PATIENT INFORMATION LEAFLET

1 About RADIESSE® Injectable Implant

1.1 Introduction

This leaflet is designed to give you useful information about RADIESSE® Injectable Implant by Merz but is not intended to provide advice regarding any specific case. It does not replace the need for a thorough consultation, and you should seek the advice of a suitably qualified medical professional if you wish to be treated with this product.

- Only you and your healthcare professional can decide whether RADIESSE® Injectable Implant is right for you. Other treatment options may also be discussed during your consultation.
- Please read all the information in this guide and discuss any questions with your healthcare professional before you are treated with RADIESSE® Injectable Implant.

Keep this information. You may want to read it again.

Name or Trade Name

RADIESSE® Injectable Implant

What is RADIESSE® Injectable Implant?

RADIESSE® Injectable Implant is a dermal filler containing nature-identical mineral calcium hydroxylapatite (CaHA) suspended in a gel matrix that is mainly made up of water (sterile water for injection) together with glycerin and sodium carboxymethylcellulose (NaCMC).

How does RADIESSE® Injectable Implant work?

After injection, the gel matrix gradually spreads away from the injection site and is degraded, which leads to soft tissue growth. The CaHA remains in place until it also is degraded over time. The result is an immediate and long-term, but not permanent, smoothing of wrinkles and folds, enhancement of facial contours and improvement of skin quality.

What is RADIESSE® Injectable Implant made of?

RADIESSE® Injectable Implant is an implant, that is over time being taken up by surrounding cells/tissue and subsequently broken down and dissolved. It is used to replace lost volume, thus achieving soft tissue enhancement. The principal components consist of CaHA particles suspended in a gel matrix made up as follows:

- 56% 25-45µm CaHA particles (w/w [by weight])
- 44% Gel (w/w), which consists of
  - 36.0% sterile Water for Injection
  - 6.6% Glycerin
  - 1.4% Carboxymethylcellulose (NaCMC)

What is RADIESSE® Injectable Implant used for?

RADIESSE® Injectable Implant is injected into the skin through a thin needle or cannula (blunt needle) to plump the skin and add volume so as to smooth wrinkles and folds of the face and other body areas, enhance facial contours, stimulate the production of collagen and elastin, and improve the quality of the skin. Your healthcare professional will inject the product into your skin to make wrinkles shallower and less visible, however RADIESSE® Injectable Implant will not correct the underlying causes of the wrinkles and folds.

RADIESSE® Injectable Implant is for aesthetic purpose only.

What will RADIESSE® Injectable Implant accomplish?

RADIESSE® Injectable Implant will provide a temporary lifting effect, enhance contours, smooth wrinkles and improve the quality of the skin, thus giving a more youthful appearance.

How long do treatment effects last?

Studies have shown that when the product is used for the purposes listed above, the effect will last a year or more in most people. The durability of correction provided by CaHA depends on multiple factors, including injection technique, site of material placement, patient age, and metabolism.

Which anatomic regions can be treated with RADIESSE® Injectable Implant?

RADIESSE® Injectable Implant is intended for:

- treatment of nasolabial folds (laugh lines)
- plumping the cheeks
- restoring volume to the backs of the hands
- restoring and/or correcting signs of facial fat loss (lipoatrophy) in people infected with human immunodeficiency virus (HIV)
- RADIESSE® Injectable Implant diluted 1:2 with 0.9% sterile saline for injections is intended for the treatment of moderate and severe lines and wrinkles of the décolleté.

For whom is RADIESSE® Injectable Implant suitable?

RADIESSE® Injectable Implant may be used in adult people taking into account the indications and contraindications, etc. stated in the instructions for use.

RADIESSE® Injectable Implant diluted 1:2 with saline is intended to be used in adult female persons who do not have any contraindications.

Please seek the advice of a suitably qualified healthcare professional to find out whether RADIESSE® Injectable Implant is right for you.

In what kind of environment and by whom should RADIESSE® Injectable Implant be applied?

RADIESSE® Injectable Implant should be used by healthcare professionals who have appropriate training and experience, and who are knowledgeable about the anatomy at and around the site of injection.

How is RADIESSE® Injectable Implant sterilized?

RADIESSE® Injectable Implant is provided in a pre-filled syringe sterilized by moist heat. It is for single use only.

The needles are provided sterile as well. They are sterilized by a gas called ethylene oxide, which has the ability to destroy microbes.

Are there any reasons why I should not receive RADIESSE® Injectable Implant?

RADIESSE® Injectable Implant is contraindicated (must not be used) in the following cases:

- in people with active or chronic skin inflammation or infection in or near the treatment area.
- in people with severe allergies and a history of anaphylactic or allergic reactions.
- in people with a tendency to develop skin inflammation or scars.
- in the presence of foreign bodies such as liquid silicone or other particulate materials.
- in people with bleeding disorders.
- in people with known hypersensitivity to any of the components.
- in people with systemic disorders that cause poor wound healing or could have a detrimental effect on the tissue over the implant.
- in areas of the body, which are poorly covered by soft tissue and which are not well supplied with blood.
- in people younger than 18 years.
- in breastfeeding and pregnant women.

It must not be injected into:

- **the upper layers of the skin or be used as a skin replacement because this could lead to complications such as fistula formation (hole through the skin), infections, extrusions (the product emerges through the skin onto the surface), nodule formation and hardening of the skin (induration).**
- **frown lines and nose since there is a risk of necrosis (tissue death) and of arteries in the retina of the eye becoming blocked.**

What are some warnings to consider?

It is important to share your medical information with your healthcare professional. Together you can make an informed decision as to whether or not RADIESSE® Injectable Implant is right for you. There are risks associated with the use of the product, which might or might not apply in your case.

Accidental injection of RADIESSE® Injectable Implant into a blood vessel is a very rare event but can lead to serious and/or permanent complications such as embolization (blocked vessel by product) or thrombosis (local coagulation or clotting of the blood in a part of the circulatory system, i.e. veins), occlusion or blockage of vessels, ischemia (restricted blood supply to blood vessels), or infarction (tissue death). Complications reported after facial injections include vision abnormalities, blindness, stroke, temporary scabs, and permanent scarring of the skin. If you experience changes in your vision, signs of a stroke (including sudden difficulty speaking, numbness or weakness of your 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, notify your healthcare professional immediately.

- RADIESSE® Injectable Implant should not be injected in people taking aspirin on a permanent basis.
- RADIESSE® Injectable Implant should not be injected in people taking medicines that could inhibit the healing process.
- RADIESSE® Injectable Implant should not be used in any person with active skin inflammation or infection in or near the treatment area until the inflammation or infection has been controlled.
- 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 happen 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.
- Injection in the back of the hand may result in temporary difficulty performing activities. Darker skin types (Fitzpatrick Skin Types IV-VI) may have an increased risk in difficulty performing activities.

Which topics should I discuss with my healthcare professional as a matter of precaution?

- Tell your healthcare professional about medicines you are taking because if you are using medications that can prolong bleeding, such as aspirin or warfarin, you may, as with any injection, experience increased bruising or bleeding at the injection site.
- Tell your healthcare professional if you have a history of herpes because it can become reactivated by injection of RADIESSE® Injectable Implant.
- Tell your healthcare professional if you have concomitant dermal therapies such as epilation, UV irradiation, or laser, mechanical or chemical peeling procedures. The safety of RADIESSE® Injectable Implant with these procedures has not been evaluated in controlled clinical trials.
- You should limit the exposure of the treated area to sun or heat for 24 hours after treatment or until any initial swelling and redness has disappeared.
- The CaHA microspheres of RADIESSE® Injectable Implant are visible in CT scans and may also be visible in X-rays and MRI scans. Tell your healthcare professional, as well as your radiologists, that you have had RADIESSE® Injectable Implant injected into your face, hands or décolleté, so they are aware it is present when they are looking at your CT scans or X-rays. Consider presenting your implant card to your healthcare professional, as well as your radiologists for information.
- Contour irregularities may occur which may require a surgical procedure to correct.

Specific precautions related to injections into hands

- Use of RADIESSE® Injectable Implant in the back of the hand in people with diseases, injuries or disabilities of the hand has not been studied. Your healthcare professional will take special care if you have an autoimmune disease affecting the hand, hand implants, Dupuytren's contracture (abnormal thickening of skin on the palm), history of hand tumor, blood vessel malformations, Raynaud's disease (your fingers turn blue or white when you are cold), or if you are at risk for tendon rupture.
- You may experience significant swelling of the back of the hand after it has been injected with RADIESSE® Injectable Implant. You will be asked to remove jewelry (rings) before treatment and not to wear it again until the swelling has gone down in order to avoid affecting the blood supply to the fingers.
- The effects of RADIESSE® Injectable Implant injection on hand function are uncertain.
- The safety of RADIESSE® Injectable Implant injected into the back of the hand in people younger than 26 years and older than 79 years has not been studied.

Which side effects may occur?

- Injection-related reactions including bruising, redness, swelling, pain, itching, discoloration, rash, or tenderness, may occur at the site of the injection. These usually disappear spontaneously within one to two days.
- The tissue may split if too much is injected. RADIESSE® Injectable Implant can be easily added in subsequent injections but cannot be easily removed.
- Additional side effects could also include pain, discomfort, tenderness, tightness, numbness, headache, fever, or nausea.

What can I do to prevent or reduce side-effects?

Your healthcare professional will advise you on what you need to do after the procedure in order to promote normal healing and avoid complications. General guidelines include the following:

- You must avoid applying make-up (including skin care products) for at least 24 hours
- Repeatedly apply cool compresses to the injected areas s needed during the first 24 hours after injection.
- Avoid the sun, tanning (ultraviolet) lamps, sauna and intense treatments in the area, which was treated with RADIESSE® Injectable Implant.
- If palpable nodules appear, massage the area gently.
- Rest your face for a week by talking, smiling, and laughing as little as possible.
- You must avoid drinking alcohol for 24 hours before and after treatment. Alcohol may cause the blood vessels to dilate and cause more bruising

- You should avoid strenuous physical activity for 24 hours after treatment
- You may be asked to stay for a certain time in the premises of the HCP, in order to identify any potential undesirable side-effects.

Swelling and numbness are common side effects. Swelling will usually disappear within 7 to 10 days, although it may persist for several weeks in some cases. Numbness should disappear within 4 to 6 weeks.

Which side-effects have occurred in the past overall?

The following side effects have been identified during the use of RADIESSE® Injectable Implant. Because they are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or be sure that they were caused by RADIESSE® Injectable Implant. Those listed have been chosen because of their seriousness, frequency of reporting, or likelihood of being caused by RADIESSE® Injectable Implant:

Vomiting, flu-like symptoms, fever, malaise, weakness and lack of energy, dizziness, headache fainting, nausea, warmth at the injection site, cyst at the injection site, inflammation, pericarditis (inflammation of the tissue surrounding the heart), allergic or anaphylactic reaction (including breathlessness), rapid breathing, swelling/ edema (a type of swelling), angioedema (a type of swelling), tightness, enlarged lymph nodes, obstructed lymph flow, hives, infection (including infection of the deeper layers of the skin), abscess, granuloma (area of chronic inflammation), nodule, hardness, redness, herpes infection, blistering, injection site ulceration, scarring, skin discoloration/ pale skin, papule/ pustule/ pimples, scab, abrasion, bruising, bleeding at the injection site, pain (including pain while chewing and muscle and joint pain), itching, rash, difficulty chewing, pins and needles, decreased sensation, sensitivity to cold, drooping eyelids, nerve injury, nerve compression, facial paralysis or weakness of facial muscles, Guillain-Barre syndrome (autoimmune disease affecting the nerves), dissatisfaction, worsening of pre-existing conditions, loss of effect, product displacement/migration, asymmetry, bags under the eyes, xanthelasma (yellowish spots around the eyes), prominent surface veins, inflammation of blood vessels, blocked or injured vessels, necrosis (local tissue death), ocular ischemia (insufficient blood supply to eye tissues), double vision, impairment/loss of vision, optic nerve injury, swelling inside the eye, disorder of the eye retina, hair loss.

People of specific ethnicities, e.g. Asians, have a higher risk of tissue reactions, such as inflammation, changes in pigmentation (including post-inflammatory increases in pigmentation), post-inflammatory hyperpigmentation (excessive pigmentation, PIH) or formation of thick raised scars (keloids), e.g. after subsequent injury to the skin.

Based on information reported to Merz about the use of RADIESSE® Injectable Implant, your healthcare professional may recommend additional interventions after RADIESSE® Injectable Implant such as: antibiotics, anti-inflammatories, corticosteroids, antihistamines, analgesics, massage, warm compress, removal of the implant, drainage, and surgery. This information does not constitute and is not intended to be medical advice, a recommendation for treatment or an exhaustive list of possible interventions.

Your healthcare professional should always evaluate each individual case, and independently determine what treatments(s), if any, are right for you.

Which residual risks may occur in spite of correct treatment and in spite of all precautionary measures being taken?

In the course of its lifetime, all risks that may occur in connection with RADIESSE® Injectable Implant are analyzed and reduced as far as possible. This so-called risk management spans all steps from design and production of RADIESSE® Injectable Implant to disposal of the syringe and even to its degradation in the body. However, after all possible measures have been taken some risks inherent to treatment with RADIESSE® and to biology of our skin still remain. These risks are listed above in the Section “Which side-effects have occurred in the past overall?” Most of the listed problems are very rare. They are listed nevertheless for your information.

What should I do if I have problems after a RADIESSE® Injectable Implant treatment?

If you believe you have experienced a serious problem related to your RADIESSE® Injectable Implant treatment, you should call your healthcare professional.

Any side effects at the injection site, which last for more than one week, should be reported to your healthcare professional. Immediately report any side effects such as changes in your vision, signs of a stroke (including sudden difficulty speaking, numbness or weakness in your face, arms, or legs, difficulty walking, face drooping, severe headache, dizziness or confusion), white appearance of the skin, unusual pain during or shortly after treatment. Your healthcare professional may refer you for appropriate treatment.

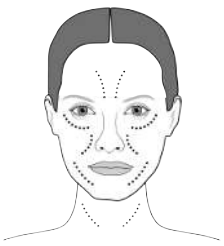
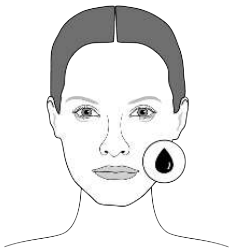
The relevant contact information is included on your implant card.

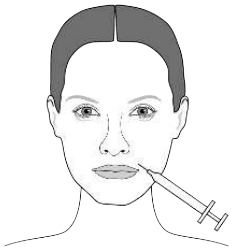
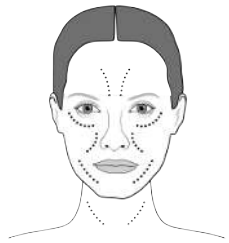
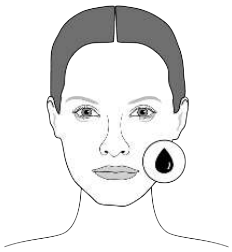
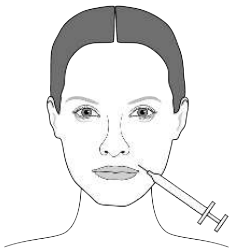
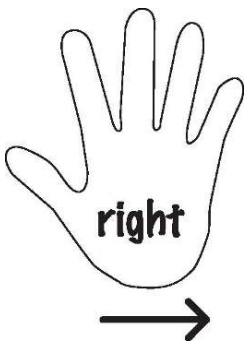
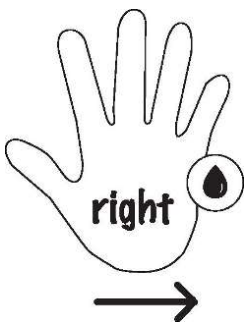
You may also contact *Merz Aesthetics GmbH* to report any side effects via Ax-Safety@merz.de .

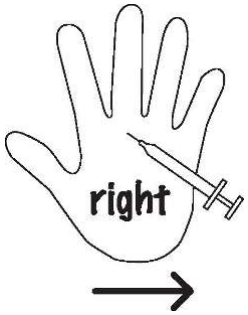
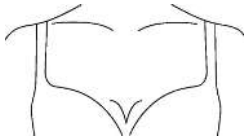
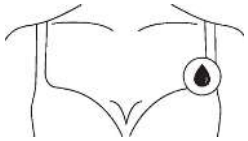
3 Additional Information

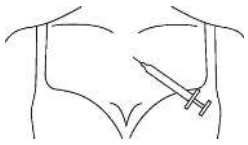
3.1 Implant Card

After the injection, your doctor will provide you with an implant card. This card contains all information related to your injection:

Details	No.	Content
 *First name, last name*	1	Patient name or patient ID
 *YYYY-MM-DD*	2	Date of implantation
 *HCP name and address*	3, 4	Name and address of healthcare professional
 *Naso-labial folds (NLF)*	5	Injection site(s) *Indicate sites*
 *x mL*	6	Total volume injected *e.g. 1mL*

Details	No.	Content
	7	Number of injections *e.g. 5 injection points*
 *Cheeks*	5	Injection site(s) *Indicate sites*
 *x mL*	6	Total volume injected *e.g. 1mL*
	7	Number of injections *e.g. 5 injection points*
 *right hand*	5	Injection site(s) *Indicate sites*
	6	Total volume injected *e.g. 1mL*

Details	No.	Content
x mL		
	7	Number of injections *e.g. 5 injection points*
 *left hand*	5	Injection site(s) *Indicate sites*
 *x mL*	6	Total volume injected *e.g. 1mL*
	7	Number of injections *e.g. 5 injection points*
 *Décolleté*	5	Injection site(s) *Indicate sites*
 *x mL*	6	Total volume injected *e.g. 1mL*

Details	No.	Content
	7	Number of injections *e.g. 5 injection points*

Keep this card with you and show it to your healthcare professional during any other appointments. Information about previous treatment must be shown to your healthcare professional before new treatment is started.

3.2 Electronical Patient Information (PI)

A printable PDF version of the patient information leaflet in your local language can be found on the following website: **www.patientinfo.merzaesthetics.com**. For the most recent version of the patient information leaflet, please always refer to the website.

4 Legal Manufacturer / Authorized Representative

MANUFACTURED BY

MERZ NORTH AMERICA, Inc.
4133 Courtney St. Suite 10
Franksville, WI 53126
USA
Telephone: +1 844.469.6379
E-Mail: mymerzsolutions@merz.com

If the manufacturer is located outside of the Union:

EC REP

Merz Aesthetics GmbH
Eckenheimer Landstraße 100
60318 Frankfurt am Main
Germany
Telephone: + 49 (0) 69 1503 - 0
E-Mail: service-aesthetics@merz.de

Used Harmonised Standards & Common Specifications:

All harmonised standards and common specifications applied are listed within the Summary of Safety and Clinical Performance.

The current Summary of Safety and Clinical Performance 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 in the search field “Basic UDI-DI/EUDAMED DI” the number 018629500DF30001LK. Until EUDAMED is fully functional the SSCP may be requested via Ax-Safety@merz.de.