

# RHA® Redensity™ Patient Information Brochure

Please read this document carefully before your treatment, it contains important information about RHA® Redensity™.

## TABLE OF CONTENTS

1. GLOSSARY .....	1
2. PRODUCT DESCRIPTION .....	2
3. CONTRAINDICATIONS .....	3
4. PRECAUTIONS.....	3
5. HOW WAS RHA® Redensity™ STUDIED?.....	5
6. BENEFITS .....	5
7. RISKS .....	6
8. PROCEDURE .....	9
9. ADDITIONAL INFORMATION.....	11

## 1. GLOSSARY

Note: the terms in the glossary are **bold** throughout the document.

**Allergic reaction:** allergic reactions occur when a person's immune system (needed to fight infections) overreacts to substances that are harmless for most people. Symptoms could include a rash, sneezing, itching, congestion or difficulty breathing

**Anaphylaxis:** a severe **allergic reaction** which needs medical treatment right away

**Anesthetic:** a medication that reduces pain; it can be added to a cream or a **dermal filler**; sometimes called a numbing medicine

**Anticoagulants:** medications that thin your blood

**Anti-inflammatory:** a medicine which reduces pain, heat, redness, and swelling, which are symptoms of inflammation

**BDDE:** 1,4-butanediol diglycidyl ether, a chemical compound used in very small amount to bind the chains of **HA** together to form a gel

**Common treatment reaction:** reactions which can be expected after injection of a **dermal filler**. It includes bruising, firmness, swelling, pain, tenderness, redness, lumps/bumps, change in skin color, and itching

**Dermal filler:** material which is injected under the skin to help smooth and plump wrinkles and folds

**Dynamic:** able to move, not fixed in place, such as the skin on the face

**Granuloma:** localized hardening under the skin, like a lump, appearing weeks or months after the injection

**Herpes:** a virus which causes certain skin conditions, such as cold sores

**Hyaluronic Acid (HA):** a naturally occurring substance found in the human body which helps maintain skin structure and feel. The HA found in RHA® Redensity™ is a different form than the HA found in the human body

**Immunosuppressive therapy:** medications that reduce the body's normal response to infections, allergens, anything not normally found in the body

**Keloid:** a thick tough scar

**Lidocaine:** a type of **anesthetic** medication which helps reduce pain

**Perioral rhytids:** the medical term for moderate and severe lines around the mouth

**Pigmentation disorders:** general term to refer to health conditions that affect the color of the skin

**Severe common treatment reaction:** reaction following an injection with symptoms that caused severe discomfort, compromised the performance of daily activities and for which treatment of the symptoms was needed. The severity is determined by the patient.

**Streptococcus equi:** a bacteria, which does not cause illness in people, used to make the **hyaluronic acid**

**Therapy:** treatment intended to reduce, heal or cure pain, disease or physical reaction

**Touch-up:** an additional injection, performed 2 to 4 weeks after the initial injection. Some patients may require a touch-up treatment to achieve the desired aesthetic results

**Treatment Related Adverse Events (TRAEs):** any unusual medical occurrence in a subject following the injection which is related to the dermal filler as determined by the doctor. It may be any symptoms, disease or reaction associated with the use of the dermal filler.

## **2. PRODUCT DESCRIPTION**

### **What is RHA® Redensity™?**

RHA® Redensity™ is an injectable gel (also called a **dermal filler**) used to treat moderate and severe lines and wrinkles around the mouth. It is injected in the moving (**dynamic**) area around the mouth (see Figure 1). It is approved for use in adults over 22 years of age.

RHA® Redensity™ is produced with **hyaluronic acid (HA)**, using an advanced technology to obtain a soft and long-lasting injectable gel to smooth facial wrinkles and folds. Chains of **HA** are linked together through a chemical reaction triggered by a small quantity of **BDDE** to create the gel texture of RHA® Redensity™. The **HA** of the gel is made from a non-animal source.

RHA® Redensity™ contains a small amount of an **anesthetic** medicine (**lidocaine**), to help reduce discomfort during injection.

**Hyaluronic acid (HA)** is a naturally occurring substance found in the human body. Your body's own **HA** helps maintain the skin's structure and its natural feel.

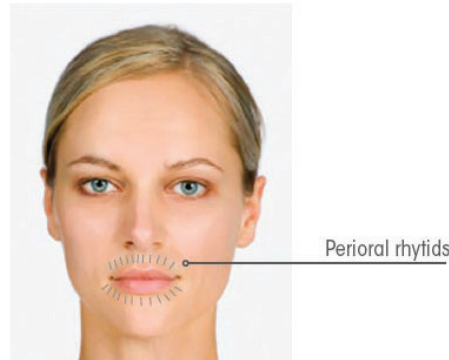


Figure 1: Location of the **moderate and severe lines around the mouth** (perioral rhytids)

### ***How does it work?***

RHA® Redensity™ is injected into the skin with an ultrafine needle to plump the skin to fill in and smooth away lines and wrinkles around the mouth (perioral rhytids). This smoothing effect has been shown to last 24 weeks (6 months) in 73% of the patients (137 out of 188 patients), and 52 weeks (12 months) in 67% of the patients (125 out of 188 patients).

RHA® Redensity™ is not a permanent gel. It slowly goes away as the body absorbs the gel. The smoothing and plumping effect will gradually disappear.

### **3. CONTRAINDICATIONS**

#### ***Are there any reasons why I should not receive RHA® Redensity™?***

Your doctor will ask about your medical history to see if RHA® Redensity™ is right for you. You should not use RHA® Redensity™ if you have a history of:

- severe **allergic reactions (anaphylaxis)** or history or presence of multiple severe allergies. An injection of RHA® Redensity™ may result in an **allergic reaction**.
- **allergic reactions** to the material (from ***Streptococcus equi***) used to make the **HA** in RHA® Redensity™. An injection of RHA® Redensity™ may result in an **allergic reaction**.
- **allergic reactions** to **lidocaine** or other similar substances used to reduce pain. An injection of RHA® Redensity™ may result in an **allergic reaction**.
- bleeding disorders. Any injection, including RHA® Redensity™ and other **dermal fillers**, may result in a higher risk of bruising or bleeding in the treated area.

### **4. PRECAUTIONS**

#### ***Are there precautions that I should discuss with my doctor?***

The following are important treatment considerations that you should discuss with your doctor. These hazards, if not avoided, could result in unsatisfactory results or complications.

- Tell your doctor if you are under 22 years of age. RHA® Redensity™ has not been studied in people younger than 22 and the effects are not known.
- Tell your doctor if you are pregnant (or plan to be) or breastfeeding. RHA® Redensity™ has not been studied in women who were pregnant or breastfeeding and the effects are not known.
- Tell your doctor if you are taking medicine that reduces your body's ability to fight infection (**immunosuppressive therapy**). Taking this type of medicine may increase the risk of infection following the injection of RHA® Redensity™ or other **dermal fillers**.
- Be sure to tell your injecting doctor if you are using "blood thinners" (**anticoagulants**) or any other medications that affect bleeding. Do not stop taking them until you speak with the doctor who prescribed them for you. Tell your prescribing doctor that you are considering having your wrinkles treated with RHA® Redensity™. These blood thinning medications may cause increased bleeding and/or bruising in the treated area.
- Tell your doctor if you have a history of cold sores (**herpes**). Any injection, including RHA® Redensity™, in the general area may trigger a recurrence of your cold sores (**herpes**).
- Tell your doctor if you have an injury, or other skin condition near the injection site(s). Injection of a **dermal filler** in this situation may lead to a worsening of your condition or infection. You may have to wait until you are completely healed before using RHA® Redensity™.
- Tell your doctor if you have ever developed a thick tough scar (**keloid**) or had problems with skin discoloration. It is possible that injection of any **dermal filler**, including RHA® Redensity™, may make the skin thicker and change color. However, when RHA® Redensity™ was studied in patients with different skin tones (pale to dark), there were no reports of this happening.
- Tell your doctor if you have a history of **pigmentation disorders**. The safety of RHA® Redensity™ in patients with history of **pigmentation disorders** has not been studied. Use in these patients may result in changes in pigmentation.
- Tell your doctor if you have already been injected with **dermal fillers** in the same area as the one(s) you are about to be treated for. This information helps your doctor decide when and whether you should get treatment with RHA® Redensity™.
- Tell your doctor if you have recently had (within 6 months), or are considering, laser treatment, chemical peeling or any other facial procedure. Use of RHA® Redensity™ with these skin treatments may lead to an increased severity of the **common treatment reactions** such as redness, swelling, heat or pain in the area.
- You should not take Vitamin E, aspirin, or **anti-inflammatories** during the week prior to the injection. Taking these medications can thin your blood and may result in increased bleeding and/or more bruising in the treated area.

If you have any additional questions about any topic in this section, please discuss further with your

doctor.

## **5. HOW WAS RHA® Redensity™ STUDIED?**

RHA® Redensity™ was tested in a clinical study to make sure it worked as intended, and was safe to use. The study looked at how well RHA® Redensity™ smoothed away moderate and severe lines (rhytids) in the moving (dynamic) perioral area.

This study lasted 52 weeks (12 months) and involved 202 patients. The wrinkles to be treated were considered to be moderate or severe, based on their depth. At the beginning of the study, a group of 150 patients was injected with RHA® Redensity™ in the perioral area, whereas a group of 52 patients was assigned to the No-Treatment group, in order to compare the effects of treatment with RHA® Redensity™ against a non-treated group, during the first 8 weeks of the study. After 8 weeks, the patients who were initially in the No-Treatment group were also injected with RHA® Redensity™. They followed all the same schedule for 12 months as the initial treatment group, at which point they were offered a repeat treatment at the end of the study. All subjects were followed for an additional 4 weeks if they had received repeat treatment at the end of the study.

Study patients were mostly females, with light to very dark skin color. The majority of patients had light to medium skin tone. The study took place at 8 different locations across the United States and Canada.

Two weeks after the initial injection, the study patients were examined by their doctor. If their doctor felt it was necessary, he / she injected more RHA® Redensity™ (**touch-up**) to get the desired result.

Study patients kept a diary for 14 days after each injection to record **common treatment reactions** at the injection site. These diaries were then shared with their doctor.

Each patient saw their doctor at regular intervals during 12 months after the procedure. At each visit, the doctor measured the effects of the treatment and checked the patient to evaluate any potential problem. Each patient was also examined by a doctor who did not know whether they had been injected with RHA® Redensity™ or not. This allowed the new doctor to objectively assess changes in how the patient looked compared to before the first injection.

Patients also evaluated themselves for changes in the appearance of the moderate and severe lines around their mouth (perioral rhytids). They looked at themselves in a mirror and compared how they looked now against their own picture taken before the first injection. They rated their results from “much improved” to “much worse” (the scale included the following grades: 1-Much improved – 2-Improved – 3-No change – 4-Worse – 5-Much worse).

Patients reported their level of pain during and after injection using a scale from 0 to 100, with “0” meaning “no pain” and “100” meaning “the worst pain possible”. The pain was the most at the time of injection and was on average 20 out of 100. Fifteen minutes after injection, the pain was on average 3 out of 100.

## **6. BENEFITS**

***What are the expected benefits of RHA® Redensity™?***

RHA® Redensity™ smooths lines (rhytids) in moving (**dynamic**) areas around the mouth (**perioral rhytids**).

During the clinical study, the clinical benefits of RHA® Redensity™ were evaluated in two phases. The evaluation was based on the severity of their perioral rhytids, compared to before treatment levels.

- Phase 1: First, 150 patients injected with RHA® Redensity™ and 51 patients who had not been injected (1 of the subjects intended for the “No treatment” group was mistakenly given the treatment), were compared after 8 weeks (2 months), to evaluate the benefits of RHA® Redensity™.

Afterwards, the group of patients who had not been injected received a treatment with RHA® Redensity™. Both groups were then pooled, to evaluate RHA® Redensity™ benefits on a long-term basis in Phase 2.

- Phase 2: all patients of the pooled population (i.e. first group of patients who were injected with RHA® Redensity™ and the second group who were injected 8 weeks after starting in the study) were evaluated periodically after their last treatment (initial injection or touch-up) with RHA® Redensity™. This allowed to evaluate how long the aesthetic improvement lasted during the 12 months after treatment. Of note, some patients (17.6 %, 35 out of 199 patients) received an additional injection throughout the course of the study, to maintain the aesthetic improvement.

Please note that some patients were excluded from the analysis due to procedural disruption, explaining the population size of 199 patients. Moreover, not all patients of the pooled population were available at each study time point, therefore the results presented below are all reported to the number of patients at each specific time point (194 after 8 weeks, 188 after 24 and 52 weeks).

RHA® REDENSITY™ was shown to last in 73 % of the patients evaluated after 24 weeks (137 out of 188 patients), and 67 % of the patients evaluated after 52 weeks (12 months) (125 out of 188 patients).

At each clinic visit, a doctor who did not know whether the patient had been injected with RHA® Redensity™ or not, examined the patient. He/she evaluated the changes in appearance of the treated rhytids compared to their appearance in the patient's picture taken before starting the treatment. These doctors reported that 92 % of the patients (179 out of 194 patients) showed improvement at 8 weeks, 84% (158 out of 188 patients) at 24 weeks, and 81% (152 out of 188 patients) at 52 weeks (12 months).

At each clinic visit, study patients were asked whether their appearance had improved or gotten worse. The patient compared the appearance of his/her treated wrinkles against their own picture taken before the first injection. Almost 95 % of the patients (186 out of 196) reported that their perioral lines (rhytids) were improved or much improved at 8 weeks after the first injection. At 52 weeks (12 months) after the first injection, 83 % (156 out of 188) still reported an improvement.

## **7. RISKS**

***What were the common treatment reactions seen in the clinical study?***

Most patients (87.9 % or 175 out of 199 patients) experienced at least one **common treatment reaction** following their injection. Some patients experienced more than one. The expected reactions at the injection site are:

- Redness
- Pain
- Tenderness
- Firmness
- Swelling
- Lumps/bumps
- Bruising
- Itching
- Discoloration

The duration of the **common treatment reactions** that occurred after the initial injection varied. The majority (76% or 722 of the 945 reactions) of the **common treatment reactions** were gone by 7 days after injection. Most (89.8% or 849 of the 945 reactions) of the **common treatment reactions** were gone by 14 days after injection. Of those **common treatment reactions** which lasted for 14 days or more, the most frequent and majority were feeling lumps/bumps, firmness and bruising at the site of injection (61%, 59 of the 96 events on the last day of the diary).

For most of these reactions, patients reported that they were mild or moderate (92% or 873 of the 945 reactions). This means that the patient had little to no discomfort and their daily life was not affected. They may have used medication and/or make-up. Of the **common treatment reactions** that were reported as **severe** by the patients (7.6%, or 72 of the 945 reactions), approximately 1/3 were for bruising.

Table 1 gives the percentage of study patients who experienced each **common treatment reaction** following the initial injection.

*Table 1: **Common treatment reactions** observed in the clinical study*

<b>Common Treatment Reactions</b>	<b>Study patients who reported the common treatment reaction</b>
Bruising	77% (154 out of 199* patients)
Swelling	73% (146 out of 199* patients)
Redness	66% (131 out of 199*patients)
Lumps/Bumps	58% (115 out of 199* patients)
Firmness	58% (115 out of 199* patients)
Tenderness	52% (105 out of 199* patients)
Discoloration	47% (94 out of 199* patients)
Pain	27% (54 out of 199* patients)
Itching	16% (31 out of 199* patients)

*\*199 is the number of patients who provided diary answers*

When **common treatment reactions** lasted longer than the 14 days of the diary, they were called

**Treatment-Related Adverse Events (TRAEs)**. The duration of TRAEs spanned from 1 to 90 days except for one event of discoloration which lasted for 384 days (bluish appearance) and one event of involuntary muscle contraction which did not resolve before study exit but had resolved, without treatment approximately 1 month later.

***What other possible reactions could occur?***

Other possible reactions can occur after the injection of a **dermal filler** such as RHA® Redensity™, although they were not observed in the clinical study. Possible reactions may be:

- Infection – Any time a **dermal filler** is injected under the skin there is a risk of infection at the site of injection. It may create hard and swollen lumps that may contain pus. Infection may require antibiotic treatment or other medical intervention.
- Granuloma – Red raised lumps that may appear weeks or months after injection. They may need to be treated by a doctor to make them go away. It may require additional procedures.
- Acne-like rashes – If you have a sensitive skin, the injection of a **dermal filler** may create an irritation or rash at the site of the treatment that can be compared to acne.
- Displacement of the gel – It is possible the injected gel may move out of the desired treatment area. Your appearance may be affected.
- Blisters – Any injection, including with RHA® Redensity™, may lead to formation of blisters at the point of injection.
- Scars – With any type of injection, including with RHA® Redensity™, scarring may occur.
- Scab – The injection of a **dermal filler**, such as RHA® Redensity™, may result in the skin becoming dry and crusty.
- Skin peeling (shedding) – The skin may dry as a reaction to the cleansing agent. The dry skin may be stressed with the injection and result in peeling or shedding.

You should contact your doctor if you experience any of these reactions or if you notice anything unusual at the site of the treatment. Most of these reactions go away within a few days on their own but some may persist for more than 30 days. Your doctor may choose to treat them with medications.

Other serious reactions may occur following the injection of **dermal fillers** to smooth wrinkles. Contact your doctor immediately if any of these happen:

- One of the risks with using this product is unintentional injection into a blood vessel. The chances of this happening are very small, but if it does happen, the complications can be serious, and may be permanent. These complications, which have been reported for facial injections, can include vision abnormalities, blindness, stroke, temporary scabs, or permanent scarring of the skin. If you have 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, or unusual pain during or shortly after treatment, you should notify your health care practitioner immediately.



- **Severe allergic reactions (anaphylaxis)** - An **allergic reaction** to a material used to make a **dermal filler** that could occur shortly after the injection. Symptoms could include a rash, sneezing, itching, congestion or difficulty breathing.

You should discuss the potential treatment risks and benefits with your doctor before the injection.

## **8. PROCEDURE**

### ***What happens in the doctor's office before the treatment?***

Note that each doctor may have their own process for treating patients.

Before the injection procedure, your doctor will ask you questions about your medical history. He/she will ask about your treatment goals. Your doctor will discuss whether you are a good candidate for RHA® Redensity™. He/she will review with you what to expect during and after treatment, including possible risks.

During this discussion, it is very important to tell your doctor about:

- all medications you are taking, both over the counter and prescription
- any previous facial treatment you may have received
- and any health conditions for which you are receiving medical attention

Your doctor will also examine your skin in and around the treatment area, and may take photos. The treatment area will be cleaned and prepared with a cleansing agent. Your doctor may use a pen to mark your face in the planned areas of injection.

### ***Do the injections hurt?***

Injections may cause some pain during and after the procedure. Your doctor will discuss different options for pain management with you. RHA® Redensity™ contains an **anesthetic** medicine (**lidocaine**) to help reduce injection site pain. This pain is temporary and usually lessens within a few minutes. To prevent or reduce pain from the injection, your doctor may use ice packs, or other **anesthetic**, both before and after the injection.

### ***What happens during the treatment?***

RHA® Redensity™ is slowly injected into the facial skin in small amounts until your doctor sees the desired result which creates a more youthful appearance of the face. For most patients, the procedure only takes 15-30 minutes.

Once your doctor has finished injecting the treatment area, he/she may gently massage the area around your mouth to help smooth and distribute the gel evenly.

Your doctor may also apply an ice pack to help decrease swelling and pain.

The amount of RHA® Redensity™ used depends on the depth of your wrinkles and your treatment goals. The right amount to be injected will be decided by your doctor during the procedure. Injection of additional RHA®1 (**touch-up** treatment) may be needed 2 to 4 weeks after initial treatment to achieve the desired aesthetic outcome. In the clinical study, 69% of the patients received a **touch-up** treatment 2 weeks after initial treatment to achieve their desired results. Your doctor will decide how much RHA® Redensity™ is needed for the **touch-up** treatment.

### **What happens after the treatment?**

Your doctor may advise you to apply cold compresses to the treated area to help reduce pain and swelling. In order to prevent injury, ask your doctor how long you can leave ice packs on the treated area.

Be aware that numbness, short term loss of touch or feeling, and tingling around the injection area may occur due to the numbing medicine (**anesthetic**). It usually goes away within a few hours. Due to this numbness, you may not have normal feeling of hot or cold in this area.

Ask your doctor about any limits for exercising and exposure to sun, cold or heat (sauna, steam room). Exposure to any of these for the first 24 hours may increase short term redness, swelling, and/or itching at the injection site.

You should ask your doctor when make-up may be applied after your treatment. Using make-up too soon may increase the risk of infection or change in skin color.

Most **common treatment reactions** like bruising, swelling, redness, firmness, lumps/bumps, tenderness, change of skin color, pain, and itching go away on their own within a few days, but your doctor may choose to treat them with medications. Refer to section 7, RISKS.

### **When should I call my doctor?**

Call your doctor if you have any questions or concerns after your procedure.

Call your doctor immediately if you have:

- 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)
- Changes in your vision
- Pain which increases after your treatment
- Significant pain away from the injection site
- Significant whitening or darkening of the skin
- Any treatment reaction other than bruising, firmness, swelling, pain, tenderness, redness, lumps/bumps, itching, which occurs in the first two weeks
- Any treatment reaction in the injected area, including lump or hardening under the skin, that appears weeks or months after your injection.

The following are common reactions often seen after treatment with **dermal fillers**. They usually go away within 2 weeks. If you are concerned, or if they last more than 2 weeks, call your doctor:

- Bruising
- Swelling
- Redness
- Firmness
- Lumps/bumps
- Tenderness

- Change in skin color
- Pain
- Itching

## **9. ADDITIONAL INFORMATION**

In case you have any further questions, please contact Revance Therapeutics, Inc. at 877-3REV-NOW (877-373-8669).

[www.revance.com](http://www.revance.com)

RHA® Redensity™ is a registered trademark of TEOXANE S.A.

**TEOXANE S.A.** - Rue de Lyon, 105 – CH 1203 Geneva (Switzerland)