RADIESSE®+ LIDOCAINE

MERZ AESTHETICS®

INSTRUCTIONS FOR USE

Only to be administered by appropriately trained healthcare professionals who are qualified or accredited in accordance with national law.

GENERAL INFORMATION

NAME OR TRADE NAME

RADIESSE® + Lidocaine Injectable Implant

DEVICE DESCRIPTION

RADIESSE® + Lidocaine Injectable Implant is a sterile, latex-free, non-pyrogenic, semi-solid, cohesive implant. The principal component is synthetic calcium hydroxylapatite (CaHA), suspended in a gel carrier that consists primarily of water (sterile water for injection USP), glycerin (USP/EuP), sodium carboxymethylcellulose (USP/EuP) and 0.3% lidocaine hydrochloride. The gel is dissipated *in vivo* and replaced with soft tissue growth, while the calcium hydroxylapatite remains at the site of injection. The lidocaine provides short-term local anesthetic effect. The result is long-term yet non-permanent restoration and augmentation.

RADIESSE® + Lidocaine Injectable Implant (1.5 mL) has a calcium hydroxylapatite particle size range of 25-45 microns and should be injected with a 27G needle with a standard Luer fitting.

RADIESSE® + Lidocaine Injectable Implant is steam-sterilized using a parametric release cycle. The steam sterilization process is considered validated to a Sterility Assurance Level (SAL) of at least 10^{-6}.

LIST OF INGREDIENTS

RADIESSE® + Lidocaine Injectable Implant is a resorbable implant used as a space filling material for soft tissue augmentation. The principal components consist of CaHA particles suspended in a sodium carboxymethylcellulose gel carrier with glycerin and 0.3% (w/v) lidocaine HCl, buffered with sodium phosphate salts in the following formulation:

- 30% 25-45µm CaHA particles (v/v)
- 70% Gel (v/v)

	Low (w/w)	High (w/w)	As Determined By
Glycerin	6.3%	6.5%	LOD* on Nonsterile Media (gravimetric analysis), and Sterile Media Rheology
Sterile Water for Injection	35.4%	36.2%	LOD on Nonsterile Media (gravimetric analysis)
Lidocaine HCl Monohydrate	0.22%	0.23%	HPLC
Phosphates	0.30%	0.31%	pH testing of the Buffer
NaCMC	1.06%	1.36%	LOD on Nonsterile Media (gravimetric analysis), and Sterile Media Rheology
CaHA	55.6%	56.5%	% solids after ashing (gravimetric analysis)

* Loss on drying

The particle size of CaHA is determined by a test procedure consisting of sieving and weighing at CaHA final release testing.

INTENDED USE / INDICATIONS

RADIESSE® + Lidocaine Injectable Implant is a device for non-medical purpose only.

INTENDED PURPOSE

RADIESSE® + Lidocaine Injectable Implant is intended for deep dermal and sub-dermal soft tissue augmentation.

INDICATIONS

RADIESSE® + Lidocaine Injectable Implant is indicated for

- the treatment of nasolabial folds
- the augmentation of cheeks
- the treatment of marionette lines
- the treatment of jawline
- the hand augmentation to correct volume loss in the dorsum of the hands

PERFORMANCE CHARACTERISTICS

Currently available scientific, pre-clinical, clinical, and post-marketing surveillance data of RADIESSE® + Lidocaine Injectable Implant support and demonstrate the performance and safety of the product. Highly viscoelastic CaHA is well suited for supraperiostal, sub-dermal, and deep dermal placement and can deliver considerable volumizing effect.

RADIESSE® + Lidocaine Injectable Implant has shown a lifetime of at least a year or more in most persons based on clinical data in most of the following indications:

Indication	Lifetime
Treatment of nasolabial folds	At least 6-7 months
Augmentation of cheeks	At least 12 months
Treatment of marionette lines	At least 6-7 months
Treatment of jawline	At least 12 months
Hand augmentation to correct volume loss in the dorsum of the hands	At least 12 months

No clinical benefit can be expected from the injection of RADIESSE® + Lidocaine Injectable Implant. The device is for aesthetic purpose only.

Link to Summary of Safety and Clinical Performance

The current Summary of Safety and Clinical Performance (SSCP) can be found in the European database on medical devices (Eudamed) under the URL: https://ec.europa.eu/tools/eudamed.

Please open the option “Search for devices” and enter the Basic UDI-DI number 018629500DF40001LW, in the respective search field. Until EUDAMED is fully functional the SSCP may be requested via Ax-Safety@merz.de.

TARGET TREATED POPULATION

RADIESSE® + Lidocaine Injectable Implant shall be used in persons who are 18 years or older regardless of gender of all ethnicities and all Fitzpatrick skin types with respect to indications and contraindications stated in the instructions for use.

INTENDED USER / USE ENVIRONMENT

RADIESSE® + Lidocaine Injectable Implant should be used by healthcare professionals (HCPs) who are qualified or accredited in accordance with national law, have appropriate training, experience, and who are knowledgeable about the anatomy at and around the site of injection. RADIESSE® + Lidocaine Injectable Implant must be injected under appropriate aseptic conditions into healthy, non-inflamed skin. Before injection, thoroughly disinfect the area to be treated.

CONTRAINDICATIONS

- RADIESSE® + Lidocaine Injectable Implant is contraindicated in the presence of acute and/or chronic inflammation or infection when these involve the area to be treated.
- RADIESSE® + Lidocaine Injectable Implant is contraindicated in persons with severe allergies manifested by a history of anaphylaxis, or history or presence of multiple severe allergies.
- RADIESSE® + Lidocaine Injectable Implant is not to be used in persons with known hypersensitivity to any of the components.
- RADIESSE® + Lidocaine Injectable Implant is not intended to be used in persons with known hypersensitivity to lidocaine or anesthetics of the amide type.
- RADIESSE® + Lidocaine Injectable Implant is contraindicated in persons prone to developing inflammatory skin conditions or those persons with a tendency for developing hypertrophic scars and keloids.
- **Do not implant in the epidermis or use as a skin replacement. Implantation into the epidermis or superficial dermis could lead to complications such as fistula formation, infections, extrusions, nodule formation and induration.**
- **RADIESSE® + Lidocaine Injectable Implant is not intended to be used for the correction of glabellar folds and nose area. A higher incidence of localized necrosis has been associated with glabellar and nose injections. Complications indicate that forceful injection into superficial dermal vessels of the glabellar or nose area could cause retrograde movement into the retinal arteries resulting in vascular occlusion.**
- RADIESSE® + Lidocaine Injectable Implant is contraindicated in the presence of foreign bodies such as liquid silicone or other particulate materials.
- RADIESSE® + Lidocaine Injectable Implant should not be used in areas where there is inadequate coverage of healthy, well vascularized tissue.
- RADIESSE® + Lidocaine Injectable Implant should not be used in persons with systemic disorders which cause poor wound healing or will lead to tissue deterioration over the implant.
- RADIESSE® + Lidocaine Injectable Implant is contraindicated in persons with bleeding disorders.
- RADIESSE® + Lidocaine Injectable Implant is contraindicated in persons under 18 years.
- RADIESSE® + Lidocaine Injectable Implant is contraindicated during pregnancy and in breastfeeding females.

WARNINGS

- **Introduction of RADIESSE® + Lidocaine Injectable Implant 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 RADIESSE® + Lidocaine Injectable Implant slowly and apply the least amount of pressure necessary. Rare but serious 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 person 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. Persons should receive prompt medical attention and possibly evaluation by an appropriate HCP specialist should an intravascular injection occur.**
- RADIESSE® + Lidocaine Injectable Implant should not be injected into organs or other structures that could be damaged by a space occupying implant.
- Do not overcorrect (overfill) the injection site as the soft tissue volume is expected to increase within several weeks as the treatment effect of RADIESSE® + Lidocaine Injectable Implant occurs.
- RADIESSE® + Lidocaine Injectable Implant should not be implanted in persons while the person is on an aspirin regimen or while taking other medications that could inhibit the healing process.
- RADIESSE® + Lidocaine Injectable Implant should not be implanted in infected or potentially infected tissue or in open cavities because infection or extrusion may occur. A significant infection may result in damage or loss to the skin overlying the implant. Hematomas or seromas may require surgical drainage.
- Use of RADIESSE® + Lidocaine Injectable Implant in persons with active skin inflammation or infection in or near the treatment area should be deferred until the inflammatory or infectious process has been controlled.
- In the event of a hypersensitivity or allergic reaction, a significant inflammation or infection may occur requiring the removal of the implant.

- Some injectable implants have been associated with hardening of the tissues at an injection site, migration of particles from an injection site to other parts of the body and/or allergic or autoimmune reactions.
- As with any implant material, possible adverse reactions which may occur include, but are not limited to, the following: inflammation, infection, fistula formation, extrusion, hematoma, seroma, induration formation, inadequate healing, skin discoloration and inadequate or excessive augmentation.

SPECIFIC WARNINGS RELATED TO INJECTIONS INTO HANDS

- Special care should be taken to avoid injection into veins or tendons in the hand. Injection into tendons may weaken tendons and cause tendon rupture. Injection into veins may cause embolization or thrombosis.
- Injection into the hand may cause side effects/adverse events that last for more than 14 days. Refer to Section "Side Effects and Adverse Events" for details.
- Injection in the dorsum of the hand may result in temporary difficulty performing activities (48% of study persons reported this adverse event). Fitzpatrick Skin Types IV-VI may have an increased risk in difficulty performing activities (68% of Fitzpatrick Skin Types IV-VI reported this event).
- RADIESSE® + Lidocaine Injectable Implant may cause nodules, bumps, or lumps in the dorsum of the hand (12% reported this event) and can last up to one year.
- Injection into persons with very severe loss of fatty tissue with marked visibility of veins and tendons has not been studied. The safety and effectiveness in this population has not been established.
- Possible acute carpal tunnel syndrome or exacerbation of pre-existing compressive median neuropathy in the wrist may occur. Volumes over 3 mL of RADIESSE® + Lidocaine Injectable Implant per hand in a treatment session have not been studied. Increased bruising is associated with higher volume injection. Re-treatment with RADIESSE® + Lidocaine Injectable Implant of volumes greater than approximately 1.6 mL per hand in a treatment session can result in increased side effects/adverse events (redness, pain, swelling, and difficulty performing activities).

PRECAUTIONS

- In order to minimize the risks of potential complications, RADIESSE® + Lidocaine Injectable Implant should only be used by HCPs 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, HCPs should fully familiarize themselves with the product, the product educational materials and the entire package insert.
- The safety and effectiveness of a cannula used for deep injection (subdermal and/or supraperiosteal) for soft tissue augmentation to improve the contour of the jawline has been clinically evaluated in a blunt-tip cannula that was 27G and 40mm in length and a 25G Pre-Hole Needle (clinical US study with RADIESSE® + Lidocaine Injectable Implant).
- HCPs 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.
- As with all transcutaneous procedures, RADIESSE® + Lidocaine Injectable Implant injection carries a risk of infection. Infection may necessitate attempted surgical removal of RADIESSE® + Lidocaine Injectable Implant. Standard precautions associated with injectable materials should be followed.
- Persons who are using medications that can prolong bleeding, such as aspirin or warfarin, may, as with any injection, experience increased bruising or bleeding at the injection site.
- The calcium hydroxylapatite (CaHA) particles of RADIESSE® + Lidocaine Injectable Implant are radiopaque and are clearly visible on CT and MRI scans, or mammograms and may be visible in standard, plain radiography. Persons need to be informed of the radiopaque nature of RADIESSE® + Lidocaine Injectable Implant, so that they can inform their primary care HCPs as well as radiologists. In a radiographic study of 58 persons, there was no indication of RADIESSE® Injectable Implant (without lidocaine) potentially masking abnormal tissues or being interpreted as tumors in CT scans.
- RADIESSE® + Lidocaine Injectable Implant requires soft tissue for easy percutaneous injection. Scar tissue and significantly compromised tissue may not accept the implant appropriately.
- Infection requiring treatment may occur at the injection site. If such infection cannot be corrected, it may become necessary to remove the implant.
- Injection related reactions, including bruising, erythema, swelling, pain, itching, discoloration or tenderness, may occur at the site of the injection. These usually resolve spontaneously within one to two days after the injection.
- Nodule(s) may form requiring treatment or removal.

- Contour irregularities may occur which may require a surgical procedure to correct.
- Do not over-inject the area to be treated. In extreme cases site rupture could occur. RADIESSE® + Lidocaine Injectable Implant can be easily added in subsequent injections but cannot be easily removed.
- The RADIESSE® + Lidocaine Injectable Implant injection procedure, like similar injection procedures, has small but inherent risks of infection and/or bleeding. The usual precautions associated with percutaneous injection procedures should be followed to prevent infection.
- **Do not re-sterilize.** RADIESSE® + Lidocaine Injectable Implant is supplied sterile and non-pyrogenic in a sealed foil pouch and is intended for single person, single treatment use only.
- The foil pouch should be carefully examined to verify that neither the pouch nor the syringe has been damaged during shipment. Do not use if the foil pouch is compromised or the syringe has been damaged. Do not use if the syringe end cap or syringe plunger is not in place. There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is not an indication of a defective product.
- 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 re-shield used needles. Recapping by hand is a hazardous practice and should be avoided.
- The safety of RADIESSE® + Lidocaine Injectable Implant with concomitant dermal therapies such as epilation, UV irradiation, radiofrequency, ablative or non-ablative laser, mechanical or chemical peeling procedures has not been evaluated in controlled clinical trials.
- No studies of interactions of RADIESSE® + Lidocaine Injectable Implant with drugs or other substances or implants have been conducted.
- Limited clinical data is available on the combination of RADIESSE® + Lidocaine Injectable Implant with BELOTERO® products and/or botulinum toxin. As a precaution, products should be injected in different facial areas. HCPs should be experienced, and persons appropriately selected as not only benefits, but also side effects/adverse events can be cumulative, and causality of side effects/adverse events could become difficult to determine. Instructions for use, depth of injection and appropriate recommendation of each product should be followed.
- Universal precautions must be observed when there is a potential for contact with a person´s body fluids. The injection session must be conducted with aseptic technique.
- If laser treatment, chemical peeling, or any other procedure based on active dermal response is considered after treatment with RADIESSE® + Lidocaine Injectable Implant, there is a possible risk of eliciting an inflammatory reaction at the implant site. This also applies if RADIESSE® + Lidocaine Injectable Implant is administered before the skin has healed completely after such a procedure.
- Injection of RADIESSE® + Lidocaine Injectable Implant into persons with a history of previous herpetic eruption may be associated with reactivation of the herpes virus.
- Care should be taken to determine the risk versus the benefit for persons with congenital methemoglobinemia with glucose-6-phosphate dehydrogenase deficiencies, and with persons who are receiving concomitant treatment with methemoglobin-inducing agents.
- For normal healthy adults, it is recommended that the maximum total dose of lidocaine HCl (without epinephrine) does not exceed 300 mg (or 4.5 mg/kg) per session. Overdosage of lidocaine HCl usually results in signs of the central nervous system or cardiovascular toxicity.

SPECIFIC PRECAUTIONS RELATED TO INJECTIONS INTO HANDS

- Use of RADIESSE® + Lidocaine Injectable Implant in the dorsum of the hand in persons with diseases, injuries or disabilities of the hand has not been studied. Care should be taken when treating persons with autoimmune disease affecting the hand, hand implants, Dupuytren's contracture, history of hand tumor, vascular malformations, Raynaud's disease, and persons at risk for tendon rupture.
- Use of RADIESSE® + Lidocaine Injectable Implant in the dorsum of the hand may result in severe swelling of the dorsum of the hand (a maximum duration of 48 days was reported based on clinical data). Persons should be instructed to remove jewelry (rings) before treatment and until swelling has resolved to avoid compromise of finger circulation.
- The effects of RADIESSE® + Lidocaine Injectable Implant injection on hand function are uncertain.
- Safety of RADIESSE® + Lidocaine Injectable Implant injected into the dorsum of the hand in persons under 26 years old and over 79 years old has not been studied.
- Safety of RADIESSE® + Lidocaine Injectable Implant beyond two years in the hand has not been investigated in clinical trials.

SIDE EFFECTS AND ADVERSE EVENTS

Persons must be informed that as with any implant material possible adverse reactions may occur. The Patient Information Leaflet annexed to this document can be used as support.

The following side effects/adverse events have been identified during post-approval use of RADIESSE® Injectable Implant (without lidocaine). Because they are reported voluntarily from a population (including from literature) of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to RADIESSE® Injectable Implant (without lidocaine) These events have been chosen for inclusion due to the combination of their seriousness, frequency of reporting, or potential causal connection to RADIESSE® Injectable Implant (without lidocaine):

infection (incl. biofilm formation), cellulitis, impetigo, loss of effect, product displacement/migration, allergic reaction, anaphylaxis, hives, rash, pruritus, urticaria, angioedema, inflammation, necrosis, granuloma, nodules, induration, erythema, skin discoloration (including hypo- and hyperpigmentation), irritation, dissatisfaction, pustule/pimple, skin pallor, hair loss, paresthesia, ptosis, pain (incl. mastication pain), headache, swelling/edema, tightness, asymmetry, abscess, herpetic infection including herpes simplex and herpes zoster, hematoma, injection site haemorrhage, blanching, blistering, scab, abrasion dry skin, dizziness, festoons, flu-like symptoms, fever, Guillain-Barre syndrome, tachypnea, ischemic reaction, lymphoid hyperplasia, lymphatic obstruction, nausea, pericarditis, scarring, sensitivity to cold, vascular occlusion/obstruction, vascular compromise, ocular ischemia, diplopia, visual impairment/blindness, facial muscle paralysis, Bell's palsy, syncope, difficulty performing activities (e.g., difficulty drinking, chewing or speaking), erosion, injection site cyst, injection site warmth, aggravation of preexisting conditions, superficial vein prominence, vasculitis, nerve injury, nerve compression, xanthelasma, anxiety, laceration, purpura, calcinosis, capillary fragility, contact dermatitis, dysphagia, dyspnoea, ear pain, eye pain, eyelid function disorder, hypoesthesia, nerve damage, vesicles, lip disorder, mouth ulceration, muscle twitching, nasal congestion, nasopharyngitis, neoplasm, rhinorrhea, exfoliation, fissures, wounds, sneezing, toothache, vomiting.

Numbness (hypoesthesia), (systemic) allergic reaction/ anaphylaxis, CNS reactions (e.g., dizziness, blurred vision), erythema (redness) and (cardiac) arrhythmia may also be associated with lidocaine hydrochloride.

Persons with specific ethnic characteristics, e.g., Asian population, should be informed of a higher risk of tissue reactions, e.g., inflammatory reactions, pigmentary disorders, post-inflammatory hyperpigmentation (PIH), scarring, and keloid formation upon cutaneous injury.

The following interventions have been reported: antibiotics, anti-inflammatories, corticosteroids, antihistamines, analgesics, massage, warm compress, excision, drainage, and surgery. This information does not constitute and is not intended to be medical advice, a recommendation on how to treat a side effect/adverse event or an exhaustive list of possible interventions. HCPs should evaluate each case on an individual basis, and independently determine, based on their professional experience, what treatment(s) are appropriate, if any, for their patients.

TREATMENT OF MOST COMMON SIDE-EFFECTS

Persons may experience side effects following injection of dermal fillers that typically resolve within a few days. These injection site reactions are generally of mild or moderate intensity.

Side effects treatments after RADIESSE® + Lidocaine Injectable Implant injections are dependent on medical need and as defined by the treating HCP and the region-specific standard of care. The HCP should refer to their standard medical care procedures for advice on treatment of side effects.

The most common side effects of RADIESSE® + Lidocaine Injectable Implant and possible treatment examples are listed below. This information is not intended to be read as medical advice.

Side effect	Treatment
Injection Site Swelling / Edema	Swelling and edema may be treated by applying a manual or cold compress, oral antihistamines, or oral corticosteroids.
Injection Site Erythema / Redness	Vitamin K cream can be used, if persistent, isotretinoin or steroids can be used.
Injection Site Pain	Pain may be treated with pain reducing agents, like paracetamol.
Ecchymosis	Ecchymosis may be treated with cold compresses, arnica, aloe vera, or vitamin K creams.
Injection Site Bruising	Bruising may be treated with cold compresses after the procedure, arnica, aloe vera, or vitamin K creams.

RESIDUAL RISKS

The residual risks are covered under Section “Side Effects and Adverse Events”. As evident from the RADIESSE® + Lidocaine Injectable Implant Risk Management File, after implementation of measures, no unacceptable risks have emerged and the overall residual risk of RADIESSE® + Lidocaine Injectable Implant is low. The overall residual risk is considered acceptable, and the benefits outweigh the overall risks. The product safety, including the overall residual risk, is acceptable for the intended use.

REPORTING OBLIGATION

Any incident that directly or indirectly led, might have led or might lead to any of the following: the death of a treated person or user, the temporary or permanent serious deterioration of a treated person's or user's state of health, or a serious public health threat; and that has occurred in relation to the device, should be reported to the manufacturer and the competent authority of the Member State in which the user and/or client is established.

In case of serious incident, please contact directly: Ax-Safety@Merz.de

DIRECTIONS FOR USE

DEVICE PRESENTATION

RADIESSE® + Lidocaine Injectable Implant is provided sterile and non-pyrogenic in a syringe packaged in a foil pouch and boxed for convenient storage.

Each syringe unit with needle convenience pack consists of one pre-filled syringe containing 1.5 mL of RADIESSE® + Lidocaine Injectable Implant and two Terumo K-Pack II 27G thin wall injection needle(s). The degree of accuracy of syringe graduations is ±0.025 mL.

The needles by Terumo provided within the carton package of RADIESSE® + Lidocaine Injectable Implant are sterilized by ethylene oxide. Needles are intended for single-use as well.

SINGLE USE

Do not use if packaging and/or syringe are damaged or if the syringe end cap or syringe plunger is not intact.

The contents of the syringe are intended for single person, single treatment use only and cannot be re-sterilized. Re-use may compromise the functional properties of the device and/or lead to device failure. Re-use may also create a risk of contamination of the device and/or cause person infection or cross-infection including but not limited to transmission of infectious disease(s) and blood transfer between persons. All which, in turn, may lead to person injury, illness or death.

PREPARATIONS, POSOLOGY AND ADMINISTRATION METHOD

Preparation of RADIESSE® + Lidocaine Injectable Implant for Face and Hand Treatment

The following is required for the percutaneous injection procedure:

- One RADIESSE® + Lidocaine Injectable Implant syringe 1.5 mL.
- Appropriate size needle(s) with Luer lock fittings. The preferred size is a 27G or larger needle with a standard Luer fitting. Use of needles smaller in diameter than 27G may increase the incidence of needle occlusion.
- Prepare person for percutaneous injection using standard methods. The treatment injection site should be marked by a surgical marker and prepared with a suitable antiseptic. Local or topical anesthesia at the injection site or sedation should be used at the discretion of the HCP. After anesthetizing the site, apply ice to the area to decrease local swelling/distention.
- Prepare the syringes and the injection needle(s) before the percutaneous injection. A new injection needle may be used for each syringe, or the same injection needle may be connected to each new syringe for same person treatment.
- Remove foil pouch from the carton. The pouch can be opened, and the syringe dropped onto the sterile field when required. There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is not an indication of a defective product.
- Peel or twist apart the needle packaging to expose the hub. For use of needles other than the needle(s) provided with this package, follow the directions provided with the needle(s).
- Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. The syringe can then be twisted onto the Luer lock fitting of the needle taking care not to contaminate the needle. **The needle must be tightened securely to the syringe and primed with RADIESSE® + Lidocaine Injectable Implant.** If excess implant is on the surface of the Luer lock fittings, it will need to be wiped clean with sterile gauze. Slowly

push the syringe plunger until the implant material extrudes from the end of the needle. If leakage is noted at the Luer fitting, it may be necessary to tighten the needle or to remove the needle and clean the surfaces of the Luer fitting or, in extreme cases, replace both the syringe and the needle.

- Locate the initial site for the implant. Scar tissue and cartilage may be difficult or impossible to inject. Avoid passing through these tissue types when advancing the injection needle.

Posology and Administration Method of RADIESSE® + Lidocaine Injectable Implant for Face and Hand treatment

General

NOTE: Do not inject into a blood vessel.

- The depth of the injection and the amount injected will vary depending on the site and extent of the restoration or augmentation. RADIESSE® + Lidocaine Injectable Implant should be injected sufficiently deep to prevent nodular formation at the surface of the skin or ischemia of the overlying tissue.
- **DO NOT OVERCORRECT THE INJECTION SITE.** Use a 1:1 correction factor. Mold or massage the injected implant periodically during the injection process to maintain a smooth contour of the implant.
- A maximum of 10 mL RADIESSE® + Lidocaine Injectable Implant is recommended as yearly dose for facial indications and hands. The dose may be adapted or increased according to the person's indication(s), tissue, age, injection depth and technique for implantation.
- If significant resistance is encountered when pushing the plunger, the injection needle may be moved slightly to allow easier placement of the material. If significant resistance is still encountered, it may be necessary to pull the needle entirely out of the injection site and try again in a new position. If significant resistance continues to persist, it may be necessary to try a different injection needle. If this is not successful, replace the syringe and injection needle.
- Advance the needle bevel down at approximately a 30° angle to the skin into the sub-dermis to the starting location. [Refer to additional instructions, below, for treatment of facial areas.] Carefully push the plunger of the syringe to start the injection and slowly inject the implant material while withdrawing the needle, placing a line of material in the desired location. Continue placing additional lines of material until the desired level of augmentation is achieved. The thread of implant material should be completely surrounded by soft tissue without leaving globular deposits.
- The injected area may be massaged as needed to achieve even distribution of the implant.

Injection Procedure for Facial Indications

- Insert needle with bevel down at approximately a 30° angle to the skin. The needle should slide into the deep dermis to the point where you wish to begin the injection. This should be easily palpable with the non-dominant hand.
- Apply slow continuous even pressure to the syringe plunger to inject the implant as you withdraw the needle, leaving behind a single thin thread or strand of implant material. The thread of implant material should be completely surrounded by soft tissue without leaving globular deposits.
- Individual threads of implant material should be placed parallel and adjacent to each other and layered when deeper folds are corrected. As an option, the threads can be cross layered in a deeper plane for structural support.
- After injection, use the index finger and thumb to smooth the areas and better distribute the implant in case of any slight nodular deposition of material.
- Injection treatments in the same anatomical location must be spaced by at least 4 weeks.

Injection Procedure for Hand Treatment

- Prepare person for percutaneous injection using standard methods. Have the person wash both hands with soapy water producing friction for 5-10 minutes and then prepare hands with suitable antiseptic. The treatment injection site may be marked for planned injection sites. Jewelry should be removed prior to injection and until post-procedure swelling has resolved.
- Using the syringe of RADIESSE® + Lidocaine Injectable Implant fitted with the injection needle, slowly push the syringe plunger until RADIESSE® + Lidocaine Injectable Implant extrudes from the end of the needle. Perform aspiration before bolus injection to avoid intravascular injection. If leakage is noted at the Luer fitting, wipe it clean with sterile gauze. It may be necessary to tighten the needle, remove the needle and clean the surfaces

of the Luer fitting or, in extreme cases, replace both the syringe and the needle. A new injection needle may be used for each syringe, or the same injection needle may be connected to each new syringe for same person treatment.

- Locate the initial site for injection. Persons are to receive injections in the dorsum of the hands between the 1st and 5th metacarpals. Injection should initially occur between the 2nd and 4th metacarpals, taking care not to inject close to the metacarpophalangeal joints. If necessary to achieve optimal correction, injection is also allowed between the 1st and 2nd and 4th and 5th metacarpals.
- Skin tenting should be performed to separate the skin from vascular and tendinous structures by using the thumb and forefinger of the non-injecting hand to lift skin over the dorsal aspect of the hand being treated.
- Advance the needle between the subcutaneous layer and superficial fascia with the syringe parallel to the dorsum of the hand. Carefully push the plunger of the RADIESSE® + Lidocaine Injectable Implant syringe to start the injection and inject the RADIESSE® + Lidocaine Injectable Implant material in small boluses, 0.2 – 0.5 mL/bolus. No more than 0.5 mL should be injected per bolus. The number of boluses will vary depending on the extent of treatment desired. No more than 3 mL of RADIESSE® + Lidocaine Injectable Implant will be injected per hand.
- If significant resistance is encountered when pushing the plunger, the injection needle may be moved slightly to allow easier placement of the material, or it may be necessary to change the injection needle.
- Immediately after injection, cover the injection site with a sterile 4x4 gauze and have person sit on this hand while the contralateral hand is being injected. This warms the RADIESSE® + Lidocaine Injectable Implant making it more malleable for later massaging.
- Treat the contralateral hand in the same manner as described in the steps above.
- Immediately after injection of the contralateral hand, cover the injection site with a sterile 4x4 gauze and have the person sit on this hand.
- While the contralateral hand is warming, remove the gauze from the hand that was initially injected, have the person make a fist with this hand, and gently massage the dorsum of the hand until RADIESSE® + Lidocaine Injectable Implant has been evenly spread across the dorsum remaining distal to the wrist crease and proximal to the metacarpophalangeal joints.
- Use a 1:1 correction factor. No overcorrection is needed.
- Injection treatments in the same anatomical location of hands must be spaced by at least 6 months.

POST-ADMINISTRATION MONITORING

It is recommended, that the treated person should stay for a post-administration monitoring time in the premises of the HCP, in order to identify any potential undesirable side-effects.

Persons should be instructed to report any side effects which last for more than one week and any adverse event as soon as it occurs to his/ her HCP, especially if the person has changes in his/ her vision, signs of a stroke (including sudden difficulty speaking, numbness or weakness in his/ her 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. The HCP may then refer the person to the appropriate treatment.

COUNSELING INFORMATION

The person should be instructed in appropriate post-procedural care, which may include the following, to promote normal healing and avoid complications.

- Apply cool compresses to areas of injection for approximately 24 hours.
- Avoid the sun, tanning (ultraviolet) lights, sauna, and intense treatments in the area, which was treated with RADIESSE® + Lidocaine Injectable Implant, post procedurally.
- Massage the area gently if palpable nodules become present.
- Advise facial rest for one week by encouraging persons to limit talking, smiling and laughing.
- 24 hours after injection avoid any skin care or make-up products, manipulation of the treated area, strenuous exercise, exposure to extreme cold or heat.
- 24 hours prior and after injection avoid excessive consumption of alcoholic beverages.

Inform the person that postoperative swelling and numbness are common. Swelling will usually resolve within 7 to 10 days but may persist for several weeks. Numbness should resolve within 4 to 6 weeks.

The Patient Information Leaflet and the Implant Card filled with treatment information must be provided to the person, before the person is treated with RADIESSE® + Lidocaine Injectable Implant.

Healthcare professionals should instruct persons to present their implant card to the radiologist prior to undergoing an X-ray, CT, or MRI scan.

STORAGE AND HANDLING INFORMATION

Packaged RADIESSE® + Lidocaine Injectable Implant should be stored at a controlled room temperature between 15°C and 25°C (59°F and 77°F). Keep dry and away from sunlight. Do not use if the expiration date has been exceeded. The expiration date is printed on the product labels.

DISPOSAL

Used and partially used syringes and injection needles could be biohazardous and should be handled and disposed of in accordance with facility medical practices and local, state or federal regulations.

ADDITIONAL DEVICE SPECIFIC INFORMATION

Explanation of Symbols used on Packaging


Manufacturer



Authorized Representative in the European Community


Importer



Catalogue number



Batch code



Unique device identifier


Contains a medicinal substance: Lidocaine Hydrochloride


Use-by date



Do not resterilize


Do not use if package is damaged


Temperature limit


Date of manufacture

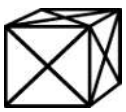

Keep away from sunlight


Keep dry


Single use. Do not re-use



Consult instruction for use (electronic instruction for use)


Contents



Sterilized using steam or dry heat



Sterilized using ethylene oxide



Not made with Natural Rubber Latex


Single sterile barrier system with protective packaging inside

Needle

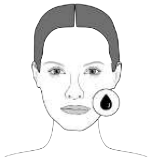
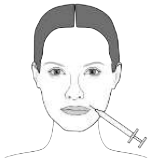
Website for more information

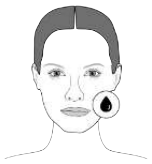
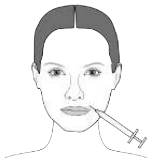
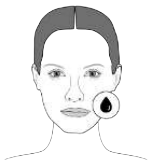
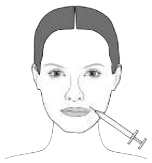
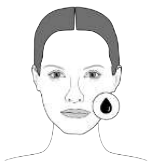
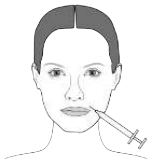
CE mark in accordance with Regulation (EU) 2017/745. This mark is followed by the notified body number.

Peel-off symbol

Explanation of Symbols used on Implant Card

Information to be Added by the Health Care Professional

No.	Content	Details
1	Patient name or patient ID	 *First name, last name*
2	Date of implantation	 *YYYY-MM-DD*
3, 4	Name and address of HCP	 *HCP name and address*
5	Injection site(s) *Indicate sites*	 *Naso-labial Folds (NLF)*
6	Total volume injected *e.g. 1mL*	 *x mL*
7	Number of injections *e.g. 5 injection points*	
5	Injection site(s) *Indicate sites*	 *Marionette Lines (ML)*

No.	Content	Details
6	Total volume injected *e.g. 1mL*	 *x mL*
7	Number of injections *e.g. 5 injection points*	
5	Injection site(s) *Indicate sites*	 *Cheeks*
6	Total volume injected *e.g. 1mL*	 *x mL*
7	Number of injections *e.g. 5 injection points*	
5	Injection site(s) *Indicate sites*	 *Jawline*
6	Total volume injected *e.g. 1mL*	 *x mL*
7	Number of injections *e.g. 5 injection points*	

No.	Content	Details
5	Injection site(s) *Indicate sites*	 *right hand*
6	Total volume injected *e.g. 1mL*	 *x mL*
7	Number of injections *e.g. 5 injection points*	
5	Injection site(s) *Indicate sites*	 *left hand*
6	Total volume injected *e.g. 1mL*	 *x mL*
7	Number of injections *e.g. 5 injection points*	
8	Place one of the two peel-off stickers from pouch packaging here.	

Pre-printed Information

Content	Details	
Information website for patients		*www.patientinfo.merzaesthetics.com*
Name and address of the manufacturer		MERZ NORTH AMERICA, Inc. 4133 Courtney St. Suite 10 Franksville, WI 53126 USA Telephone: +1 844.469.6379 E-mail: *mymerzsolutions@merz.com*
Name and address of the EU Representative		Merz Aesthetics GmbH Eckenheimer Landstraße 100 60318 Frankfurt am Main Germany Telephone: + 49 (0) 69 1503 - 0 E-mail: *service-aesthetics@merz.de*
Device type		Injectable Implant

Electronical IFU (eIFU) Information

A printable PDF version of the IFU in your local language can be found on the following website: www.ifu.merzaesthetics.com. For the most recent version of the IFU please always refer to the website. An update of the IFU may have happened due to safety reasons.

Training

Training on RADIESSE® + Lidocaine Injectable Implant is available upon request to your Merz Aesthetics contact or authorized distributor.

Used Harmonised Standards and Common Specifications

All harmonised standards and common specifications applied are listed in detail within the Summary of Safety and Clinical Performance (SSCP). The SSCP is available in the European database on medical devices (Eudamed), where it is linked to the UDI-DI as presented on the labelling. Eudamed may be accessed using following URL: https://ec.europa.eu/tools/eudamed. Until EUDAMED is fully functional the SSCP may be requested via Ax-Safety@merz.de.

In brief, the Instructions for Use were primarily created according to the requirements of

- Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices
- The Commission Implementing Regulation (EU) 2022/2346 of 1 December 2022 (Common Specifications)
- ISO 20417
- ISO 15223



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