

INSTRUCTIONS FOR USE

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

1 GENERAL INFORMATION

1.1 NAME OR TRADE NAME

RADIESSE[®] Injectable Implant

1.2 DEVICE DESCRIPTION

RADIESSE[®] 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) and sodium carboxymethylcellulose (USP/EuP). The gel is dissipated *in vivo* and replaced with soft tissue growth, while the calcium hydroxylapatite remains at the site of injection. The result is long-term yet non-permanent restoration and augmentation.

RADIESSE[®] 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[®] 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.

1.3 LIST OF INGREDIENTS

RADIESSE[®] 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 an aqueous formulation of USP/EuP grade pharmaceutical excipients in the following formulation:

Ingredient

- 56% 25-45µm CaHA particles (w/w)
- 44% Gel (w/w)
 - 36.0% sterile water for Injection
 - 6.6% glycerin
 - 1.4% sodium carboxymethylcellulose (NaCMC)

As determined by

% solids after ashing
(gravimetric analysis)

LOD* (gravimetric analysis)

Refractive index

Viscosity

* Loss on drying

2 INTENDED USE / INDICATIONS

RADIESSE[®] Injectable Implant is a device for non-medical purpose only.

2.1 INTENDED PURPOSE

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

2.2 INDICATIONS

RADIESSE[®] Injectable Implant is indicated for

- the treatment of nasolabial folds
- the augmentation of cheeks
- the hand augmentation to correct volume loss in the dorsum of the hands
- the restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus.

- RADIESSE® Injectable Implant diluted 1:2 with 0.9% sterile saline for injections is intended for the treatment of moderate and severe décolleté wrinkles.

2.3 PERFORMANCE CHARACTERISTICS

Currently available scientific, pre-clinical, clinical, and post-marketing surveillance data of RADIESSE® Injectable Implant in a non-diluted form (RADIESSE® Injectable Implant) support and demonstrate the performance and safety of the product. Highly viscoelastic CaHA is well suited for subdermal, and deep dermal placement and can deliver considerable volumizing effect. Dilution makes the product less viscous and therefore more suitable for rejuvenation treatments of larger areas, such as décolleté.

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

Indication	Lifetime
Treatment of nasolabial folds	At least 12 months
Augmentation of cheeks	At least 12 months
Hand augmentation to correct volume loss in the dorsum of the hands	At least 12 months
Restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus	At least 12 months
Treatment of moderate and severe décolleté wrinkles	At least 12 months

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

2.4 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 018629500DF30001LK, in the respective search field. Until EUDAMED is fully functional the SSCP may be requested via Ax-Safety@merz.de.

3 TARGET TREATED POPULATION

RADIESSE® 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.

Clinical data for Fitzpatrick skin types V and VI are limited for hand augmentation.

For décolleté wrinkles treatment, RADIESSE® Injectable Implant diluted 1:2 with 0.9% sterile saline for injections is intended to be used for adult female persons who do not meet contraindications. Differences in clinical use within different Fitzpatrick skin types were not investigated in detail for décolleté wrinkles treatment.

4 INTENDED USER / USE ENVIRONMENT

RADIESSE® 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® Injectable Implant must be injected under appropriate aseptic conditions into healthy, non-inflamed skin. Before injection, thoroughly disinfect the area to be treated.

5 CONTRAINDICATIONS

- RADIESSE® Injectable Implant is contraindicated in the presence of acute and/or chronic inflammation or infection when these involve the area to be treated.
- RADIESSE® Injectable Implant is contraindicated in persons with severe allergies manifested by a history of anaphylaxis, or history or presence of multiple severe allergies.
- RADIESSE® Injectable Implant is not to be used in persons with known hypersensitivity to any of the components.

- Radiesse® 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® 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® Injectable Implant is contraindicated in the presence of foreign bodies such as liquid silicone or other particulate materials.
- Radiesse® Injectable Implant should not be used in areas where there is inadequate coverage of healthy, well vascularized tissue.
- Radiesse® 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® Injectable Implant is contraindicated in persons with bleeding disorders.
- Radiesse® Injectable Implant is contraindicated in persons under 18 years.
- Radiesse® Injectable Implant is contraindicated during pregnancy and in breastfeeding females.

6 WARNINGS

- **Introduction of Radiesse® Injectable Implant into the vasculature may lead to embolization or thrombosis, occlusion of the vessels, ischemia, or infarction. Take extra care when injecting, soft tissue fillers, for example inject Radiesse® 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® 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® Injectable Implant occurs.
- Radiesse® 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® 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® 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.

6.1 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® 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® Injectable Implant per hand in a treatment session have not been studied. Increased bruising is associated with higher volume injection. Re-treatment with RADIESSE® 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).

6.2 SPECIFIC WARNINGS RELATED TO INJECTIONS IN THE DECOLLETÉ AREA

- RADIESSE® Injectable Implant diluted 1:2 with 0.9% sterile saline should be injected in the subdermal plane sufficiently deep to prevent nodular formation at the surface of the skin or ischemia of the overlying tissue or discoloration of the skin.

7 PRECAUTIONS

- In order to minimize the risks of potential complications, RADIESSE® 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.
- 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® Injectable Implant injection carries a risk of infection. Infection may necessitate attempted surgical removal of RADIESSE® 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® 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® 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 potentially masking abnormal tissues or being interpreted as tumors in CT scans.
- RADIESSE® 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® Injectable Implant can be easily added in subsequent injections but cannot be easily removed.
- The RADIESSE® Injectable Implant injection procedure, like similar injection procedures, has small but inherent risks of infection and/or bleeding. The person may experience slight discomfort during and following the procedure. Therefore, anesthetic techniques common with this treatment should be considered. The usual precautions associated with percutaneous injection procedures should be followed to prevent infection.
- **Do not re-sterilize.** RADIESSE® 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® 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® Injectable Implant with drugs or other substances or implants have been conducted.
- Limited clinical data is available on the combination of RADIESSE® 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® Injectable Implant, there is a possible risk of eliciting an inflammatory reaction at the implant site. This also applies if RADIESSE® Injectable Implant is administered before the skin has healed completely after such a procedure.
- Injection of RADIESSE® Injectable Implant into persons with a history of previous herpetic eruption may be associated with reactivation of the herpes virus.

7.1 SPECIFIC PRECAUTIONS RELATED TO INJECTIONS INTO HANDS

- Use of RADIESSE® 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® Injectable Implant in the dorsum of the hand may result in significant swelling of the dorsum of the hand. 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® Injectable Implant injection on hand function are uncertain.
- Safety of RADIESSE® 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® Injectable Implant beyond one year in the hand has not been investigated in clinical trials.

8 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 the use of RADIESSE® Injectable Implant. 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. 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:

infection (incl. biofilm formation), cellulitis, impetigo, loss of effect, product displacement/migration, allergic reaction, anaphylaxis (incl. dyspnoea), hives, rash, pruritus, urticaria, angioedema, inflammation, necrosis, granuloma, nodules, induration, erythema, skin discoloration (including hypo- and hyperpigmentation), dissatisfaction, papule/pustule, skin pallor, hair loss, paresthesia, hypoesthesia, ptosis, pain (incl. mastication pain, arthralgia, myalgia), headache, swelling/edema, tightness, asymmetry, abscess, herpetic infection including herpes simplex and herpes zoster, hematoma, petechiae/purpura, injection site hemorrhage, blanching, blistering, scab, abrasion, dizziness, festoons, flu-like symptoms, fever, malaise, asthenia, Guillain-Barre syndrome, tachypnea, ischemic reaction, lymphoid hyperplasia, lymphatic obstruction, nausea, vomiting, pericarditis, scarring, sensitivity to cold, vascular occlusion/obstruction, vascular compromise, vascular injury, ocular ischemia,

diplopia, visual impairment/blindness, optic nerve injury, papilloedema, retinal disorder, facial muscle paralysis, Bell's palsy, syncope, chewing problems, injection site erosion, injection site cyst, injection site warmth, aggravation of preexisting conditions, superficial vein prominence, vasculitis, nerve injury, nerve compression, xanthelasma.

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.

9 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® 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® 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.

10 RESIDUAL RISKS

The residual risks are covered under Section "Side Effects and Adverse Events". As evident from the RADIESSE® Injectable Implant Risk Management File, after implementation of measures, no unacceptable risks have emerged and the overall residual risk of RADIESSE® 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.

11 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

12 DIRECTIONS FOR USE

12.1 DEVICE PRESENTATION

RADIESSE® 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® Injectable Implant and a Terumo K-Pack II with two 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® Injectable Implant are sterilized by ethylene oxide. Needles are intended for single-use as well.

12.2 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.

12.3 PREPARATIONS, POSOLOGY AND ADMINISTRATION METHOD

12.3.1 Preparation of RADIESSE® Injectable Implant for Face and Hand Treatment

The following is required for the percutaneous injection procedure:

- One RADIESSE® 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® 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.

12.3.2 Preparation of RADIESSE® Injectable Implant diluted with saline 1:2 for the Treatment of the Décolleté

Only one (1) RADIESSE® Injectable Implant syringe 1.5 mL is used for the preparation of RADIESSE® Injectable Implant diluted with saline 1:2.

The injection of RADIESSE® Injectable Implant diluted with saline 1:2 for décolleté treatment needs to be done within 30 minutes after dilution.

The following needle is recommended for injection:

Description	Manufacturer	Qty.
Injection needles (27G x 3/4")	Terumo Europe N.V.	3

Use of needles smaller in diameter than 27G may increase the incidence of needle occlusion.

The following cannula is recommended for injection:

Description	Manufacturer	Qty.
Cannula, blunt tip, 25G x 2" (0.5 x 50 mm)	TSK STERiGLIDE™	3
Needle Guide, 23 G x ¾" (0.60 x 19 mm; for pre-hole)	TSK STERiGLIDE™	3

For décolleté treatment RADIESSE® Injectable Implant is diluted with sterile physiological saline solution (0.9% NaCl) for injections. Dilution of RADIESSE® Injectable Implant is to be performed with the following auxiliary components:

Description	Manufacturer	Qty.	Article number
RADIESSE® Injectable Implant 1.5 mL	Merz North America, Inc.	1	8071
RAPIDFILL Connector Luer Lock to Luer Lock	Baxter Healthcare Corporation	1	H93813901
BD Luer-Lock® Tip Syringe (5 mL)	Becton, Dickinson and Company	2	309649
Blunt needle (18G x 1½")	Terumo Europe N.V.	1	N/A
Sterile physiological saline solution (0.9% NaCl)	Sterile solution for injections, not specified by Merz	3.0 mL	N/A

Dilution Table

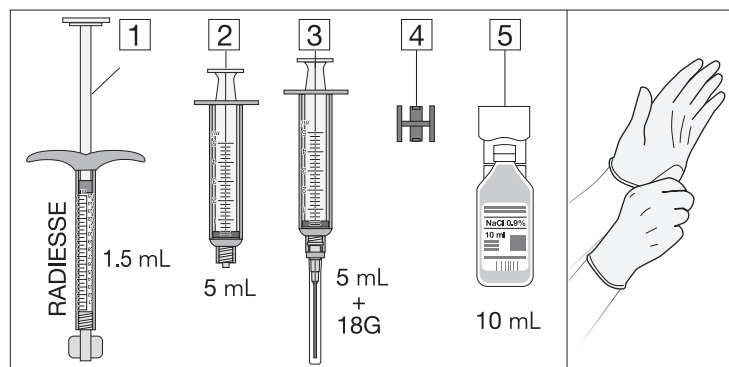
The following table shows the ratio of RADIESSE® Injectable Implant and saline for the preparation of RADIESSE® Injectable Implant diluted with saline 1:2.

Dilution factor	Amount of RADIESSE® Injectable Implant (mL)	Amount of saline (mL)	Total volume of the implant (mL)
1:2	1.5	3.0	4.5

Dilution Protocol

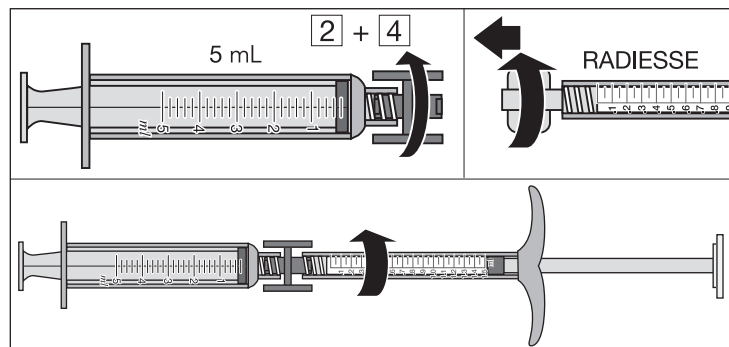
- **CAUTION:** Only use RADIESSE® Injectable Implant diluted with saline 1:2 within 30 minutes after preparation.
- **CAUTION:** The procedure has to be performed in an ambulatory setting under aseptic conditions. The person's skin should be healthy and not inflamed. The skin should be rigorously cleaned with a topical antiseptic prior to any injection.
- **CAUTION:** The components used for preparation of RADIESSE® Injectable Implant diluted with saline 1:2 are intended for single-use only.
- **CAUTION:** Use only sterile 0.9% NaCl solution for injection to prepare RADIESSE® Injectable Implant diluted with saline 1:2.
- **CAUTION:** Check diluted RADIESSE® Injectable Implant for absence of foreign particles before use and discard the product, if foreign particles are visible.

A. Auxiliary components incl. solution



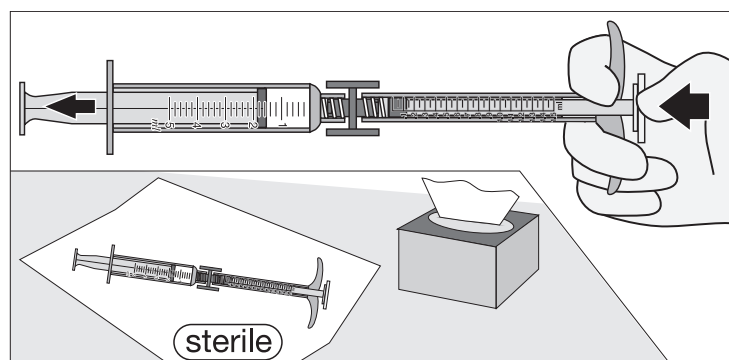
1. Provide sterile 0.9% saline solution for injection.
2. Select a RADIESSE® Injectable Implant and mixing components and check their expiry date.
3. Open the RADIESSE® Injectable Implant and mixing components and place the content on a clean and disinfected working surface.
4. **Wear gloves for the following procedure.**
5. Assemble the components and perform the dilution using aseptic technique.

B. Connect the Dilution Syringe and the RADIESSE® Injectable Implant Syringe



6. Firmly connect the RAPIDFILL Connector by screwing clockwise to a 5 mL BD Luer-Lock Syringe (Dilution syringe).
There is no preferred direction for the Luer Connector.
7. Firmly connect the RADIESSE® Injectable Implant syringe to the opposite site of the RAPIDFILL Connector.

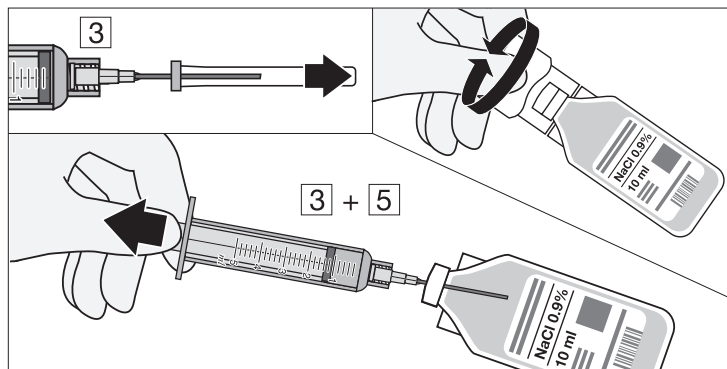
C. Transfer of RADIESSE® Injectable Implant



8. Transfer the entire RADIESSE® Injectable Implant into the dilution syringe.
9. Place the interconnected syringes on a cleaned and disinfected surface.

Do not disconnect.

D. Filling Dilution Syringe with Saline

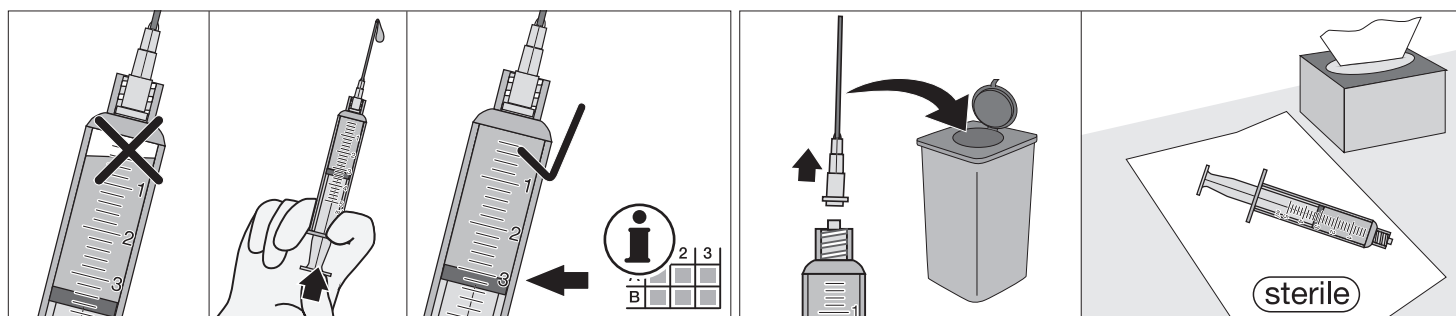


10. Open the saline solution vial.

11. Fit the second dilution syringe with a blunt 18G-needle (pink needle hub).

12. Use the blunt needle to withdraw the desired amount of saline (see dilution table) into the dilution syringe.

E. Disconnect Needle

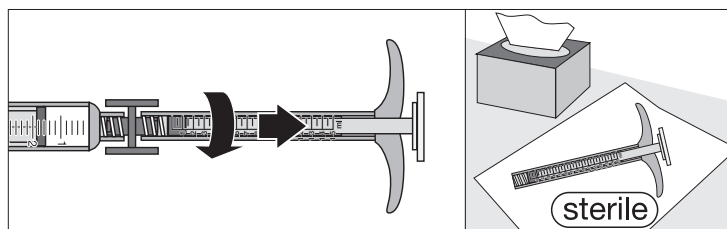


13. Remove all excess air – adjust to desired volume if necessary. Refer to dilution table above.

14. Disconnect the needle and discard.

15. Place the syringe filled with saline on a clean and disinfected surface.

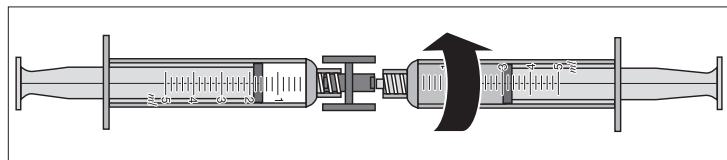
F. Connect Dilution Syringes



16. Disconnect the RADIESSE® Injectable Implant syringe from the connector.

17. Place the RADIESSE® Injectable Implant syringe on a clean and disinfected surface – avoid contamination.

Do not discard the RADIESSE® Injectable Implant syringe, it will be used again!



18. Connect the dilution syringe filled with RADIESSE® Injectable Implant to the dilution syringe filled with saline.

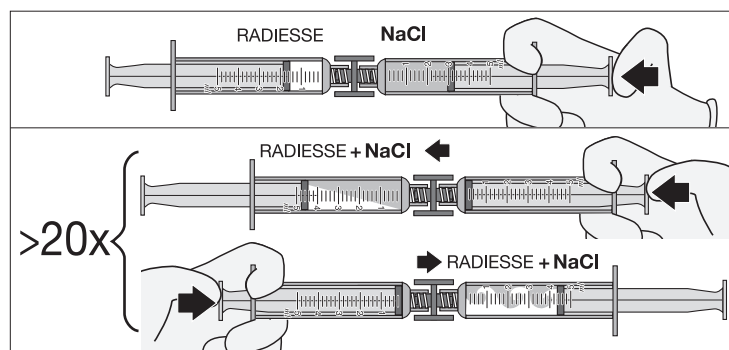
G. Dilution of RADIESSE® Injectable Implant and saline

Each mixing stroke is one complete compression of the first mixing syringe plunger followed by one complete compression of the second mixing syringe plunger. Plungers are compressed firmly and quickly.

1 mixing stroke = 2 pump moves (back and forth)

Mixing has to be repeated before every new transfer of product from mixing syringe to injection syringe.

H. Dilution of RADIESSE® Injectable Implant

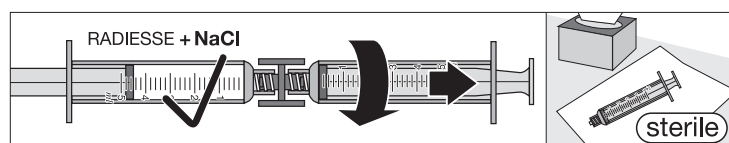


19. Mix the saline and RADIESSE® Injectable Implant by alternately depressing the plungers until the product is mixed homogeneously (at least 20 mixing strokes).

1 mixing stroke = 2 pump moves

The formation of air bubbles in the dilution is normal.

I. Check for Homogeneity

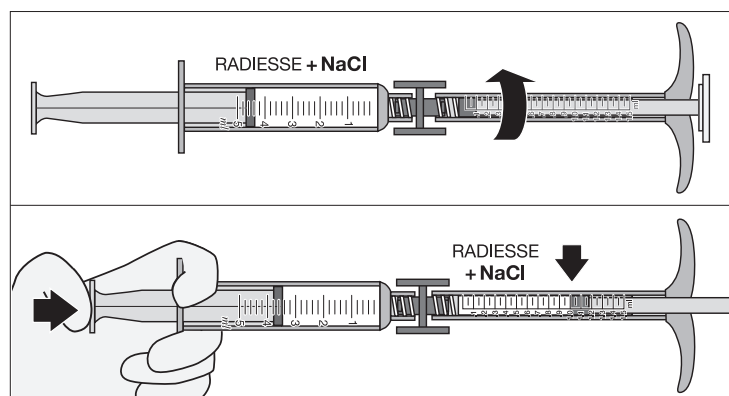


20. Check if the product is mixed homogeneously – if necessary, mix again.

21. After mixing, please assure that the whole product is located in one syringe.

22. Remove the empty syringe from the connector and place it on a clean and disinfected surface.

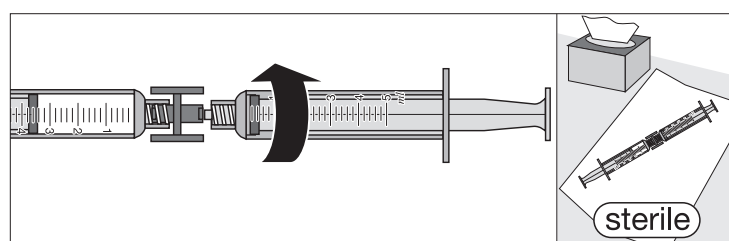
J. Transfer into RADIESSE® Syringe



23. Connect the empty RADIESSE® Injectable Implant syringe to the connector and transfer the desired amount of product into the injection syringe by pushing the product into the empty syringe. (Injection with the mixing syringe would cause a too high finger force.)

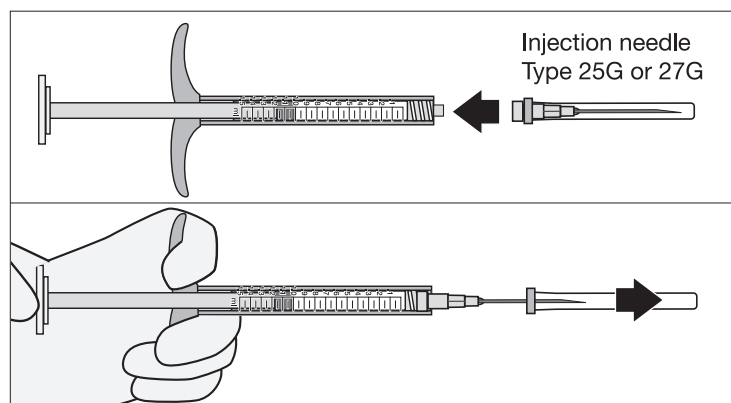
Mixing has to be repeated before every new transfer of product from mixing syringe to injection syringe (see last instruction step).

K. Avoid Contamination



24. To avoid contamination and dry out of the product please attach the empty 5 mL dilution syringe again to the RAPIDFILL Connector to close the syringe with the remaining product and place it on a clean and disinfected surface.

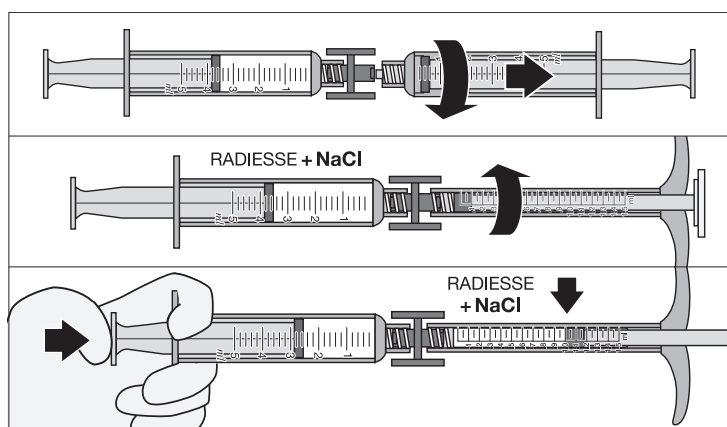
L. Fit with needle/cannula and inject



25. Fit the RADIESSE® Injectible Implant syringe with an injection needle (27G x 3/4") or cannula, blunt tip, 25G x 2" (0.5 x 50 mm).

26. Proceed with the injection.

M. Filling of the remaining product



27. If more product is needed repeat the mixing steps 19 to 26.

Ensure that the product is homogenously mixed before transferring into Injection syringe.

Discard all components and all remaining product according to local regulations for potentially infectious and sharp materials.

12.3.3 Posology and Administration Method of RADIESSE® Injectible 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® Injectible 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® Injectible 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

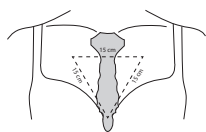
- Prepare person for percutaneous injection using standard methods. Have the person wash both hands with soapy water producing friction for 5-10 minutes and then prepare hands with suitable antiseptic. The treatment injection site may be marked for planned injection sites. Jewelry should be removed prior to injection and until post-procedure swelling has resolved.
- Using the syringe of RADIESSE® Injectable Implant fitted with the injection needle, slowly push the syringe plunger until RADIESSE® 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® Injectable Implant syringe to start the injection and inject the RADIESSE® 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® Injectable Implant (two 1.5 mL syringes) 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® 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® 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.

Posology and Administration Method for Décolleté Treatment

- Prepare person for percutaneous injection using standard methods. The treatment injection site is to be prepared with a suitable antiseptic. Local or topical anesthesia could be applied at the injection site, ice could be applied to the area to decrease local swelling/distention, or sedation could be used at the discretion of the HCP.
- It is recommended to perform the injection procedure with a 27G x 3/4" sharp needle or 25G x 50 mm blunt cannula.
- The injection needle or cannula has to be tightened securely to the syringe and primed with diluted 1:2 RADIESSE® Injectable Implant. If excess implant is on the surface of the Luer lock fittings, it needs to be wiped clean with sterile gauze.
- The syringe plunger can then slowly be pushed until the implant material extrudes from the end of the needle or cannula. If leakage is noted at the Luer fitting, it may be necessary to tighten the needle or cannula, remove the needle or cannula and clean the surfaces of the Luer fitting or, in extreme cases, replace both the syringe and the needle/cannula.
- The HCP locates the initial site for the implant. The HCP is not allowed to inject into scar tissue or into a blood vessel.
- Diluted RADIESSE® Injectable Implant 1:2 is to be injected in the subdermal plane sufficiently deep to prevent nodular formation at the surface of the skin or ischemia of the overlying tissue.
- Over-correction is not allowed.
- The injection of 4.5 mL of diluted 1:2 RADIESSE® Injectable Implant is in the central area of the décolleté in an area of approximately 100 cm² (see Figure 1), limited by an equilateral triangle of approximate side length up to 15 cm.

Figure 1: Treatment Area



- If significant resistance is encountered when pushing the plunger, the needle/cannula can be moved slightly to allow easier placement of the material.
- If significant resistance is still encountered, the HCP should pull the needle or cannula entirely out of the injection site and try again in a new position.
- If significant resistance continues to persist, the HCP should try a different needle or cannula. If this is not successful, the syringe and needle/cannula should be replaced. The needle or cannula is to be advanced into the sub-dermis to the starting location; the plunger of the syringe is to be carefully pushed to start the injection by slowly injecting the implant material.
- The technique of retrograde linear threads has to be utilized (see Figure 2).

Figure 2: Linear threading retrograde technique when using 27G x 3/4" needle or 25G x 50 mm cannula (2).

Injection technique
with needle:



Injection technique
with cannula:



- The linear threading retrograde technique with using a 27G x 3/4" needle: beginning in the lower corner and moving from the medial line towards the lateral rim of the triangle (as shown on Figure 2), linear threads of 0.1 – 0.25 mL per thread has to be placed in a retrograde way in the sub-dermal plane. The procedure has to be repeated from the other body side. In whole, from 18 to 45 linear threads have to be placed in a retrograde way to cover the entire central décolleté area (up to 100 cm²) and to distribute evenly the RADIESSE® Injectable Implant volume of 4.5 mL.

- The linear threading retrograde technique with using 25G x 50mm cannula: three cannula entry points have to be made with a 23G pre-hole needle (see Figure 2). From each of the entry points, linear threads of 0.1 to 0.25 mL of diluted 1:2 RADIESSE® Injectable Implant per thread have to be placed in a retrograde way in the subdermal plane. In total, 18 to 45 linear threads have to be placed to cover the entire central décolleté area (up to 100 cm²) and to evenly distribute the RADIESSE® Injectable Implant volume of 4.5 mL.
- After every repeated transfer of diluted 1:2 RADIESSE® Injectable Implant from the mixing syringe into the injection RADIESSE® Injectable Implant syringe, another sterile needle or cannula has to be utilized and the used injection needles and cannulas must be discarded.
- Following treatment, manual massage of the entire treatment area has to be performed by the HCP in order to promote even distribution of diluted 1:2 RADIESSE® Injectable Implant.

To achieve optimal results, a re-treatment is recommended at week 16 after initial treatment. If indicated, persons may be treated up to 3 times within 16 weeks.

A maximum of 13.5 mL diluted 1:2 RADIESSE® Injectable Implant is recommended as maximum yearly dose, when treating the décolleté. The dose may be adapted according to the person's tissue, age and technique for implantation.

12.4 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.

13 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® 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® 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.

14 STORAGE AND HANDLING INFORMATION

Packaged RADIESSE® 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.

15 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.

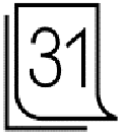
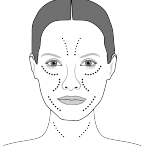
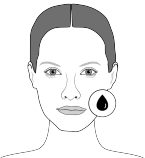
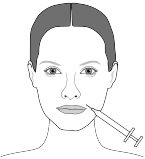
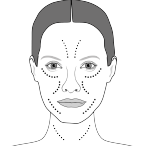
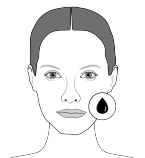
16 ADDITIONAL DEVICE SPECIFIC INFORMATION

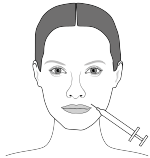
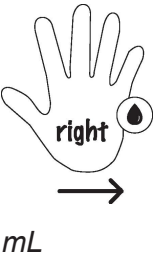
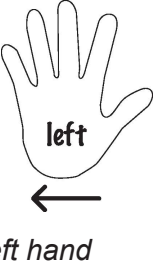
16.1 Explanation of Symbols used on Packaging

	Manufacturer		Authorized Representative in the European Community
	Importer		Catalogue number
	Batch code		Medical device
	Unique device identifier		Use-by date
	Do not resterilize		Do not use if package is damaged
	Temperature limit		Keep away from sunlight
	Keep dry		Single use. Do not re-use
	Date of manufacture		Consult instruction for use (electronic instruction for use)
	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

16.2 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	 <i>First name, last name</i>
2	Date of implantation	 <i>YYYY-MM-DD</i>
3, 4	Name and address of HCP	 <i>HCP name and address</i>
5	Injection site(s) <i>Indicate sites</i>	 <i>Naso-labial Folds (NLF)</i>
6	Total volume injected <i>e.g. 1mL</i>	 <i>x mL</i>
7	Number of injections <i>e.g. 5 injection points</i>	
5	Injection site(s) <i>Indicate sites</i>	 <i>Cheeks</i>
6	Total volume injected <i>e.g. 1mL</i>	 <i>x mL</i>

No.	Content	Details
7	Number of injections <i>e.g. 5 injection points</i>	
5	Injection site(s) <i>Indicate sites</i>	
6	Total volume injected <i>e.g. 1mL</i>	
7	Number of injections <i>e.g. 5 injection points</i>	
5	Injection site(s) <i>Indicate sites</i>	
6	Total volume injected <i>e.g. 1mL</i>	
7	Number of injections <i>e.g. 5 injection points</i>	
5	Injection site(s) <i>Indicate sites</i>	 <i>Décolleté</i>

No.	Content	Details
6	Total volume injected <i>e.g. 1mL</i>	 <i>x mL</i>
7	Number of injections <i>e.g. 5 injection points</i>	
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 EC 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

16.3 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.

16.4 Training

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

16.5 Used Harmonized Standards and Common Specifications

All harmonized 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

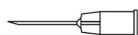
- Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices
- The Commission Implementing Regulation (EU) 2022/2346 of 1 December 2022 (Common Specifications)
- ISO 20417
- ISO 15223



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