

# **RADIESSE™**

## **INJECTABLE IMPLANT**

### **INSTRUCTIONS FOR USE**

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**CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed physician, or properly licensed practitioner.**

#### **DESCRIPTION**

Radiesse is a sterile, latex-free, non-pyrogenic, semi-solid, cohesive subdermal implant. The principle durable component of Radiesse 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 Radiesse 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 collagen and other soft tissue ingrowth, while the calcium hydroxylapatite remains at the site of injection to form a scaffold for the new tissue formation. The result is intended to be long-term soft tissue augmentation. Radiesse (0.3 cc and 1.3 cc) has a particle size range of 25-45 microns and should be injected with a 25 to 27 gauge needle.

#### **INTENDED USE**

Radiesse is indicated for subdermal implantation for the correction of moderate to severe facial wrinkles and folds such as nasolabial folds.

#### **CONTRAINDICATIONS**

- Radiesse is not to be used in patients with known hypersensitivity to any of the components.
- Radiesse must not be injected into blood vessels. Introduction of Radiesse into the vasculature may occlude the vessels and could cause infarction or embolization.

#### **WARNINGS**

- Use of Radiesse 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 to Radiesse have been observed consisting mainly of short-term bruising, redness and swelling. Refer to adverse events section for details.
- The safety and efficacy of Radiesse for use in the lips has not been established.

#### **PRECAUTIONS**

- The calcium hydroxylapatite (CaHA) particles of Radiesse have been shown to be radiopaque. Studies have shown that the CaHA particles are clearly visible on CT Scans and may be visible in standard, plain radiography. The study did not provide any evidence of significant risk of the injected Radiesse potentially masking abnormal tissues or being interpreted as tumors in CT Scans. Patients need to be informed of the radiopaque nature of Radiesse, so that they can inform their primary care health professionals as well as radiologists.

- Radiesse is 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.
- Long-term safety and effectiveness of Radiesse beyond one year have not been investigated in clinical trials.
- The safety of Radiesse in patients with increased susceptibility to keloid formation and hypertrophic scarring has not been studied. Radiesse should not be used in patients with known susceptibility to keloid formation or hypertrophic scarring.
- As with all transcutaneous procedures, Radiesse injection carries a risk of infection. Standard precautions associated with injectable materials should be followed. No infections have been reported in the clinical study. Refer to adverse events section for details.
- Safety of Radiesse 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.
- 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.

## ADVERSE EVENTS

In a study of 117 patients in 4 US investigational sites, adverse events reported in patient diaries and by physicians after injections are contained in Tables 1 and 2. Patients in the study received Radiesse in one side of the face and a collagen dermal implant (Cosmoplast) as the Control in the other side of the face. Ecchymosis and edema were reported at a significantly higher rate for Radiesse than for Control. This was not an unexpected result, as Radiesse was typically injected with a larger (27 gauge) and longer (1¼") needle than the needle used with Control (30 or 31 gauge, ½").

**Table 1**  
**Adverse Events**  
**Number of Patients With at Least One Adverse Event by Adverse Event Type**  
**N = 117**

<b>Adverse Event Type</b>	<b>Radiesse N(%)</b>	<b>Control N(%)</b>	<b>p-Value</b>
Allergic Reaction	0 (0.0%)	0 (0.0%)	N/A
Ecchymosis (bruising)	74 (63.2%)	51 (43.6%)	0.0038
Edema (swelling)	86 (73.5%)	66 (56.4%)	0.0090
Embolization	0 (0.0%)	0 (0.0%)	N/A
Erosion	0 (0.0%)	0 (0.0%)	N/A
Erythema	82 (70.1%)	88 (75.2%)	0.4636
Extrusion	0 (0.0%)	0 (0.0%)	N/A
Granuloma	0 (0.0%)	0 (0.0%)	N/A
Hematoma	0 (0.0%)	0 (0.0%)	N/A
Infection	0 (0.0%)	0 (0.0%)	N/A
Necrosis	0 (0.0%)	0 (0.0%)	N/A
Needle Jamming	1 (0.9%)	0 (0.0%)	1.0000
Nodule	1 (0.9%)	3 (2.6%)	0.6218
Pain	34 (29.1%)	27 (23.1%)	0.3717
Pruritis (itching)	22 (18.8%)	26 (22.2%)	0.6275
Other	36 (30.8%)	28 (23.9%)	0.3046

## STUDY DESIGN

The safety and effectiveness of Radiesse for the treatment of nasolabial folds was evaluated in a multi-center, prospective, randomized clinical trial. Patients were randomized to receive Radiesse in one fold and a commercially available control material (Cosmoplast) in the contra-lateral fold. Patients were injected with enough material to receive optimal correction.

The primary efficacy endpoint of the study was to determine whether Radiesse was non-inferior to the control material for the correction of nasolabial folds 3 months after treatment using the Lemperle Rating Scale (LRS). LRS ratings were determined via blinded, photographic assessments by 3 board certified physicians (dermatologists or plastic surgeons).

The secondary endpoints of the study were to determine whether Radiesse was superior to the control material for the correction of nasolabial folds at months after treatment on the LRS and non-inferior to the control material at 3 and 6 months using the Global Aesthetic Improvement Scale (GAIS). LRS and GAIS ratings were again determined via blinded, photographic assessments by 3 board certified physicians (dermatologists or plastic surgeons).

## OUTCOMES

### Demographics

As indicated in Table 2, the study enrolled a population of predominantly female, Caucasian non-smokers.

**Table 2**  
**Patient Demographics**  
**N = 117**

<b>Age (Years)</b>	
Mean	54.7
Standard Deviation	8.9
Minimum	31.0
Maximum	76.0
<b>Gender</b>	
Female	105 (89.7%)
Male	12 (10.3%)
<b>Race</b>	
American Indian	0 (0.0%)
Asian	0 (0.0%)
Black	2 (1.7%)
Caucasian	102 (87.2%)
Hispanic	11 (9.4%)
Other	2 (1.7%)
<b>Smoking History</b>	
Quit Smoking	26 (22.2%)
Never Smoked	83 (70.9%)
Smokes	8 (6.8%)

Patients were eligible to receive up to three injections during the initial treatment phase (week 0, week 2 and week 4). This treatment regimen was chosen to be consistent with the instructions for use for the control material. Volumes injected during the initial treatment phase are detailed in Table 4 below. The total mean volume for Radiesse was 1.2ml and was 2.4ml for the Control. There was significantly less Radiesse injected when compared to the amount of Control injected ( $p < 0.0001$ ).

**Table 3**  
**Total Volume of Material Injected (ml)**  
**N = 117**

	<b>Radiesse</b>	<b>Control</b>	<b>Difference</b>	<b>p-Value</b>
Mean	1.2	2.4	1.1	< 0.0001
Median	1.1	2.2	1.1	
Standard Deviation	0.5	0.9	0.8	
Minimum	0.3	0.8	-0.4	
Maximum	2.7	4.7	3.0	

### **Effectiveness**

As indicated in Table 4 below, a vast majority (84.6%) of Radiesse treated folds were determined to be superior to the Control treated folds while 12.8% were determined to be equivalent at three months using the LRS demonstrating that the primary endpoint was met.

**Table 4**  
**Primary Effectiveness Endpoint**  
**Non-Inferiority - LRS**  
**3 Months**  
**N = 117**

<b>Radiesse Compared to Control</b>			
Superior	Equivalent	Inferior	p-Value
99 (84.6%)	15 (12.8%)	3 (2.6%)	< 0.0001

As indicated in Tables 5, 6, and 7 below, at 6 months on the LRS and 3 and 6 months on the GAIS, the vast majority of Radiesse treated folds were determined to be superior to the Control treated folds. In addition, the mean LRS change from baseline was greater than 1 point better in Radiesse treated folds when compared to the Control treated folds. The mean change was 1.59 at 3 months was 1.18 and 6 months. These data demonstrate that the secondary endpoint of superiority was met.

**Table 5**  
**Secondary Effectiveness Endpoint**  
**Superiority - LRS**  
**6 Months**  
**N = 117**

<b>Radiesse Compared to Control</b>			
Superior	Equivalent	Inferior	p-Value
92 (78.6%)	19 (16.2%)	6 (5.1%)	< 0.0001

**Table 6**  
**Secondary Effectiveness Endpoint**  
**Non-Inferiority – GAIS**  
**3 Months**  
**N = 117**

<b>Radiesse Compared to Control</b>			
Superior	Equivalent	Inferior	p-Value
98 (83.8%)	16 (13.7%)	3 (2.6%)	< 0.0001

**Table 7**  
**Secondary Effectiveness Endpoint**  
**Superiority - GAIS**  
**6 Months**  
**N = 117**

<b>Radiesse Compared to Control</b>			
Superior	Equivalent	Inferior	p-Value
88 (75.2%)	25 (21.4%)	4 (3.4%)	< 0.0001

These outcomes indicate that Radiesse is safe and effective for its intended use of soft tissue augmentation in the treatment of nasolabial folds. The clinical trial confirmed that Radiesse clearly met all the primary and secondary endpoints of the study as defined in the clinical protocol with an acceptable level of risk.

#### **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 with Radiesse 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.

#### **DIRECTIONS FOR USE**

##### **GENERAL**

The following is required for the percutaneous injection procedure:

- Radiesse syringe(s)
  - 25-27 gauge needle 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. Local or topical anesthesia at the injection site should be used at the discretion of the physician.
  2. Prepare the syringes of Radiesse 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 notch, 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. Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. The syringe of Radiesse can then be twisted onto the Luer lock fitting of the needle. **The needle must be tightened securely to the syringe and primed with Radiesse.** If excess Radiesse 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 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 to replace the needle.
5. The amount injected will vary depending on the site and extent of the restoration or augmentation desired. Radiesse should be injected subdermally.
6. Use a 1:1 correction factor. No overcorrection is needed.
7. 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 possible with needles smaller than 27g or if the needle is not properly tightened onto the syringe.
8. Advance the needle into the subdermis to the starting location. Carefully push the plunger of the Radiesse syringe to start the injection and slowly inject the Radiesse material in linear threads while withdrawing the needle. Continue placing additional lines of material until the desired level of correction is achieved.
9. The 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. 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 material.

## **PATIENT COUNSELING INFORMATION**

Refer to Radiesse Patient Information Guide.

## **STORAGE**

Radiesse 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 three 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**

BioForm Medical Inc. warrants that reasonable care has been exercised in the design and manufacture of this product.

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