REVANESSE® LIPS + PATIENT INFORMATION SHEET

If you have any questions about your treatment with Revanesse® Lips +, or do not understand something about dermal filler injections, you should ask your doctor, or his or her staff, to explain. You should feel free to discuss your concerns openly with your doctor in order to better understand your options for treatment of the lips. A glossary is included at the end of this document to assist with any terms that are unfamiliar to you (Attachment 1 – Glossary includes items underlined in the text)

What is Revanesse® Lips +?

Revanesse® Lips + is hyaluronic acid dermal filler. Hyaluronic acid is a naturally occurring substance that is found within the body. Hyaluronic acid is produced by bacteria and purified for use as injectable soft tissue filler in order to enhance the appearance of lips. Revanesse® Lips+ is crosslinked with 1,4-butanediol diglycidyl ether (BDDE). BDDE is a chemical used to crosslink the hyaluronic acid in the dermal filler. Crosslinking is the process of chemically joining two or more molecules to form a network. The product also contains lidocaine.

The product should not be used in patients with a history of allergies or sensitivities to such material and you should not be treated with the product if you have a previous hypersensitivity to local anesthetics of the amide type, such as lidocaine.

The product is approved for submucosal implantation for lip augmentation in patients 22 years of age or older.

How does Revanesse® Lips + work?

Revanesse® Lips+ is a gel that is injected directly into the lips using an ultrafine needle to temporarily plump the lips for lip enhancement in adults 22 years of age or older. The lidocaine in the gel improves the comfort of the injection by reducing sensitivity to pain.

Are there any reasons why I should not (contraindications) receive the Revanesse® Lips + injection?

Your doctor will ask about your medical history to determine if Revanesse® Lips + is right for you. You should not be treated with Revanesse® Lips + if you:

- Have severe allergies which have resulted in anaphylaxis or have a history of

multiple severe allergies

- Have heightened immune responses to common allergens, especially inhaled allergens and food allergens (atopy).
- Have an allergy to natural rubber latex.
- Have an allergy to hyaluronic acid products,
- Have a history of allergies to Streptococcal proteins or have plans to undergo administration of graded doses of allergens (desensitization therapy) during treatment with Revanesse® Lips +;
- Have a history of hypersensitivity to lidocaine
- Have a history of bleeding disorders
- Are pregnant or nursing. Safety of Revanesse® Lips + has not been established in breastfeeding or pregnant women.
- Revanesse® Lips + should not be used in spaces other than the lip
- Have a history of hypertrophic scarring or keloid formation
- Have evidence of scars at the intended treatment sites
- Have acne and / or other inflammatory diseases of the skin, such as rosacea, seborrheic dermatitis, and psoriasis
- Have a cold sore (herpes virus) in the area of the lips
- Have acute or chronic skin disease, such as seborrheic dermatitis or rosacea, in or near the injection sites, or any infection or unhealed wound of the face
- Are under concomitant anticoagulant therapy, antiplatelet therapy, or have a history of bleeding disorders, clotting disorders such as hemophilia or connective tissue disorders such as systemic lupus erythematosus

You should never use Revanesse® Lips + in conjunction with a laser treatment, intense pulsed light, chemical peeling, dermabrasion treatments or any other procedure based on active dermal response, including over-the-counter (OTC) wrinkle products or prescription wrinkle treatments within 4 weeks (28 days) prior to treatment, as there is a possible risk of inflammation at the treatment site if these procedures are performed before treatment.

Are there any warnings I should be aware of?
If you are under the age of 22 you should not be treated with Revanesse® Lips +.

Limited safety and effectiveness information is available for this product for injection into the lips in men. The same product has been evaluated in men for the treatment of facial wrinkles and creases, (nasolabial folds).

Warning: One of the risks with using this product is unintentional injection into a blood vessel. The chances of this happening are 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. It is imperative that you contact your health care practitioner immediately if you have any adverse inflammatory reactions that persist for more than one week.

If you have an adverse inflammatory reaction, such as redness, pain and swelling that persist for one week or more after treatment with Revanesse® Lips +, you should report this immediately to your doctor.

Ask your doctor if you have questions about any of the side effects, and please tell your doctor or your doctor's staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel, whether or not you think these problems are related to the products.

Revanesse® Lips+ has the same formulation as Revanesse® Versa+ which is marketed in the US for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds. Revanesse® products are distributed in many foreign countries. The reported side effects are described in the rest of this brochure.

Is there anything else I can do to improve the appearance of my lips?

Your doctor will talk to you about other options, including the important risks and benefits. In addition, you may discuss your options with your regular health care provider if you have questions. Some other products that can be used to enhance your lips are:

- Topical products such as retinoids and peptides
- Other dermal fillers such as Restylane Silk, or Juvederm Volbella XC
- Fat Injections
- Botox
- Lip Implants
- Surgical correction

All devices and procedures involve a certain amount of risk. You should be aware of the expected and normal occurrences following dermal filler injections, as well as the possible complications.

What are the risks?

- Bleeding and Bruising: Bleeding is usually minimal and resolves within a few minutes. It is possible to have a bleeding episode from the injection of the local anesthesia or filler that requires treatment, but it is unusual. Bruising in the area is also an expected reaction and can take up to a week to resolve.
- Swelling: Swelling is also expected and may take several days to a week to resolve. It is unusual but medical treatment may be necessary if swelling is slow to resolve.
- Pain: Some discomfort is expected with injections but usually lasts less than a day.

Other risks that are less likely, but may occur, include the following**:**

- Acne-like skin eruptions
- Skin hypersensitivity (rash, prolonged swelling, redness, hardness)
- Skin infection
- Damage to nerves or blood vessels
- Skin lumpiness
- Skin abscess
- Scarring
- Skin necrosis (death of the skin)
- Hyperpigmentation (darkening of the skin)
- Reactivation of herpes infection (blisters or skin sores)

As with using any dermal filler, there is a risk of allergic reaction. If you have a very serious allergic reaction (anaphylactic shock) you may require emergency medical help and be at risk of death. Some symptoms of allergic reactions are:

- a rash
- having a hard time breathing
- wheezing when you breathe
- sudden drop in blood pressure
- swelling of the face
- fast pulse
- sweating
- dizziness or fainting
- inability to breathe without assistance
- a feeling of dread

One of the risks with using this product is unintentional injection into a blood vessel. The chances of this happening are 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 or blindness. These complications may 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.

Ask your doctor if you have questions about any of the side effects, and please tell your doctor or your doctor's staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel, whether or not you think these problems are related to the products.

How long does Revanesse® Lips+ last?

The length of time for lip augmentation and wrinkle correction varies. Many people maintain correction at six months. In the clinical study, sixty five percent of patients (46/71) treated with Revanesse® Lips+ rated themselves as much improved or very much improved at Month 6 after injection. Revanesse® Lips+ is absorbed by the body over time.

What happens before the procedure?

Your doctor will examine you and will explain the procedure and the potential risks. You will be asked about your health, your medical history, and the medications you take and have recently taken. You should advise your doctor of any of your concerns before the procedure, and discuss any questions related to the procedure.

What happens during the procedure?

The doctor will prepare the area to be treated. There is some pain associated with the injection of the product. You should discuss your concerns about injection related pain with your doctor.

The doctor will inject the filler, during which you may experience tenderness or a stinging sensation in the area of the injection. The procedure does not take long, often 15 to 30 minutes.

What should I expect after the procedure?

Following treatment, a cold compress or ice may be applied for any bruising or swelling at the injection site. You may also gently massage the area with constant pressure for several minutes. The most common side effects include: bruising, redness, swelling, pain, and itching.

You should contact your doctor if you experience redness, itching or pain at the injection site for recommendations for over-the-counter treatment (such as Tylenol, Motrin or Benadryl). Most side effects occur shortly after injection and go away within two weeks. If you experience a reaction that lasts longer than two weeks, or what you think may be a delayed reaction to the product, contact your doctor.

You should seek immediate medical attention if you develop symptoms such as unusual pain, vision changes, a white appearance of skin near the injection site (blanching) or any other unexpected symptoms. While rare, unexpected symptoms include unusual pain, vision changes, or any signs of a stroke (including sudden difficulty speaking, numbness or weakness in your face, arms, or legs, difficulty walking, visual changes, face drooping, severe headache, dizziness, or confusion) during or shortly after the procedure.

Additional side effects of dermal fillers less commonly reported include: infections, lumps and bumps, discoloration or change in pigmentation. It is rare for patients to have a delayed onset reaction or an infection such as cold sores (herpetic sores).

Rare, but serious risks, of dermal fillers include: scarring, blurred vision, partial vision loss, and blindness if the dermal filler is inadvertently injected into a blood vessel. In occasionally rare cases, there have been reports of unintentional injection of the product into a blood vessel with dermal filler products. It is recommended that doctors take care to avoid injection into blood vessels (especially around the forehead, nose and eye area) for these reasons. In rare cases patients have experienced allergic reaction to dermal fillers that may lead to a severe reaction (anaphylactic shock) that requires emergency medical help.

What did the clinical study show?

The company completed a US clinical study to evaluate Revanesse® Lips + for lip augmentation (PRO 2018-02). This study included 158 patients that were treated at 6 investigational sites. Up to 2 treatments approximately 1 month apart (initial treatment and up to 1 touch-up treatment) were allowed. The 158 patients were followed for 24 weeks after injection with either Revanesse® Lips + (80 patients) or a Comparator (another FDA-approved dermal filler, 78 patients) in the lips and lines around the lips.

The purpose of the study was to compare the safety and effectiveness profiles of Revanesse® Lips+ to an approved dermal filler for patients seeking lip augmentation. All patients returned for routine safety and effectiveness follow-up visits at 1, 2, 3, and 6 months after the last treatment during the primary safety and effectiveness phase. Safety was assessed by monitoring side effects through a patient diary and adverse events (AEs) monitored by the study doctor at all study visits. Safety was also assessed with vision evaluations performed by a trained evaluator. These vision assessments were performed prior to any treatment. These vision assessments were also repeated 30 minutes following any treatment and at all follow-up visits. In addition, safety was assessed with the following functional evaluations: Lip Function, Lip Sensation, Lip Texture, Lip Firmness, Lip Symmetry, Lip Movement/Function.

After 24 weeks patients were offered the option of retreatment with Revanesse® Lips+ to assess the safety of repeat treatment. There were 84 retreated patients, 94.0% of the patients participated for 6 months to complete the retreatment study, which lasted 8 months from the first patient enrolled to the last patient exiting the study.

The clinical studies demonstrated that Revanesse® Lips + is safe and has relatively the same performance as the FDA approved dermal filler (non-inferior to Comparator) in patients undergoing lip augmentation. Of the 158 patients in the study:

- 141 patients completed the study
  17 patients discontinued (left the study) early
- 73 patients did not continue into the retreatment study.

Adverse events, which include side effects reported by patients in the study and adverse effects reported by the study doctor were reported for 75 patients (75/80, 94%). The most frequently reported adverse events were injection site swelling (88%), injection site bruising (71%), injection site pain (21%), and facial asymmetry (15%). Most adverse events were reported as mild or moderate in intensity. Most adverse events lasted 30 days or less (Table 1 and Table 2).

Table 1. Overall Summary of Adverse Events after Treatment

Duration	Revanesse® Lips + Number of Events N=257
0-7 days	171 (67%)
8-14 days	40 (16%)
15-30 days	22 (9%)
>31 days	24 (9%)

Table 2. Duration of Adverse Events after Treatment by Adverse Event Type

Adverse Event	0-7 days	8-14 days	15-30 days	>31 days
	N=171 events (67%)	N=40 events (16%)	N=22 events (9%)	N=24 events (9%)
Injection site bruising	59/171 (78%)	14/40 (35%)	4/22 (18%)	0 (0%)
Injection site redness	7/171 (4%)	0 (0%)	1/22 (5%)	0 (0%)
Injection site mass	1/171 (1%)	0 (0%)	1/22 (5%)	4/24 (17%)
Injection site movement impairment	2/171 (1%)	1/40 (3%)	0 (0%)	0 (0%)
Injection site pain	14/171 (8%)	5/40 (13%)	4/22 (18%)	0 (0%)
Injection site itching	3/171 (2%)	0 (0%)	0 (0%)	0 (0%)
Injection site swelling	73/171 (43%)	15/40 (38%)	2/22 (9%)	4/24 (17%)
Facial asymmetry	6/171 (4%)	1/40 (3%)	4/22 (18%)	5/24 (21%)

Eighteen patients treated with Revanesse® Lips+ experienced 24 adverse events that lasted longer than 30 days. The longest duration was 4 instances of injection site mass lasting between 47 and 56 days, swelling lasting between 53 days and ongoing at the end of the study, and facial asymmetry lasting between 45 days and ongoing at the end of the study. Events related to the injection procedure included, swelling, lip asymmetry, injection site mass or lump and mucocele. The remaining adverse events were not treatment related. The severity of the adverse events experience by the patients is presented in Table 3.

Table 3. Number of Patients Experiencing an Adverse Event by Severity

Adverse Event	Mild N= 80 patients	Moderate N= 80 patients	Severe N= 80 patients
Injection site bruising	44 (55%)	12 (15%)	1 (1%)
Injection site redness	7 (9%)	1 (1%)	0 (0%)

Adverse Event	Mild N= 80 patients	Moderate N= 80 patients	Severe N= 80 patients
Injection site mass	6 (8%)	0 (0%)	0 (0%)
Injection site movement impairment	2 (3%)	0 (0%)	1 (1%)
Injection site pain	12 (15%)	4 (5%)	1 (1%)
Injection site itching	4 (5%)	0 (0%)	0 (0%)
Injection site swelling	58 (73%)	11 (14%)	1 (1%)

The data from the study also evaluated the impact of Revanesse® Lips+ injections on different subgroups of patients based on Fitzpatrick Skin Type (FST), which range from Type I- very pale to Type VI- very dark.

The Fitzpatrick Skin Type (FST) Categories:

Type	Description of Characteristics
Type I	This FST skin type always burns, never tans (pale white; blond or red hair; blue, gray eyes; freckles)
Type II	This FST skin type usually burns, tans minimally (white; blond, brown or red hair; blue, green, or hazel eyes)
Type III	This FST skin type sometimes has a mild burn, tans uniformly (cream white; yellowish; any hair color or brown eyes)
Type IV	This FST skin type burns minimally, always tans well (light brown; olive; dark brown to black hair)
Type V	This FST skin type very rarely burns, tans very easily (brown)
Type VI	This FST skin type never burns, always tans (deeply pigmented dark brown to darkest brown, black in complexion)

In the study the incidence and severity of adverse events in 53 patients with Fitzpatrick Skin Types IV – VI (27 patients were FST IV, 9 patients were FST V, and 17 patients were FST VI) was similar to that reported in the general population and no unique adverse events associated with these patient subgroups were observed.

The study had no incidences of darkening of the skin (hyperpigmentation), or formation of excessive scarring (keloids) and/or thick scarring (hypertrophic scars). Hyperpigmentation was not observed in the Revanesse® Lips + study including the 53 patients with Fitzpatrick Skin Types IV – VI.

It is important to discuss your history of scarring with your doctor and refer to the information provided in these tables for your FST.

Limited safety and effectiveness information is available for this product for injection into the lips in men. In prior studies of Revanesse® products there was no gender related difference in safety and effectiveness. Revanesse® products have been evaluated in men for the treatment of facial wrinkles and creases, (nasolabial folds).

Three patients had adverse events and had treatment with hyaluronidase. All three patients who had treatment with hyaluronidase experienced injection site swelling, which was sometimes severe. One patient experienced severe swelling, bruising, pain, and movement impairment which resolved. This patient also had injection site mass and mild lip asymmetry which resolved. Two of the three patients chose to exit the study due to the adverse effects.

Eighty-four patients were retreated with Revanesse Lips+. Most of the 84 retreated patients had at least one adverse event (62 patients or 74%, Table 4). Most of the adverse events were mild (92%) as shown in Table 5. The following was reported:

Table 4. Adverse Events after Retreatment

Adverse Event	Total (N = 84 patients) number of patients (%)
Patients with at least 1 adverse event	62 (74%)
Injection site bruising	40 (48%)
Injection site redness	6 (7%)
Injection site mass	6 (7%)
Injection site pain	10 (12%)
Injection site swelling	48 (57%)
Facial asymmetry	5 (6%)

Table 5. Adverse Events with Severity after Retreatment

Adverse Event	Severity	Total (N=114 events)
Total reported Adverse Events	Mild	105 (92%)
	Moderate	9 (8%)
	Severe	0 (0%)
Injection site bruising	Mild	38 (33%)

Adverse Event	Severity	Total (N=114 events)
	Moderate	2 (2%)
Injection site redness	Mild	6 (5%)
Injection site mass	Mild	6 (5%)
Injection site pain	Mild	8 (7%)
	Moderate	2 (2%)
Injection site itching	Mild	1 (1%)
Injection site swelling	Mild	44 (39%)
	Moderate	4 (4%)

The average change in Lip Fullness Grading Scale (LFGS) from before injection to Month 2 after injection in overall fullness of both lips together was non-inferior (approximately the same performance) to the approved product Comparator.

Will I need more than one treatment to achieve my desired results?

You should discuss your treatment goals and plan with your doctor. In the clinical study, 46% (38/80) of patients treated with Revanesse® Lips+ received a touch-up treatment 1 month after the initial treatment in order to achieve the desired results. Of the 84 patients that entered the retreatment study, 68 of the 84 patients received Revanesse® Lips+ in the initial treatment study (68/84, 81%), while the others had received their first treatment with the Comparator.

When to Call your Doctor

Call your doctor immediately if you have:

- Changes in your vision
- Signs of a stroke (including sudden difficulty speaking, numbness of 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

Be sure to call your doctor if you have:

- Significant pain away from the injection site
- Any Redness and/or visible swelling that lasts for more than a few days
- Any side effect that occurs weeks or months after treatment
- Any other Symptoms that cause you concern

Patient Assistance Information:

If you have further questions, please contact:

Prollenium Medical Technologies, Inc.
1-866-353-3015 or +1-905-508-1469 (internationally) 9 AM and 5 PM EST Monday through Friday.

Attachment 1 - Glossary

- Abscess - a collection of pus that has built up within the tissue of the body.
- Anaphylaxis – a severe, potentially life-threatening allergic reaction. It can occur within seconds or minutes of exposure to something you're allergic to, such as peanuts or bee stings.
- Anesthetic – a substance that reduces sensitivity to pain.
- Anticoagulant - the process of hindering the clotting of blood
- Antiplatelet therapy - group of medicines that stop blood cells (called platelets) from sticking together and forming a blood clot.
- Concomitant medications – medications taken at the same time.
- Hyaluronic acid (HA) – a polysaccharide (sugar) that is naturally in the body. It keeps skin moisturized and soft. HA fillers, Including Revanesse® Lips +, are a modified form of the HA that is naturally in your body.
- Hyaluronidase – an enzyme used to breakdown HA
- Hypersensitivity – an undesirable reactions produced by the normal immune system, including allergies and autoimmunity
- Hyperpigmentation – is a common, usually harmless condition in which patches of skin become darker in color than the normal surrounding skin
- Hypertrophic Scarring - is a thickened, wide, often raised scar that develops where skin is injured. Scars are common during the wound healing process, but a hypertrophic scar is a result of an abnormal response to a trauma or injury.
- Inflammation - refers to your body's process of fighting against things that harm it, such as infections, injuries, and toxins, in an attempt to heal itself. When something damages your cells, your body releases chemicals that trigger a response from your immune system
- Keloids - a type of raised scar. They occur where the skin has healed after an injury. They can grow to be much larger than the original injury that caused the scar.
- Lidocaine – a synthetic compound used as a local anesthetic to decrease pain
- Mucocele - a salivary gland cyst, which contains mucous content.
- NSAID – Nonsteroidal anti-inflammatory drug, such as ibuprofen
- Pigmentation - Skin pigmentation disorders affect the color of your skin.
- Peptides - Peptides are amino acids that make up certain proteins needed by the skin. More specifically, collagen is made of three polypeptide chains, so adding peptides can stimulate your skin to make collagen
- Psoriasis - is a skin disease that causes red, itchy scaly patches, most commonly on the knees, elbows, trunk and scalp
- Retinoid - Retinoids reduce fine lines and wrinkles by increasing the production of collagen.
- Rosacea - is a common skin condition that causes redness and visible blood vessels in your face.
- Seborrheic dermatitis - is a common skin condition that mainly affects your scalp. It causes scaly patches, red skin and stubborn dandruff.
- Sensitivity – the quality of being tender or easily irritated.
- Site mass - abnormal growths of tissue that can be malignant (cancerous) or

benign (harmless)

- Systemic lupus erythematosus – an autoimmune disease that occurs when your body's immune system attacks your own tissues and organs.
- Touch-up – an additional injection of a small amount of Revanesse® Lips + usually given two weeks after treatment, if necessary to achieve the desired result.