REVANESSE ULTRA PATIENT INFORMATION SHEET

If you have any questions about your treatment with Revanesse Ultra, 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 facial wrinkles and creases (nasolabial folds).

What is Revanesse Ultra?

Revanesse Ultra is hyaluronic acid dermal filler. Hyaluronic acid is a naturally occurring substance that is found within the body. It may be produced by bacteria and purified for use as injectable soft tissue filler in order to correct the appearance of facial wrinkles and creases, (nasolabial folds). The product is approved for use in the U.S. by the Food and Drug Administration for the cosmetic treatment of facial wrinkles and creases.

How does Revanesse Ultra work?

Revanesse Ultra is an injection into the facial tissue to improve the appearance of facial wrinkles and creases, such as nasolabial folds. The injection results in a smoothing effect. The product is intended for individuals 22 years of age or more seeking correction of their facial wrinkles and creases.

Are there any warnings I should be aware of?

If you have an adverse inflammatory reaction, such as redness, pain and swelling that persist for one week or more after treatment with Revanesse Ultra, you should report this immediately to your doctor. If you are under the age of 22 you should not be treated with Revanesse Ultra.

Warning: 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.

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

You should not be treated with Revanesse Ultra if you:

- are pregnant or breastfeeding, as the safety of these products for use during pregnancy, or in women who are breastfeeding, has not been studied
- 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 allergic history including;
  - severe allergic reactions (anaphylaxis),
  - heightened immune responses to common allergens, especially inhaled allergens and food allergens (atopy),
  - allergy to natural rubber latex,
  - allergy to hyaluronic acid products,
  - Streptococcal proteins or have plans to undergo administration of graded doses of allergens (desensitization therapy) during treatment with Revanesse Ultra.
- 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 Ultra in conjunction with a laser, intense pulsed light, chemical peeling or dermabrasion treatments, or with 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.

Is there anything else I can do to improve the appearance of my facial wrinkles and creases?

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 correct your facial wrinkles and creases are:

- Topical products such as retinoids, peptides, and silicones
- Other dermal fillers such as Restylane® or Juvederm®
- Semi-permanent fillers such as Radiesse® and Sculptra®
- Botox®
- Dermabrasion or laser abrasion
- Surgical correction

All devices and procedures involve a certain amount of risk. You should be aware of the expected and normal occurrences following tissue 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 sensitivity (rash, itching, tenderness)
- Skin infection
- Damage to nerves or blood vessels
- Skin lumpiness
- 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 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 or blindness.

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 Ultra last?
The length of time for wrinkle correction varies. Many people maintain correction at six months, and /or continued to be happy with the level of correction at six months or more. Revanesse Ultra 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, allergic reaction that may lead to a severe reaction (anaphylactic shock) that requires emergency medical help.

What did the clinical study show?

The clinical study demonstrated that Revanesse Ultra is safe and approximately the same performance as an FDA approved dermal filler (non-inferior to comparator) in patients undergoing correction of facial wrinkles and creases (nasolabial folds). The patients in the main study were offered retreatment with Revanesse Ultra if they had returned to their previous wrinkle severity or needed optimal correction at six months post treatment. Of the 163 patients in the study:

- 4 patients discontinued the study early
- 88 did not continue to retreatment
  - 36 maintained optimal correction at 6 months
  - 32 were satisfied with the results at 6 months
  - 7 did not continue for personal reasons
  - 8 were not satisfied with the results
  - 4 did not continue because they experienced an adverse event
  - 1 was not eligible for retreatment
- 71 patients were retreated

The 71 patients that were retreated showed improvement in the Wrinkle Severity Rating Score (WSRS), a patient evaluation (Patient Global Aesthetic Improvement or pGAI), and an evaluation by the doctor (Investigator Global Aesthetic Improvement or iGAI) at the end of the retreatment study (52 weeks). The study did not demonstrate any safety concerns with retreatment of Revanesse Ultra for men or women at least 22 years of age with nasolabial folds

(NFLs) with a moderate or severe Wrinkle Severity Rating Score (WSRS) score at baseline who had previously received 1 or 2 treatments with Revanesse Ultra or an FDA approved marketed dermal filler.

In the clinical study the most commonly observed side effects were swelling, redness, pain, bruising, headache, tenderness, lump formation, and itching at the injection site. These are typically mild in severity and typically resolved in less than 7 days. These side effects are expected with most dermal filler products.

The company completed three US clinical studies to evaluate Revanesse Ultra in the correction of nasolabial folds. In the main study (SYM2014-02 Main Study) 163 patients were followed for 24 weeks after injection with Revanesse Ultra injectable gel in one nasolabial fold (NLF) and a Comparator in the other NLF. In the retreatment study (SYM2014-02 Retreatment), 71 patients from the main study were retreated with Revanesse Ultra and followed for a total of 52 weeks. In the third study (SYM2016-02), 100 patients were treated with Revanesse Ultra in one NLF, and the product containing lidocaine in the other NLF and were followed for 24 weeks. The data from these studies was combined to evaluate the impact of Revanesse Ultra injections on different subgroups based on race and ethnicity. The adverse event incidence was evaluated by race and 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)

The combined studies had no incidences of darkening of the skin (hyperpigmentation), or formation of excessive scarring (keloids) and/or thick scarring (hypertrophic scars).

There were 97 injections of Revanesse Ultra in the Fitzpatrick Skin Type IV-VI category, with 308 injections in the I-III category. The percentage of incidences of each type of adverse event was greater for the I-III FST (pale to cream white or yellowish) than for the IV-VI FST (olive or light brown skin to very dark brown).

There were 42 injections of Revanesse Ultra in the Fitzpatrick Skin Type V-VI with 363 injections in the I-IV category. The percentage of incidences of each AE was greater for the I-IV FST (pale to olive or light brown) than for the V-VI FST (brown to very dark brown).

The incidence of swelling for the Combined Analysis (SYM 2014-02 Main, SYM 2014-02 Retreatment, and SYM 2016-02) was greatest in the FST I:

I 50.00% (There were 4 injections in FST I skin type of which 2 had swelling)
II 38.14% (There were 118 injections in FST II skin type of which 45 had swelling)
III 34.41% (There were 186 injections in FST III skin type of which 64 had swelling)
IV 25.45% (There were 55 injections in FST IV skin type of which 14 had swelling)
V 31.82% (There were 22 injections in FST V skin type of which 7 had swelling)
VI 20.00% (There were 20 injections in FST VI skin type of which 4 had swelling)

The incidence of injections site swelling in the Main Study (SYM 2014-02 Main) was greatest in FST V, of the four injections in patients that were FST V there were three incidences of swelling at the injection site:

I 66.67% (There were 3 injections in FST I skin type of which 2 had swelling)
II 50% (There were 50 injections in FST II skin type of which 25 had swelling)
III 45.78% (There were 83 injections in FST III skin type of which 38 had swelling)
IV 43.75% (There were 16 injections in FST IV skin type of which 7 had swelling)
V 75% (There were 4 injections in FST V skin type of which 3 had swelling)
VI 28.57% (There were 7 injections in FST VI skin type of which 2 had swelling)

In the Retreatment Study (SYM 2014-02 Retreatment) the most injection site swelling was observed in the FST IV with 4 incidences out of 12 injections:

I 0% (There were 0 injections in FST I skin type of which 0 had swelling)
II 31.48% (There were 54 injections in FST II skin type of which 17 had swelling)
III 30% (There were 60 injections in FST III skin type of which 18 had swelling)
IV 33.33% (There were 12 injections in FST IV skin type of which 4 had swelling)
V 16.67% (There were 6 injections in FST V skin type of which 1 had swelling)
VI 20% (There were 10 injections in FST VI skin type of which 2 had swelling)

In all three studies there were no incidences of darkening of the skin (hyperpigmentation), excessive scarring (keloids) and/or thick scarring (hypertrophic scars). It is important to discuss your history of scarring with your doctor, and refer to the information provided in these tables for your FST.

In these studies, most adverse events lasted 30 days or less.

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.