67)
Median	45.0	45.0	45.0
Minimum, maximum	22, 73	24, 63	22, 73
Age category, n (%)			
22-29 years	33 (11.5)	8 (17.4)	41 (12.3)
30-44 years	106 (36.9)	14 (30.4)	120 (36.0)
45-59 years	120 (41.8)	17 (37.0)	137 (41.1)
60-73 years	28 (9.8)	7 (15.2)	35 (10.5)
Sex, n (%)			
Female	252 (87.8)	38 (82.6)	290 (87.1)
Male	35 (12.2)	8 (17.4)	43 (12.9)
Race, n (%)			
White	257 (89.5)	39 (84.8)	296 (88.9)
Black or African American	17 (5.9)	4 (8.7)	21 (6.3)
Asian	4 (1.4)	1 (2.2)	5 (1.5)
Native Hawaiian or Other Pacific Islander	1 (0.3)	0	1 (0.3)
Other	8 (2.8)	2 (4.3)	10 (3.0)
Ethnicity, n (%)			
Hispanic or Latino	66 (23.0)	9 (19.6)	75 (22.5)
Not Hispanic or Latino	221 (77.0)	37 (80.4)	258 (77.5)
Fitzpatrick skin type, n (%)			
I	5 (1.7)	0	5 (1.5)
II	75 (26.1)	11 (23.9)	86 (25.8)
III	117 (40.8)	20 (43.5)	137 (41.1)
IV	62 (21.6)	10 (21.7)	72 (21.6)
V	13 (4.5)	3 (6.5)	16 (4.8)
VI	15 (5.2)	2 (4.3)	17 (5.1)
Body mass index (kg/m^2)	n = 285	n = 46	n = 331
Mean (standard deviation)	25.30 (4.772)	25.98 (4.866)	25.40 (4.783)
Median	24.30	26.10	24.40
Minimum, maximum	17.5, 46.3	19.4, 42.5	17.5, 46.3
Blinded Evaluator GIHS score - left, n (%)			
0	0	0	0
1	0	0	0
2	147 (51.2)	24 (52.2)	171 (51.4)
3	140 (48.8)	22 (47.8)	162 (48.6)
Blinded Evaluator GIHS score - right, n (%)			
0	0	0	0
1	0	0	0
2	147 (51.2)	27 (58.7)	174 (52.3)
3	140 (48.8)	19 (41.3)	159 (47.7)

Treatment Characteristics

Injections into the infraorbital hollows were supraperiosteal with a 29 G x ½" needle, or supraperiosteal and other with a 25 G x 1½" or 27 G x 1½" cannula. Injection techniques were linear threading (antegrade and retrograde), fanning, micro-bolus and serial puncture or a combination of these. The total volume of injection used for both infraorbital hollows together (up to 3 treatments) ranged from 0.1 to 6.0 mL with a mean volume of 2.6 mL. For the treatment group the median volume used for both infraorbital hollows together for the initial treatment was 1.2 mL, 1.0 mL for touch-up and 1.0 mL for retreatment.

Analysis populations

There are different analysis populations in the clinical study:

- The Intention To Treat (ITT) population was defined as all subjects who were randomized and includes 333 subjects. The ITT population is analyzed based on their randomization group; treatment or no treatment.
- The modified ITT (mITT) population was defined as all subjects who were randomized and who did not have a remote Month 3 study visit. The mITT population includes 245 subjects and is analyzed based on their randomization group; treatment or no treatment.
- The safety population was defined as all subjects that were treated or randomized to the no treatment group. The safety population includes in total 316 subjects that were treated with Restylane Eyelight in the study. This also include subjects in the no treatment control group that received the optional treatment at Month 12.

The mITT population is used for analysis of the primary effectiveness endpoint only. The ITT population is used for analyses of all other effectiveness endpoints, and the safety population is used for analysis of safety data.

Effectiveness Results

Restylane Eyelight provided a clinically and statistically significant improvement in the correction of volume deficit in the infraorbital hollows compared to the no-treatment control group. The primary effectiveness endpoint was met in that the treatment group responder rate was 87.4% which was statistically greater ($p < 0.001$) than the no-treatment control group (17.7%) at month 3 using the mITT population. The result was consistent with the result when using the ITT population. A responder was defined as a subject with at least a 1-point improvement from baseline, on both sides of the face, concurrently.

A mean clinically significant improvement (at least 1 point) was seen for the majority of the participants through 12 months based on the GIHS (Table 5).

Table 5: Responder Rates Based on GIHS as Assessed by the Blinded Evaluator through 12 Months

	Restylane Eyelight
Month 6 Responder rate, m/n (%)	221/257 (86.0)
Month 9 Responder rate, m/n (%)	197/254 (77.6)
Month 12 Responder rate, m/n (%)	162/255 (63.5)

The proportion of subjects in the *Restylane Eyelight* group having at least "Improved" on the GAIS, as assessed live by the Subject and Treating Investigator separately, demonstrated high improvement rates at each visit up until Month 12. The treated subjects rated their GAIS to 93.0% at Month 1 and 79.8% at Month 12 and the Treating Investigator rated the treated subjects to 97.4% at Month 1 and 87.5 % at Month 12.

The FACE-Q Satisfaction with Outcome showed that there were high total satisfaction scores throughout the study from Month 1 through Month 12 for subjects in the *Restylane Eyelight* group (mean range 64.3 to 73.5, with 0 as the worst and 100 as the best).

The majority of the subjects in the *Restylane Eyelight* group responded with "very satisfied" or "satisfied" in each response category for questions in the Subject Satisfaction Questionnaire at all visits across Month 1 to Month 12 (mean range 58.8% to 87.3%).

The median time to feeling comfortable returning to social engagement for subjects treated using needle was within 4 hours after treatment, and for subjects treated using cannula the time to feeling comfortable was within 12 hours after treatment.

Effectiveness Subgroup Analysis

Subgroup analyses were performed for injection tool, study site, Fitzpatrick skin types (I-III and IV-VI), race, ethnicity, gender, BMI, age, baseline GIHS, and cannula type for potential association with the primary effectiveness outcomes at Month 3. The Responder rates in the Restylane Eyelight cannula group based on the Blinded Evaluators' GIHS assessments at Month 3 was higher in subjects who had injection via a TSK 27-gauge × 1.5 inch cannula (91.2%) compared with subjects who had injection via a TSK 25-gauge × 1.5 inch cannula (69.6%). The Responder rates in the Restylane Eyelight group based on the Blinded Evaluators' GIHS assessments across all visits were generally similar across injection tool, race, ethnicity and age.

The GIHS and GAIS endpoints were analyzed in the needle group and the cannula group separately. The responder rates based on the Blinded Evaluators' GIHS assessment and the subjects' and Treating Investigators' GAIS assessments were generally similar across all visits, between subjects who received *Restylane Eyelight* via needle and subjects who received *Restylane Eyelight* via cannula.

8. INSTRUCTIONS FOR USE

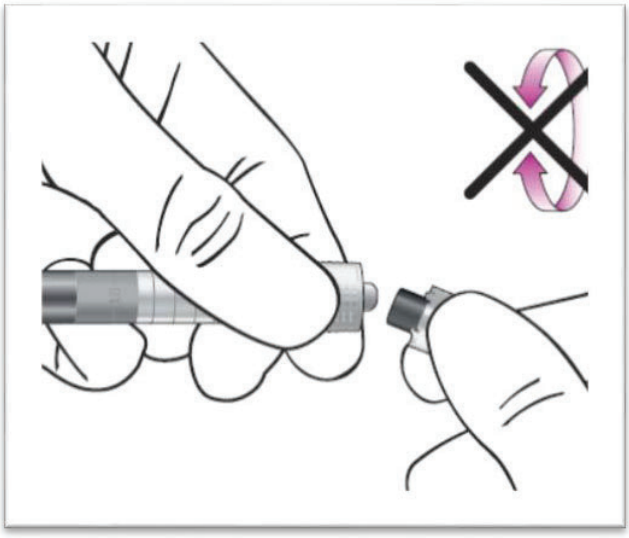
DIRECTIONS FOR ASSEMBLY

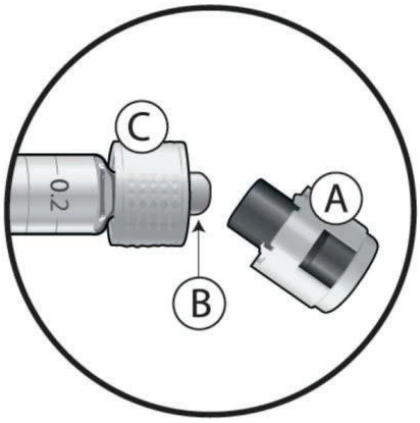
Syringe with white cap:

It is recommended to use medical gloves. Use your thumb and forefinger to hold firmly around both the syringe barrel and the luer-lock adapter part (C) of the closure system. With your other hand, take hold of the white cap (A) at the end of the closure system and gently tilt back and forth carefully until cap disconnects and can be pulled off (seal will be broken).

Do not rotate.

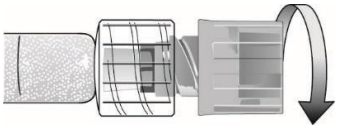
Do not touch the syringe tip (B) to keep it sterile.





Syringe with transparent cap:

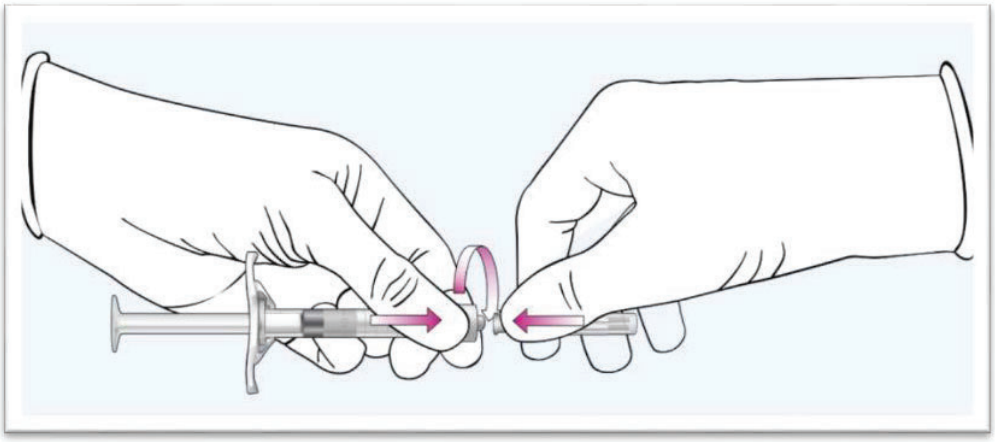
Unscrew the tip cap of the syringe carefully.



ASSEMBLY OF NEEDLE TO SYRINGE

Use the thumb and forefinger to hold firmly around both the glass syringe barrel and the luer-lock adapter (C). Grasp the needle shield with the other hand. To facilitate proper assembly, both push and rotate firmly clockwise. Make sure the needle is screwed on all the way so that the needle shield touches the luer-lock adapter (C). To remove the needle shield, hold the syringe and the luer-lock adapter. With your other hand hold the needle shield and pull straight out. Do not rotate. 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.

Assembly instruction also applies to cannulas.



9. HEALTH CARE PROFESSIONAL INSTRUCTIONS

PRE-TREATMENT GUIDELINES

Prior to treatment, the patient should avoid taking aspirin, nonsteroidal anti-inflammatory medications, St. John's Wort, or high doses of Vitamin E supplements. These agents may increase bruising and bleeding at the injection site.

TREATMENT PROCEDURE

1. Use of this product should be used by only qualified health care professionals with expertise in dermal filler injections.
2. Educational resources are available through myGAINtraining.com, which provides training on the anatomy of the treatment area, effective patient assessment, and appropriate injection techniques. Health care professionals may contact Galderma for educational and training resources specific to this indication.
3. Prior to treatment, a medical history should be obtained to do a proper patient selection. The patient shall be informed about the indications, contraindications, warnings, precautions, treatment responses, potential adverse events and method of administration. Assess the patient's need for appropriate anesthetic treatment for managing comfort, i.e., topical anesthetic, local or nerve block. Patients also should be advised that supplemental "touch-up"

implantations may be required to achieve and maintain the desired level of correction.

4. Before and after treatment, health care professionals are encouraged to conduct vision assessments, including visual acuity, extraocular motility, and visual field testing.
5. Health care professionals are encouraged to be prepared with the following in the event of an intravascular injection:
    - ensuring supplies are immediately available, as recommended by the American Society for Dermatologic Surgery guidelines[1]
    - identifying a local ophthalmologist or ophthalmology subspecialist to be available in the event of an ophthalmic adverse event related to a dermal filler injection
    - conducting a basic neurologic examination in the event of an ophthalmic adverse event due to the association of such events with central nervous system deficits
6. The patient's face should be washed with soap and water and dried with a clean towel. Cleanse the area to be treated with a suitable antiseptic solution. Medical gloves are recommended during the injection procedure.
7. To avoid breakage of the needle/cannula, do not attempt to bend or manipulate it before or during treatment. If it gets bent, discard it and complete the procedure with a replacement needle/cannula.
8. Before injecting, remove air by pressing the rod carefully until a small droplet is visible at the tip of the needle/cannula.
9. When using a needle, withdraw the plunger rod slightly to aspirate and verify that the needle is not intravascular. Inject slowly while pulling the needle backwards.
10. When using a cannula, after preparation as described above, an entry point is made in the skin with an incision needle of appropriate size. Inject slowly.
11. *Restylane Eyelight* is administered using a thin gauge needle (29 G x ½") or a blunt cannula. (25-27G with cannula length of 1.5 or 2 inches). *Restylane Eyelight* should be placed in the supraperiosteal plane. If *Restylane Eyelight* is injected too superficially this may result in visible lumps and/or bluish discoloration.
12. Inject *Restylane Eyelight* applying even pressure on the plunger rod. Do not apply excessive pressure to the syringe at any time. If resistance is encountered, the needle/cannula should be partially withdrawn and repositioned, or fully withdrawn, checked for function and replaced if needed. It is important that the injection is stopped just before the needle/cannula is pulled out of the skin to prevent material from leaking out or ending up too superficially in the skin.
13. For each new treatment site, it is recommended to change needle/cannula to minimize the risk of infections and to avoid the use of blunt needles.
14. Defects should be fully corrected, but not overcorrected. In the event of overcorrection, consider removal of excessive product by aspiration, extrusion or enzymatic degradation (use of hyaluronidase has been described in scientific publications).
15. 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]
16. The correction site can be gently massaged to conform to the contour of the surrounding tissues.

17. If the treated area is swollen directly after the injection, an ice pack with adequate protective cloth can be applied on the site for a short period. Ice should be used with caution if the area is still numb from anesthetic to avoid thermal injury.
18. Patients may experience treatment site responses, which typically resolve within 1 week.
19. Typical usage for each treatment session is specific to the site as well as hollow severity. Based on U.S. clinical studies, the maximum recommended dose per treatment is 1 mL per side for the infraorbital hollow area per treatment. If a volume of more than 1 mL per side is needed to achieve optimal correction, a follow-up treatment session is recommended.

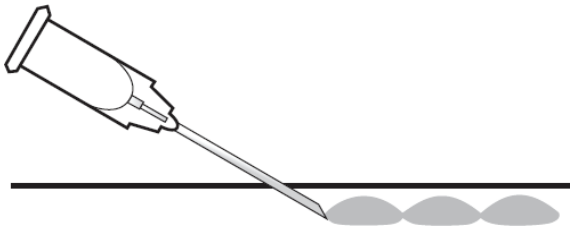
INJECTION TECHNIQUES

Restylane Eyelight can be injected by a number of different techniques; linear threading, serial puncture, fanning, micro bolus, or combination of these injection techniques. They depend on the treating physician's experience and preference, and patient characteristics.

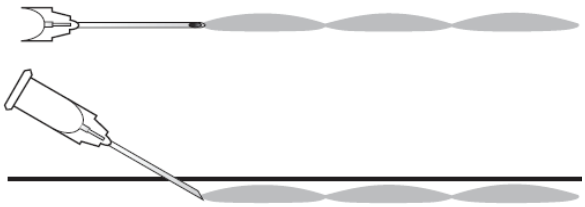
- **Serial puncture** (A) involves multiple, closely spaced injections. Although serial puncture allows precise placement of the filler, it produces multiple puncture wounds that may be undesirable to some patients.
- **Linear threading** (includes retrograde and antegrade) (B) is accomplished by fully inserting the needle into skin and injecting the filler along the track as a "thread." Although threading is most commonly practiced after the needle has been fully inserted and is being withdrawn, it can also be performed while advancing the needle ("push-ahead" technique).

Note! The correct injection technique is crucial for the final result of the treatment.

A. Serial Puncture



B. Linear Threading
(includes retrograde and antegrade)



If the infraorbital hollows need further treatment, the same procedure should be repeated until a satisfactory result is obtained. Additional treatment with *Restylane Eyelight* may be necessary to achieve the desired correction.

STERILE NEEDLE(S)

- Follow national, local or institutional guidelines for use and disposal of medical sharp devices. Obtain prompt medical attention if injury occurs.
- To help avoid needle breakage, do not attempt to straighten a bent needle. Discard it and complete the procedure with a replacement needle.
- Do not reshield used needles. Recapping by hand is a hazardous practice and should be avoided.
- Discard unshielded needles in approved sharps collectors.
- *Restylane Eyelight* is provided with a needle that does not contain engineered injury protection. Administration of *Restylane Eyelight* requires direct visualization and complete and gradual insertion of the needle making engineered protections infeasible. Care should be taken to avoid sharps exposure by proper environmental controls.

10.HOW SUPPLIED

Restylane Eyelight is supplied in a disposable glass syringe with a luer-lock fitting. *Restylane Eyelight* is co-packed with sterilized needle as indicated on the carton (29 G x ½").

A patient record label is a part of the syringe label. Remove it by pulling the flap marked with three small arrows. This label is to be attached to patient records to ensure traceability of the product.

The contents of the syringe are sterile.

The volume in each syringe and needle gauge is as stated on the syringe label and on the carton.

SHELF LIFE AND STORAGE

Restylane Eyelight must be used prior to the expiration date printed on the package.

Store at a temperature of up to 25° C (77° F). Do not freeze. Protect from sunlight.

Refrigeration is not required.

Do not resterilize *Restylane Eyelight* as this may damage or alter the product.

Do not use if the package is open or damaged or if the expiry date or lot number is missing or illegible. Immediately return the damaged product to Galderma Laboratories, L.P.

Rx only

U.S. PATENT 5,827,937; 8,455,459; 8,778,909; 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. 5.1.3	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Date of Manufacture	Indicates the date when the medical device was manu-factured
	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. 5.2.3	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Sterilized using ethylene oxide	Indicates a *medical device* that has been sterilized using ethylene oxid
	ISO 15223-1 Ref. No. 5.2.5	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Sterilized using steam or dry heat	Indicates a *medical device* that has been sterilized using steam or dry heat
	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. 5.2.6	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Do not resterilize	Indicates a medical device that is not to be resterilized
	ISO 15223-1 Ref. No. 5.2.8	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Do not use if package is dam-aged and consult instructions for use	Indicates that a medical device that should not be used if the package has been damaged or opened and that the user should consult the instructions for use for additional information

	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. 5.6.3	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Non-pyrogenic	Indicates a medical device that is non-pyrogenic
	ISO 15223-1 Ref. No. 5.7.7	Medical Devices – Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Medical Device	Indicates the item is a medical device

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 Directive 93/42/EEC, Article 17	CE marking	CE marking	Signifies European technical conformity. 0197is the notified body number for the needles

Manufactured for

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Phone: 1-855-425-8722

Manufactured by

Q-Med AB
Seminariegatan 21
SE-752 28 Uppsala
Sweden

Made in Sweden

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All other trademarks are the property of their respective owners.

Ordering Information

Galderma Laboratories, L.P. and its distributor, McKesson Specialty, are your only sources for FDA-approved *Restylane Eyelight*. Purchasing from any other agent is illegal.

To order call 1-855-425-8722

Revised: August, 2023

Part Number: 90-26597-02

References:

1. Jones, Derek; Fitzgerald, Rebecca; Cox, Sue Ellen; et al. Preventing and Treating Adverse Events of Injectable Fillers: Evidence-Based Recommendations from the American Society for Dermatologic Surgery Multidisciplinary Task Force, Dermatologic Surgery: February 2021 - Volume 47 - Issue 2 - p 214-226