# RADIESSE® (+) LIDOCAINE

**INJECTABLE IMPLANT**

# INSTRUCTIONS FOR USE

## DESCRIPTION

RADIESSE® (+) Lidocaine injectable implant is a sterile, non-pyrogenic, semi-solid, cohesive implant. The principle component is synthetic calcium hydroxylapatite suspended in a gel carrier that consists primarily of water (sterile water for injection USP), glycerin (USP), sodium carboxymethylcellulose (USP), 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. The typical duration of effect is 6 months, although RADIESSE® (+) Lidocaine injectable implant has been shown to be effective for up to one year in some subjects. Additional injections (touch-ups) may be performed, but only after sufficient time has passed to evaluate the patient (See INDIVIDUALIZATION OF TREATMENT section).

RADIESSE® (+) Lidocaine injectable implant (1.5cc and 0.8cc) has a calcium hydroxylapatite particle size range of 25-45 microns and should be injected with a 25 gauge outer diameter (O.D.) to 27 gauge inner diameter (I.D.) needle with a standard Luer fitting.

## INTENDED USE/INDICATIONS

RADIESSE® (+) Lidocaine injectable implant is indicated for plastic / reconstructive procedures, including deep dermal and subdermal soft tissue augmentation of the facial area and is also intended for restoration and correction of fat or volume loss (lipoatrophy) in the facial area and for rejuvenation of the hands.

## CONTRAINDICATIONS

- RADIESSE® (+) Lidocaine injectable implant is contraindicated in the presence of acute and/or chronic inflammation or infection involving the area to be treated.
- RADIESSE® (+) Lidocaine injectable implant is contraindicated in patients with known hypersensitivity to any of the components.
- RADIESSE® (+) Lidocaine injectable implant is not intended to be used in patients with known hypersensitivity to lidocaine or anesthetics of the amide type
- RADIESSE® (+) Lidocaine injectable implant is contraindicated in patients prone to developing inflammatory skin conditions or those patients 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. A higher incidence of localized necrosis has been associated with glabellar injection. Complications associated with injectables 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 patients with systemic disorders which cause poor wound healing or will lead to tissue deterioration over the implant.
- RADIESSE® (+) Lidocaine 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, in lactating females, or in patients under 18 years has not been established.
- The safety and efficacy of RADIESSE® (+) Lidocaine injectable implant for use in the lip mucosa has not been established.

**PRECAUTIONS**

- In order to minimize the risks of potential complications, this product should only be used by healthcare 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.
- The calcium hydroxylapatite (CaHA) particles in RADIESSE® (+) Lidocaine injectable implant are radio-opaque and are clearly visible on CT Scans and may be visible in standard, plain radiography. Patients need to be informed of the radio-opaque nature of RADIESSE® (+) Lidocaine injectable implant, so that they can inform their primary care health professionals and/or radiologists. In a radiographic study of 58 patients, there was no indication of RADIESSE® injectable implant (without lidocaine) potentially masking abnormal tissues or was interpreted as tumors in CT Scans. As with all transcutaneous procedures, RADIESSE® (+) Lidocaine injection carries a risk of infection. Standard precautions associated with injectable materials should be followed.
- 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.
- 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® (+) 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 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 <u>not</u> 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 recap 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.

- 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 patients with a history of previous herpetic eruption may be associated with reactivation of the herpes.

- Safety of RADIESSE® injectable implant (without lidocaine) beyond 3 years has not been investigated in clinical trials.

- Care should be taken to determine the risk verse the benefit for patients with congenital methemoglobinemia with glucose-6-phosphate dehydrogenase deficiencies, and with patients who are receiving concomitant treatment with methemoglobin-inducing agents.

**ADVERSE EVENTS**

Adverse events seen in a clinical trial with RADIESSE® (+) Lidocaine 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 (without lidocaine) and the other fold was injected with the RADIESSE® + Lidocaine injectable implant. The most common adverse events reported were swelling and redness. There was no significant difference in adverse event rates between the nasolabial folds injected with RADIESSE® injectable implant (without lidocaine) and those injected with RADIESSE® (+) Lidocaine injectable implant. Needle jams occurred during RADIESSE® (+) Lidocaine injections in three (3/101, 3%) subjects. In all cases, the needle was replaced and the RADIESSE® (+) Lidocaine injections were completed without further sequelae. Of 13 blanching events described, one was associated with a vascular compromise event. There were two (2/102, 2%) vascular compromises that occurred in nasolabial folds injected with RADIESSE® injectable implant (without lidocaine) and none that occurred in nasolabial folds injected with RADIESSE® (+) Lidocaine injectable implant. Both occurrences of vascular compromise were treated and resolved.

The following adverse events were reported during clinical trials performed with the RADIESSE® injectable implant (without lidocaine): ecchymosis, edema, erythema, nodule, pain, pruritus, soreness, tenderness, numbness, contour irregularity, lumps, irritation, rash, needle jamming, discoloration, hardness, headache, scab, tightness, blood shot eyes, black eye, abrasion, spot, nerve sensitivity, dry, burning sensation, warm, stretched, pimple, flushed, feverish, ear running, backed-up salivary gland, firmness, hearing loss, and puffiness.

**POST MARKET SURVEILLANCE**

The following adverse events have been identified during post-approval use of RADIESSE® injectable implant (without lidocaine). 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® injectable implant (without lidocaine). These events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to RADIESSE® injectable implant (without lidocaine): 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.

## INDIVIDUALIZATION OF TREATMENT

Before treatment, the patient's suitability for the treatment 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. In clinical trials, RADIESSE® injectable implant (without lidocaine) has been utilized in touch-up injections at 2 weeks and 4 weeks, and retreatment between 6 and 12 months has been shown to be safe and effective. Although various touch-up and retreatment options have been evaluated in clinical trials, the number of treatment sessions a patient will need ultimately depends upon their personal treatment plan as established by their physician. 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:

- One RADIESSE® (+) Lidocaine injectable implant syringe(s), 0.8cc or 1.5cc
- 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.

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.

3. 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.*

4. 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).

5. 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 need**l**e taking care not to contaminate the needle. Discard needle package. **The needle <u>must</u> 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.

6. 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.

7. **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.

8. 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.

9. Advance the needle bevel down at approximately a 30° angle to the skin into the sub-dermis to the starting location. 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.

**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 cool compresses to areas of injection for approximately 24 hours.
- Avoid the sun, tanning (ultraviolet) lights, sauna and intense facial treatments post procedurally.
- Massage area gently 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® (+) Lidocaine injectable implant is provided sterile and non-pyrogenic in a syringe packaged in a foil pouch and boxed for convenient storage.

Each syringe only unit consists of one pre-filled syringe containing either 0.8cc or 1.5cc of RADIESSE® (+) Lidocaine injectable implant.

RADIESSE® (+) Lidocaine injectable implant is supplied with two (2) sterile 27G injection needles.

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.

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.

**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 of which, in turn, may lead to patient injury, illness or death.**

## STORAGE

Packaged RADIESSE® (+) Lidocaine 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.

Please note that the 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 can directly affect the product and the results obtained from its use.

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