



## **INJECTABLE IMPLANT INSTRUCTIONS FOR USE**

### **DESCRIPTION**

RADIESSE® (+) injectable implant is a sterile, non-pyrogenic, semi-solid, whose principle component is synthetic calcium hydroxylapatite suspended in a gel carrier of glycerin, sodium carboxymethylcellulose, 0.3% lidocaine hydrochloride, sodium phosphate and sterile water for injection.

RADIESSE® (+) 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 (ID) needle.

### **INTENDED USE/INDICATIONS**

RADIESSE® (+) injectable implant is indicated for subdermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds and for the rejuvenation of the hands. The presence of lidocaine is intended to reduce the patient's pain during treatment.

### **CONTRAINDICATIONS**

- Contraindicated for patients with severe allergies manifested by a history of anaphylaxis, or history or presence of multiple severe allergies.
- Not to be used in patients with known hypersensitivity to any of the components.
- Not intended to be used in patients with known hypersensitivity to lidocaine or anesthetics of the amide type.
- Contraindicated for patients with bleeding disorders.
- Contraindicated in patients prone to developing inflammatory skin conditions or those patients with a tendency for developing hypertrophic scars.
- Do not implant in the epidermis or use as a skin replacement. Implantation into the epidermis could lead to complications such as fistula formation, infections, extrusions, nodule formation and induration.
- 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.
- Contraindicated in the presence of foreign bodies such as liquid silicone or other particulate materials.
- Should not be used in areas where there is inadequate coverage of healthy, well vascularized tissue.

- Should not be used in patients with systemic disorders which cause poor wound healing or will lead to tissue deterioration over the implant.
- Not intended for use in the breasts.
- Not intended for use in the lips.

## **WARNINGS**

- Use of RADIESSE® (+) injectable implant in any person with active skin inflammation or infection in or near the treatment area should be deferred until the inflammatory or infectious process has been controlled.
- Injection procedure reactions have been observed consisting mainly of short-term (i.e., < 7 days) bruising, redness, swelling, lumpiness, pain, itching, discoloration and tenderness.
- Special care should be taken to avoid injection into the blood vessels. An introduction into the vasculature may occlude the vessels and could cause infarction or embolism leading to ischemia, necrosis or scarring. This has been reported to occur in the lips, nose, glabellar or ocular area. Although rare, loss of vision is also possible. This has been reported to occur in the nasolabial folds, oral commissures, lips, nose, glabellar or ocular area. Complications associated with injectables indicate that forceful injection into superficial dermal vessels of the glabellar and nose area could cause retrograde movement into the retinal arteries resulting in vascular occlusion.
- Do not overcorrect (overfill) a contour deficiency because the depression should gradually improve within several weeks as the treatment effect of RADIESSE® (+) injectable implant occurs. In extreme cases site rupture could occur with overcorrection.
- The safety and effectiveness for use in the lips has not been established. There have been published reports of nodules associated with the use of RADIESSE® injectable implant injected into the lips.

## **PRECAUTIONS**

- The calcium hydroxylapatite (CaHA) particles of RADIESSE® (+) injectable implant are radiopaque 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® (+) injectable implant, so that they can inform their primary care health professionals as well as radiologists. In a radiographic study of 58 patients, there was not a significant risk of RADIESSE® injectable implant potentially masking abnormal tissues or being interpreted as tumors in CT Scans.
- Packaged for single patient use. Do not resterilize. Do not use if package is opened or damaged. Do not use if the syringe end cap or syringe plunger is not in place.
- The long-term safety of RADIESSE® (+) injectable implant has not been investigated in clinical trials.
- The safety of RADIESSE® (+) injectable implant in patients with increased susceptibility to keloid formation and hypertrophic scarring has not been studied.
- Nodules may form, requiring treatment or removal.
- Irregularity of the implant may occur which may require a surgical procedure to correct.

- As with all transcutaneous procedures, RADIESSE® (+) injectable implant injection carries a risk of infection. If such infection cannot be corrected, it may become necessary to remove the implant. Standard precautions associated with injectable materials should be followed.
- Safety of RADIESSE® (+) injectable implant for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.
- Patients 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.
- Universal precautions must be observed when there is a potential for contact with patient body fluids. The injection session must be conducted with aseptic technique.
- After use, treatment syringes and needles may be potential biohazards. Handle accordingly and dispose of in accordance with accepted medical practice and applicable local, state and federal requirements.
- The patient should be informed that he or she should minimize exposure of the treated area to extensive sun or heat exposure for approximately 24 hours after treatment or until any initial swelling and redness has resolved.
- Safety and effectiveness in the periorbital area has not been established.
- No studies of interactions of RADIESSE® (+) injectable implant with drugs or other substances or implants have been conducted.
- 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.
- 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.
- Injection of RADIESSE® (+) injectable implant into patients with a history of previous herpetic eruption may be associated with reactivation of the herpes.
- Care should be taken to determine the risk versus the benefit for patients with congenital methemoglobinemia, with glucose-6-phosphate dehydrogenase deficiencies, and patients who are receiving concomitant treatment with methemoglobin-inducing agents.

## **ADVERSE EVENTS**

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 MARKETING SURVEILLANCE**

The following adverse events were received from post-marketing surveillance for the RADIESSE® injectable implant: infection, over-injection, under-injection, loss of effect, product displacement, allergic reaction, necrosis, granuloma, exposed material, hair loss, tingling, ptosis, abscess, paralysis, superficial injection, herpetic infection, hematoma, blanching, blistering, bluish color, dark circles, did not like results, dizziness, double vision, festoons, flu-like symptoms, grey discoloration, hyperventilating, inflammation, ischemic reaction, nausea, pallor to skin, prior medical condition worsened, possible blood clot, scarring, sensitivity to cold, skin texture changed, tissue mass developed, vascular compromise, ocular ischemia, edema, vision loss, lumpiness, nodules, redness, pain, numbness, rash, headache, burning sensation, tissue plane migration, eye irritation, itching, lymphoid hyperplasia, ulceration at injection site, and pustules.

The most commonly reported serious adverse events for the RADIESSE® injectable implant (without lidocaine) (with a frequency greater than 5 reported events) were necrosis, allergic reaction, edema, and infection. The following describes these serious adverse events:

- Serious edema has been reported with an onset ranging from 1 day to 3 weeks (inflammation related to nodule formation). Treatment generally consisted of administration of antibiotics, anti-histamines and steroids. In some cases patients sought treatment in an emergency room or were hospitalized. Generally events resolved within 1 to 2 days but a few patients have been reported as having intermittent edema or persistent edema related to recurring infection. For cases where information was available, most patients had recovered or are recovering.
- Infection, often identified as cellulitis, was accompanied by swelling, hardened areas, redness, pustules, and pain. Onset of infection ranged from 1 day to 2 months and generally lasted 2 days but, in one case, persisted for 6 months. Infections were generally treated with antibiotics. For cases where information was available, patients had recovered or were recovering. Few patients experienced scarring that may require corrective surgery or discoloration at the site of the infection.
- Allergic Reaction was identified by itchiness and severe swelling, including swelling of the face and tongue. Onset ranged from immediately after injection to 2 days after injection. Allergic reaction was generally treated with anti-histamines and steroids. Some cases required hospitalization. All patients recovered from the allergic reaction with no permanent adverse outcome.
- Necrosis was generally preceded by pain and blanching of the skin at the time of injection accompanied with stinging or tingling and bruising, redness, and swelling. Onset of necrosis ranged from immediately at time of injection to 12 days after injection. Treatment for necrosis generally consisted of a combination of nitroglycerin ointment/vasodilatation, ibuprofen, acetaminophen, or aspirin, antibiotics, steroids,

non-steroidal wound treatment ointment and warm compresses. For cases where information was available, patients had recovered or were recovering with minimal to no scarring at last contact. Few cases required consultation with a plastic surgeon and possible excision and revision surgery to correct the defect resulting from the necrosis.

## INDIVIDUALIZATION OF TREATMENT

Before treatment, the patient's suitability for the treatment should be assessed. The outcome of treatment with RADIESSE® (+) injectable implant will vary between patients. In some instances, additional treatments may be necessary depending on the size of the defect and the augmentation or contouring 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)
  - 25 gauge OD - 27 gauge ID needle(s) with Luer lock fittings
1. Prepare patient for percutaneous injection using standard methods. The treatment injection site should be marked and prepared with a suitable antiseptic.
  2. Prepare the syringes of RADIESSE® (+) injectable implant 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.
  3. Remove foil pouch from the carton. Open the foil pouch by tearing at the notches (marked 1 and 2), and remove the syringe from the foil pouch. *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.*
  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 of RADIESSE® (+) injectable implant can then be twisted onto the Luer lock fitting of the needle taking care not to contaminate the needle. Discard needle package. **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 RADIESSE® (+) injectable implant 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 treat. Avoid if possible, passing through these tissue types when advancing the injection needle.

7. The amount injected will vary depending on the site and extent of the restoration, augmentation, or contouring desired. RADIESSE® (+) injectable implant should be injected subdermally.
8. Use a 1:1 correction factor. No overcorrection is needed.
9. Insert needle with bevel down at approximately a 30° angle to the skin. Needle should slide under the dermis to the point you wish to begin the injection. This should be easily palpable with the non-dominant hand.
10. 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. Needle jams are more likely with use of needles smaller than 27 gauge ID.
11. Advance the needle into the subdermis to the starting location. Carefully push the plunger of the RADIESSE® (+) injectable implant syringe to start the injection and slowly inject the implant material in linear threads while withdrawing the needle. Continue placing additional lines of material until the desired level of correction is achieved. For hand rejuvenation, DO NOT inject RADIESSE® (+) injectable implant in linear threads. Inject in a bolus form between the central tendons in the dorsum of the hand and distribute the material through massage. RADIESSE® (+) injectable implant should be injected in the areolar plane between the subcutaneous layer and superficial fascia.
12. Apply slow continuous even pressure to the syringe plunger to inject the implant as you withdraw the needle. The 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.
13. Use once and discard in accordance with local safety standards.

#### **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.
- Provide oral analgesics if desired.

#### **STORAGE**

RADIESSE® (+) injectable implant should be stored at a controlled room temperature between 15°C and 32°C (59°F and 90°F). The expiration date, when stored in these temperatures, is two years from date of manufacture. Do not use if the expiration date has been exceeded.

**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.

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**SYMBOLS**

LATEX FREE

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**MANUFACTURED BY**

Merz North America, Inc.  
4133 Courtney Road, Suite #10  
Franksville, WI 53126 U.S.A.  
Fax: 262-835-3330  
Telephone: 262-835-3300  
E-Mail: [info@merz.com](mailto:info@merz.com)

**DISTRIBUTED IN CANADA BY:**

Merz Pharma Canada Ltd.  
5155 North Service Road, Suite #202  
Burlington, ON L7L 6G4  
Fax: 905-315-1194  
Telephone: 905-315-1193  
E-Mail: [info@merzcanada.com](mailto:info@merzcanada.com)

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