RADIESSE®

INJECTABLE IMPLANT

INSTRUCTIONS FOR USE

SYMBOL DEFINITIONS

	Not Made with Natural Rubber Latex. N'a pas été fabriqué à partir de latex de caoutchouc naturel. No fabricado con látex de caucho natural. Nicht mit Naturkautschuklatex hergestellt. Niet vervaardigd met latex (natuurlijk rubber). Senza lattice di gomma naturale. Não contém látex de borracha natural. Inte tillverkat med naturligt gummilatex. Ikke fremstillet med naturlig gummilatex. Ei sisällä luonnonkumilateksia. Ikke laget av naturlig gummilateks. Doğal Kauçuk Lateksle üretilmemiştir. Δεν κατασκευάζεται με φυσικό ελαστικό λατέξ.	Изготовлено не из натурального каучукового латекса. Nu este fabricat cu cauciuc natural (latex). Není vyrobeno z latexu z přírodního kaučuku. Nem tartalmaz természetes gumi latexet. Niewykonane z naturalnej gumy lateksowej. Nie je vyrobené s latexom z prírodného kaučuku. Pagaminta be natūralios gumos latekso. Ei sisalda looduslikku kummilateksit. Ražots, neizmantojot dabīgā kaučuka lateksu. Nije izrađeno od prirodnog gumenog lateksa. Ni izdelano iz lateksa iz naravnega kavčuka. Не съдържа естествен гумен латекс.
	Do not use if package is damaged. Ne pas utiliser si le conditionnement est endommagé. No utilice el producto si el envase está dañado. Bei beschädigter Verpackung nicht verwenden. Niet gebruiken bij beschadigde verpakking. Non utilizzare se la confezione è danneggiata. Não utilize se a embalagem estiver danificada. Använd ej om förpackningen är skadad. Må ikke anvendes, hvis pakningen er beskadiget. Ei saa käyttää, jos pakkaus on vaurioitunut. Må ikke brukes dersom emballasjen er skadet. Ambalajı zarar görmüşse kullanmayın. Να μη χρησιμοποιηθεί εάν η συσκευασία έχει ζημιά.	Использование при нарушении целостности упаковки не допускается. Nu folosiţi dacă ambalajul este deteriorat. Nepoužívejte, jestliže je poškozený obal. Ne használja, ha a csomagolás sérült. Nie używać, jeśli opakowanie jest uszkodzone. Nepoužívajte, ak je obal poškodený. Nenaudokite, jei pakuotė pažeista. Mitte kasutada, kui pakend on kahjustatud. Nelietot, ja iepakojums bojāts. Nemojte upotrebljavati ako je ambalaža oštećena. Ne uporabljajte, če je paket poškodovan. Да не се използва, ако опаковката е повредена.

RADIESSE®

INJECTABLE IMPLANT

INSTRUCTIONS FOR USE

CE 0086

DESCRIPTION

RADIESSE® injectable implant is a steam sterilized, latex-free, non-pyrogenic, semi-solid, cohesive completely bio-degradable deep and sub-dermal implant. The principal component is synthetic calcium hydroxylapatite, a biomaterial with over twenty years of use in orthopedics, neurosurgery, dentistry, otolaryngology and ophthalmology. Calcium hydroxylapatite is the primary mineral constituent of bone and teeth. The semi-solid nature of the implant is created by suspending calcium hydroxylapatite in a gel carrier that consists primarily of water (sterile water for injection USP) and glycerin (USP). The gel structure is formed by the addition of a small amount of sodium carboxymethylcellulose (USP). 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 is classified as a Class III Medical Device according to Annex IX of the MDD. RADIESSE® injectable implants have a particle size range of 25-45 microns and can be injected with a 25 gauge outer diameter (O.D.) to 27 gauge inner diameter (I.D.) or larger needle with a standard Luer fitting. **Use of needles smaller than 27 gauge I.D. may increase the incidence of needle occlusion.**

INTENDED USE/INDICATIONS

RADIESSE® injectable implant is indicated for plastic and reconstructive surgery, including deep dermal and sub-dermal soft tissue augmentation of the facial area, and is also intended for restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus.

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 patients with known hypersensitivity to any of the components.
- RADIESSE® injectable implant is contraindicated in patients prone to developing inflammatory skin conditions or those patients with a tendency for developing hypertrópic scars.
- 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. A higher incidence of localized necrosis has been associated with glabellar injection. Complications associated with other injectables indicate that forceful injection into superficial dermal vessels of the glabellar 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 patients with systemic disorders which cause poor wound healing or will lead to tissue deterioration over the implant.
- RADIESSE® injectable implant is contraindicated for patients with bleeding disorders.

WARNINGS

- Introduction of product into the vasculature may lead to embolization, occlusion of the vessels, ischemia, or infarction. Take extra care when injecting soft tissue fillers, for example inject the product slowly and apply the least amount of pressure necessary. Rare but serious adverse events associated with the intravascular injection of soft tissue fillers in the face have been reported and include temporary or permanent vision impairment, blindness, cerebral ischemia or cerebral hemorrhage, leading to stroke, skin necrosis, and damage to underlying facial structures. Immediately stop the injection if a patient exhibits any of the following symptoms, including changes in vision, signs of a stroke, blanching of the skin, or unusual pain during or shortly after the procedure. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care practitioner specialist should an intravascular injection occur.
- Implant should not be injected into organs or other structures that could be damaged by a space occupying implant.
- Implant should not be implanted in patients while the patient is on an aspirin regimen or while taking other medications that could inhibit the healing process.
- 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.

- 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 that 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.
- Safety and effectiveness during pregnancy or in lactating females has not been established.
- The safety and efficacy of RADIESSE® injectable implant for use in the lip mucosa has not been established.

PRECAUTIONS

- In order to minimize the risks of potential complications, RADIESSE® should only be used by health care practitioners who have appropriate training, experience, and who are knowledgeable about the anatomy at and around the site of injection.
- In order to minimize the risks of potential complications, Healthcare practitioners should fully familiarize themselves with the product, the product educational materials and the entire package insert.
- 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.
- Irregularity of the implant 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 patient 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 patient, 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 reshield 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, or laser, mechanical or chemical peeling procedures has not been evaluated in controlled clinical trials.
- 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® into patients with a history of previous herpetic eruption may be associated with reactivation of the herpes.
- Safety of RADIESSE® injectable implant beyond 3 years has not been investigated in clinical trials.

ADVERSE EVENTS

Adverse events seen in a clinical trial with RADIESSE® injectable implant were generally expected, mild in nature, and short in duration. In a multi-center, randomized, controlled trial for the treatment of nasolabial folds by subdermal injection, one fold was injected with the RADIESSE® injectable implant and the other fold was injected with a commercially available collagen dermal implant. The most common adverse events reported were redness, swelling and bruising. There was no significant difference in adverse event rates between the nasolabial folds injected with RADIESSE® and those injected with collagen dermal filler. Needle jams occurred during RADIESSE® injections in one (1/117, 0.9%) subjects. In all cases, the needle was replaced and the RADIESSE® injections were completed without further sequelae. There were no reported vascular compromises that occurred in nasolabial folds injected with RADIESSE® or the collagen dermal filler.

The following adverse events were reported during clinical trials performed with the RADIESSE® injectable implant: ecchymosis, edema, erythema, granuloma, nodule, pain, pruritus, soreness, tenderness, numbness, contour irregularity, lumps, rash, discoloration, hardness, headache, scab, tightness, abrasion, burning sensation, papule/pustule, fever, firmness, hearing loss, swelling and nausea.

POST MARKET SURVEILLANCE

The following adverse events have been identified during post-approval use of RADIESSE®. Because they are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to RADIESSE®. These events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to RADIESSE®: infection, cellulitis, impetigo, loss of effect, product displacement/migration, allergic reaction, anaphylaxis, hives, rash, pruritus, urticaria, angioedema, inflammation, necrosis, granuloma, nodules, induration, erythema, skin discoloration, pustule, skin pallor, hair loss, paresthesia, ptosis, pain, headache, swelling, asymmetry, abscess, herpetic infection including herpes simplex and herpes zoster, hematoma, blanching, blistering, dizziness, festoons, flu-like symptoms, Guillain-Barre syndrome, tachypnea, ischemic reaction, lymphoid hyperplasia, nausea, pericarditis, scarring, sensitivity to cold, vascular occlusion/obstruction, vascular compromise, ocular ischemia, diplopia, visual impairment/blindness, facial muscle paralysis, Bell's palsy.

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 an adverse event or an exhaustive list of possible interventions. Physicians 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.

INDIVIDUALIZATION OF TREATMENT

Before treatment, the patient's suitability for the treatment and the patient's need for pain relief should be assessed. The outcome of treatment will vary between patients. In some instances additional treatments may be necessary depending on the size of the defect and the needs of the patient. Additional injections may be performed, but only after sufficient time has passed to evaluate the patient. The patient should not be re-injected sooner than seven days after the previous treatment.

DIRECTIONS FOR USE

GENERAL

The following is required for the percutaneous injection procedure:

- RADIESSE® injectable implant syringe(s) {Provided Separately}
- Appropriate size needle(s) with Luer lock fittings. The preferred size is a 25 gauge outer diameter (O.D.) to 27 gauge inner diameter (I.D.) or larger needle with a standard Luer fitting. Use of needles smaller in diameter than 27 gauge I.D. may increase the incidence of needle occlusion.

1. Prepare patient 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 physician. After anesthetizing the site, apply ice to the area to decrease local swelling/distention.

2. 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 patient 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 <u>not</u> an indication of a defective product.*

   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. **The needle <u>must</u> 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 remove the needle and clean the surfaces of the Luer fitting or, in extreme cases, replace both the syringe and the needle.

3. Locate the initial site for the implant. Scar tissue and cartilage may be difficult or impossible to inject. Avoid, if at all possible, passing through these tissue types when advancing the injection needle.

   NOTE: Do not inject into a blood vessel.

4. The depth of the injection and the amount injected will vary depending on the site and extent of the restoration or augmentation. RADIESSE® injectable implant should be injected sufficiently deep so as to prevent nodular formation at the surface of the skin or ischemia of the overlying tissue.

5. **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.

6. 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.

7. Advance the needle into the deep dermis to the starting location. [Refer to additional instructions, below, for augmentation of specific 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.

AUGMENTATION OF CHEEKS, CHIN, FACE OR CORNER OF THE MOUTH

1. Insert needle with bevel down at approximately a 30° angle to the skin. The needle should slide into the deep dermis to the point you wish to begin the injection. This should be easily palpable with the non-dominant hand.
2. 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.
3. 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.
4. 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.
5. Injection can be made in the subcutaneous tissue or muscle, but not adjacent to bone or in the epidermis.

PATIENT COUNSELING INFORMATION

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

- Apply ice or cool compresses to areas of injection for approximately 24 hours.
- Avoid the sun, tanning (ultraviolet) lights, sauna and intense facial treatments postoperatively.
- Massage area if palpable nodules become present.
- Promote facial rest for one week by encouraging patients to limit talking, smiling and laughing.
- Inform patient that postoperative swelling and numbness is common. Swelling will usually resolve within 7 to 10 days, but may persist for several weeks. Numbness should resolve within 4 to 6 weeks.

HOW SUPPLIED

RADIESSE® injectable implant is provided sterile and non-pyrogenic in a syringe packaged in a foil pouch and boxed for convenient storage. Each unit consists of one pre-filled syringe of RADIESSE® injectable implant. The degree of accuracy of syringe graduations is ±0.025cc. 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 patient, 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 patient infection or cross-infection including but not limited to transmission of infectious disease(s) and blood transfer between patients. All which, in turn, may lead to patient injury, illness or death.

STORAGE

Packaged RADIESSE® injectable implant should be stored at a controlled room temperature between 15°C and 32°C (59°F and 90°F). 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.

WARRANTY

Merz North America, Inc. warrants that reasonable care has been exercised in the design and manufacture of this product.

THIS WARRANTY IS IN LIEU OF AND EXCLUDES ALL OTHER WARRANTIES NOT EXPRESSLY SET FORTH HEREIN, WHETHER EXPRESSED OR IMPLIED BY OPERATION OF LAW OR OTHERWISE, INCLUDING BUT NOT LIMITED TO, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR ITS PARTICULAR PURPOSE.

Handling and storage of this product, as well as factors relating to the patient, diagnosis, treatment, surgical procedures and other matters beyond Merz North America, Inc.'s control directly affect the product and the results obtained from its use. Merz North America, Inc.'s obligation under this warranty is limited to the replacement of this product and Merz North America, Inc. shall not be liable for any incidental or consequential loss, damage, or expense, directly or indirectly, arising from the use of this product. Merz North America, Inc. neither assumes, nor authorizes any person to assume for Merz North America, Inc., any other or additional liability or responsibility in connection with this product.

MANUFACTURED BY
Merz North America, Inc.
4133 Courtney St., Suite 10
Franksville, WI 53126 USA
Telephone: 844.469.6379
E-Mail: mymerzsolutions@merz.com

EC REP

Merz Pharmaceuticals GmbH
Eckenheimer Landstraße 100
D-60318 Frankfurt am Main
Germany
+ 49 (0) 69 1503 - 0