RENÚ®

INSTRUCTIONS FOR USE

DESCRIPTION

RENÚ® Calcium Hydroxylapatite (CaHA) Soft Tissue Filler Implant is a sterile, semi-solid, cohesive implant. The principle durable component is synthetic calcium hydroxylapatite. The semi-solid nature is created by suspending the calcium hydroxylapatite particles in a durable high yield strength thixotropic gel. The aqueous gel carrier consists of sodium carboxymethylcellulose, glycerin, and phosphate buffer. The carrier resorbs in vivo so that the calcium hydroxylapatite remains at the site of implantation, providing a scaffold for local tissue infiltration. This cellular infiltrated hydroxyapatite scaffold provides the long-term non-permanent restoration and augmentation.

INTENDED USE / INDICATIONS

RENÚ® is indicated for vocal fold medialization, vocal fold insufficiency, subdermal implantation for the correction of moderate to severe facial wrinkles and folds and for the restoration or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus that may be improved by injection of a soft tissue-volumizing agent. RENÚ replaces, fills, and augments the size of the displaced or deformed tissue so that it may enhance the structure needing correction.

CONTRAINDICATIONS

- Contraindicated in patients with known hypersensitivity to any of the components.
- Contraindicated in patients with severe allergies manifested by a history of anaphylaxis, or history or presence of multiple severe allergies.
- Contraindicated in the presence of acute and/or chronic inflammation or infection when these involve the area to be treated.
- Contraindicated in the presence of foreign bodies, such as liquid silicone or other particulate materials.
- Contraindicated in patients prone to developing inflammatory skin conditions or those patients with a tendency for developing hypertrophic scars.
- Contraindicated in patients with inadequate coverage of healthy, well vascularized tissue.
- Contraindicated in patients with systemic disorders which cause poor wound healing or will lead to tissue deterioration over the implant.
- Contraindicated in bilateral laryngeal paralysis and vocal disorders of psychogenic or emotional origin.

WARNINGS

- Special care should be taken when injecting soft tissue fillers to avoid injection into blood vessels/vasculature. Rare but serious adverse events associated with intravascular injection of soft tissue fillers have been reported. Associated complications can be serious, and may be permanent. Complications can include vision abnormalities/impairment, blindness, stroke, temporary scabs, platelet aggregation, vascular occlusion, infarction, hemolysis, embolization, embolic phenomena, necrosis, ischemia, cerebral ischemia or cerebral hemorrhage leading to stroke, permanent scarring of the skin, and damage to underlying facial structures. Immediately stop the injection if a patient exhibits any of the following: changes in 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 (blanching) of the skin, or unusual pain during or shortly after treatment. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care practitioner should an intravascular injection occur.
- Airway obstruction may result from aggressive vocal fold injection, over-injection, or laryngeal edema from trauma and manipulation of the larynx. Under no circumstance should excessive force be used to overcome resistance during injection, since sudden and uncontrolled over injection may occur. Airway obstruction following vocal fold injection can occur immediately, or at any time up to seven (7) days following injection. Airway obstruction can often be prevented by minimizing laryngeal trauma and manipulation during the injection and can be treated by administering intraoperative and postoperative steroid treatment.
- RENÚ should not be injected into the airway. Confirm placement of needle tip visually before initiating the injection.
- With any implant materials, possible adverse reactions that may occur include, but are not limited to the following: inflammation, infection, fistula formation, inadequate healing, skin discoloration, vocal fold paralysis, breathing difficulty, swelling of throat, implant extrusion, poor phonatory function post injection, permanent hoarseness due to inadequate or excessive augmentation.
- Do not inject superficially. Implantation could lead to complications such as infections, extrusion, tissue erosion, nodule formation and induration.
- Viable tissue is required for effective injection. Scar tissue, cartilage, and significantly compromised tissue may not respond to treatment. If possible, avoid passing through these tissue types when advancing the injection needle.
- Should not be injected into organs or other structures which could be damaged by space occupying implant. Some injectable implant devices have been associated with hardening of the tissues at an injection site, migration from an injection site to other parts of the body, and/or allergic or autoimmune reactions. Based on clinical usage, animal studies, and supporting literature, this has not been observed nor is it expected with RENÚ.
- Do not overcorrect (overfill) a deficiency because the depression should gradually improve within several weeks as the treatment effect of RENÚ occurs (see INDIVIDUALIZATION OF TREATMENT). Inject the product slowly and apply the least amount of pressure necessary.
- There have been published reports of nodules associated with the use of CaHA based injectable implant injected into the lips. The safety and effectiveness for use in the lips has not been established.
- There have been published reports of tissue necrosis associated with the use of CaHA based injectable implants.
- Injection procedure reactions have been observed consisting mainly of short-term (i.e., < 7days) bruising, redness and swelling.

PRECAUTIONS

- Therapy should be delayed at least six (6) months following the onset of vocal fold paralysis and/or until an adequate trial of voice rehabilitation has been given.
- Vocal fold injections of RENÚ should only be performed by physicians who have appropriate training, experience with diagnostic and therapeutic otolaryngology procedures including vocal fold injection, are knowledgeable about the anatomy at and around the site of injection, and after fully familiarizing themselves with the product and the entire package insert.
- Tissue injections of RENÚ should only be performed by health care practitioners who have appropriate training, experience with diagnostic and therapeutic tissue injections, expertise in the correction of volume deficiencies in patients with human immunodeficiency virus, are knowledgeable about the anatomy at and around the site of injection, and after fully familiarizing themselves with the product and the entire package insert.
- Do not bend or attempt to straighten a bent 24 gauge needle; discard it and replace with a new needle**.** Renú Transoral Needles have a malleable 16G cannula, however care should be taken to avoid placing undue pressure upon or bending any portion of the 24G needle to avoid needle breakage.
- Do not over-inject the RENÚ into the tissue. RENÚ can be easily added in subsequent injections but cannot be easily removed. Inject the product slowly and apply the least amount of pressure necessary.
- In some cases, initial treatment with RENÚ may not be effective and additional injections may be indicated.
- RENÚ injection procedure and the associated instrumentation procedures have small but inherent risks of infection and/or bleeding like similar minimally invasive procedures. The patient may experience slight discomfort during and following the procedure. The usual precautions associated with vocal fold and tissue injection procedures, should be followed.
- As with any surgical or implantation procedure, Renú carries a risk of infection. Care should be taken during injection of Renú to avoid infection.
- RENÚ is supplied sterile in a sealed foil pouch and is intended for **single use only**. Do not store partially used syringes for later use. Reuse of a syringe or needle at a later time, or on multiple patients, could be biohazardous and pose a risk of contamination and infection.
- **Do not re-sterilize**; re-sterilized device safety and performance has not been validated.
- The foil pouch should be carefully examined to verify that neither the pouch nor the RENÚ syringe has been damaged during shipment. Do not use if the foil pouch is compromised or the syringe has been damaged. Do not use if the syringe end cap or syringe plunger has been displaced.
- Use of needles with a nominal inner diameter smaller than 0.26mm and/or longer than 1.5" (38.1mm) increase the incidence of needle occlusion.
- Safety and efficacy of Renú has not been evaluated when an anesthetic is mixed into the product prior to injection.
- If significant resistance is encountered when pushing the plunger, under no circumstance should excessive force be used to overcome resistance since the injection needle may disconnect from the Renú syringe. It may be necessary to try a different needle or replace both the syringe and needle.
- The CaHA particles of the injectable implant are radiopaque and are clearly visible on CT Scans and may be visible in standard, plain radiography. In a radiographic study of 58 patients, there was no indication that CaHA based injectable implants potentially masked abnormal tissues or were interpreted as tumors in CT Scans (Carruthers, Liebeskind, et al., 2008). Patients need to be informed of the radiopaque nature of CaHA based injectable implant so that they can inform their primary care health professionals as well as radiologists.
- The safety of RENÚ in patients with increased susceptibility to keloid formation and hypertrophic scarring has not been studied.
- Safety and efficacy of RENÚ during pregnancy, in breastfeeding or lactating females, or in patients under 18 years has not been established.
- Safety and effectiveness in the periorbital area has not been established.
- Safety and effectiveness of Renú with concomitant dermal therapies such as epilation, UV irradiation, or laser, mechanical or chemical peeling procedures has not been evaluated.
- Patients who are using medications that can prolong bleeding, such as aspirin or warfarin, may, as with any injection, experience increased bruising or bleeding at the injection site.
- Universal precautions must be observed during the injection procedure.
- The injection session must be conducted with aseptic technique.

- After use, treatment syringes and needles may be potential biohazards. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal requirements.
- The patient should be informed that he or she should minimize exposure of the treated area to extensive sun or heat exposure for approximately 24 hours after treatment or until any initial swelling and redness has resolved.
- No studies of interactions of RENÚ with drugs or other substances or implants have been conducted.
- Health care practitioners are encouraged to discuss all potential risks of soft tissue injection with each patient prior to treatment to ensure that patients are aware of signs and symptoms of potential complications.
- Suboptimal RENÚ injection can occur and may require surgical removal. Excessive injection resulting in persistent over-medialization may occur. Although a rare complication, superficial injection into the subepithelial space can also occur. Partial or total removal of the implant can be performed following standard surgical techniques including through phonomicrosurgery operative techniques.
- The RENÚ vocal fold injection procedure has a small but inherent risk of infection. Post injection infections which do not respond to standard medical treatment are uncommon. However, if an infection is unresponsive to treatment and removal of the implant is determined to be required, partial or total removal of the implant can be performed following standard surgical techniques including through phonomicrosurgery operative techniques.
- The RENÚ aesthetics injection procedure has a small but inherent risk of infection. Post injection infections which do not respond to standard medical treatment are uncommon. However, if an infection is unresponsive to treatment and removal of the implant is determined to be required, partial or total removal of the implant can be performed following standard surgical techniques.
- Patient movement during the RENÚ injection procedure may cause superficial injection into the subepithelial space. Although a rare complication, partial or total removal of the implant can be performed following standard surgical techniques including through phonomicrosurgery operative techniques. Confirm placement of needle tip visually before initiating the injection.

INDIVIDUALIZATION OF TREATMENT

Medical examination, including medical history and diagnostic testing, should be conducted to determine if the patient is an appropriate candidate for treatment with RENÚ. The outcome of treatment with Calcium Hydroxylapatite may vary between patients. In some patients, additional treatments may be necessary to improve and/or maintain the level of response. If symptoms persist after treatment, additional injections may be performed but only after sufficient time has passed to evaluate the patient. The patient should not be re-injected sooner than seven days after the previous treatment. Typical correction can be expected to last from 9 to 18 months.

MRI INFORMATION

RENÚ® Implant is magnetic resonance (MR) safe. There are no known hazards resulting from exposure of the RENÚ devices to any MR environment.

DIRECTIONS FOR USE FOR RENÚ SOFT TISSUE VOLUMIZING FILLER, RENÚ COSMETIC, RENÚ LIPOATROPHY AESTHETIC CORRECTION, RENÚ VOLUME FILLER, RENÚ VOCAL FOLD MEDIALIZATION, RENÚ VOICE, AND RENÚ VOICE INSUFFICIENCY:

PERCUTANEOUS VOCAL FOLD INJECTION
(RENÚ VOCAL FOLD MEDIALIZATION, RENÚ VOICE, AND RENÚ VOICE INSUFFICIENCY)

The following is required for the vocal fold injection procedure:

- RENÚ® Implant syringe(s)
- Needle(s) with Luer-loc fittings, ≤ 1.5" (38.1mm) in length, and a nominal inner diameter ≥ 0.26mm (e.g., 27G thin wall, 26G, or 25G)
- Nasopharyngoscope

CAUTION: Universal precautions must be observed during the injection procedure.

CAUTION: The injection session must be conducted with aseptic technique.

1. Prepare the syringe(s) of RENÚ®, injection needles(s), and nasopharyngoscope equipment before the surgical injection using facility medical practices for a nasopharyngoscope examination. A new injection needle may be used for each syringe or the same injection needle may be connected to each new syringe. **In all cases, when the injection needle is attached to the syringe, the needle must be securely tightened to the syringe (the needle must be tightened until the squared section of the needle's Luer fittings contacts the syringe) and be primed with RENÚ®.**

CAUTION: The foil pouch should be carefully examined to verify that neither the pouch nor the RENÚ syringe has been damaged during shipment. Do not use if the foil pouch is compromised or the syringe has been damaged. Do not use if the syringe end cap or syringe plunger has been displaced.

CAUTION: RENÚ is supplied sterile in a sealed foil pouch and is intended for **single use only**. Do not store partially used syringes for later use. Reuse of a syringe or needle at a later time, or on multiple patients, could be biohazardous and pose a risk of contamination and infection.

CAUTION: Do not re-sterilize; re-sterilized device safety and performance has not been validated.

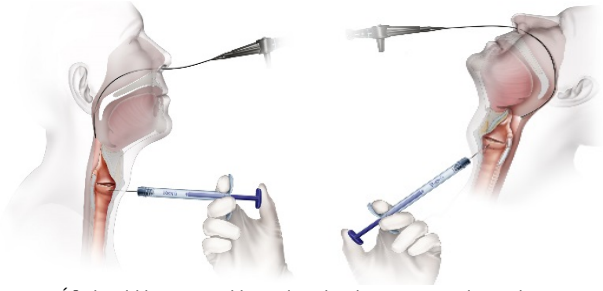
2. Remove foil pouch from the carton. The pouch can be opened and the syringe of RENÚ® placed onto the sterile field when required. **NOTE**: ***There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is not an indication of a product issue.***

CAUTION: Health care practitioners are encouraged to discuss all potential risks of soft tissue injection with each patient prior to treatment to ensure that patients are aware of signs and symptoms of potential complications.

3. Prepare patient for nasopharyngoscopy and anesthetize using standard methods. Local anesthesia is not required but may be utilized at the injection site.
4. Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. If excess RENÚ® is on the surface of the Luer-loc fittings, it will need to be wiped clean with sterile gauze. The injection needle can then be twisted onto the Luer-loc fitting of the syringe of RENÚ®.

CAUTION: Use of needles with a nominal inner diameter smaller than 0.26mm and/or longer than 1.5" (38.1mm) increase the incidence of needle occlusion.

5. **The needle must be tightened securely to the syringe and primed with RENÚ®.** Slowly push the syringe plunger until RENÚ® extrudes from the end of the injection needle. If leakage is noted at the Luer fitting, it may be necessary to remove the needle and clean the surfaces of the Luer fitting or, in some cases, replace both the syringe and the injection needle.
6. Place the nasopharyngoscope to precisely visualize the needle position and RENÚ® injection volume during augmentation.



7. RENÚ® should be injected lateral to the thyroarytenoid muscle.

WARNING: Viable tissue is required for effective injection. Scar tissue, cartilage, and significantly compromised tissue may not respond to treatment. If possible, avoid passing through these tissue types when advancing the injection needle.

8. Extend the patient's neck if possible and identify the following external landmark: the cricoid and inferior border of the thyroid cartilage and thyroid notch. Because the superior surface of the vocal fold lies at approximately half the distance between the superior notch and the inferior border of the thyroid cartilage, injection is placed below this level but above the inferior thyroid cartilage margin. Trans-cartilaginous injection is used unless cartilage calcification prevents it, in which case needle placement is through the cricothyroid membrane.

WARNING: RENÚ should not be injected into the airway. Confirm placement of needle tip visually before initiating the injection.

WARNING: Special care should be taken when injecting soft tissue fillers to avoid injection into blood vessels/vasculature. Rare but serious adverse events associated with intravascular injection of soft tissue fillers have been reported. Associated complications can be serious and may be permanent. Complications can include vision abnormalities/impairment, blindness, stroke, temporary scabs, platelet aggregation, vascular occlusion, infarction, hemolysis, embolization, embolic phenomena, necrosis, ischemia, cerebral ischemia or cerebral hemorrhage leading to stroke, permanent scarring of the skin, and damage to underlying facial structures. Immediately stop the injection if a patient exhibits any of the following: changes in 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 (blanching) of the skin, or unusual pain during or shortly after treatment. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care practitioner should an intravascular injection occur.

WARNING: Do not overcorrect (overfill) a deficiency because the depression should gradually improve within several weeks as the treatment effect of RENÚ occurs (see INDIVIDUALIZATION OF TREATMENT). Inject the product slowly and apply the least amount of pressure necessary.

CAUTION: Do not over-inject the RENÚ into the tissue. RENÚ can be easily added in subsequent injections but cannot be easily removed. Inject the product slowly and apply the least amount of pressure necessary.

9. With needle location visually confirmed through nasopharyngoscope, slowly push the plunger shaft of the RENÚ® syringe to start the injection.
10. After the initial injection, the patient should be asked to phonate and cough to disperse RENÚ®. Additional RENÚ® is injected until the vocal folds touch during phonation at a position midway between the anterior commissure and the vocal processes.

WARNING: Airway obstruction may result from aggressive vocal fold injection, over-injection, or laryngeal edema from trauma and manipulation of the larynx. Under no circumstance should excessive force be used to overcome resistance during injection, since sudden and uncontrolled over injection may occur. Airway obstruction following vocal fold injection can occur immediately, or at any time up to seven (7) days following injection.

Airway obstruction can often be prevented by minimizing laryngeal trauma and manipulation during the injection and can be treated by administering intraoperative and postoperative steroid treatment.

CAUTION: If significant resistance is encountered when pushing the plunger, under no circumstance should excessive force be used to overcome resistance since the injection needle may disconnect from the Renú syringe. It may be necessary to try a different needle or replace both the syringe and needle.

11. Some tissue planes may be difficult to inject. If significant resistance is encountered when pushing the plunger, pull back the injection needle about one (1) to three (3) millimeters (with the needle still in the vocal fold tissue) and push the plunger again slowly. If significant resistance is still encountered, it may be necessary to pull the needle entirely out of the injection site and inject in a new position.
12. The number of injection attempts is at the discretion of the treating physician and must take into account the patient's tolerance of the procedure and discomfort.

CAUTION: After use, treatment syringes and needles may be potential biohazards. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal requirements.

13. Dispose of the opened syringes, as well as used injection needles.
14. Instruct the patient to not use his/her voice for three days so as to minimize any potential extrusion of the Renú Implant through the injection site.

CAUTION: The RENÚ vocal fold injection procedure has a small but inherent risk of infection. Post injection infections which do not respond to standard medical treatment are uncommon. However, if an infection is unresponsive to treatment and removal of the implant is determined to be required; partial or total removal of the implant can be performed following standard surgical techniques including through phonomicrosurgery operative techniques.

15. A course of antibiotics maybe prescribed, as appropriate.

ORAL VOCAL FOLD INJECTION

(RENÚ VOCAL FOLD MEDIALIZATION, RENÚ VOICE, AND RENÚ VOICE INSUFFICIENCY)

The following is required for the vocal fold injection procedure:

- RENÚ® Implant syringe(s)
- Renú Transoral Needle or needle(s) with Luer-loc fittings, ≤ 1.5" (38.1mm) in length, and a nominal inner diameter ≥ 0.26mm (e.g., 27G thin wall, 26G, or 25G)
- Nasopharyngoscope

CAUTION: Universal precautions must be observed during the injection procedure.

CAUTION: The injection session must be conducted with aseptic technique.

1. Prepare the syringes of RENÚ®, injection needles(s), and nasopharyngoscope equipment before the surgical injection using facility medical practices for a nasopharyngoscope examination. A new injection needle may be used for each syringe or the same injection needle may be connected to each new syringe. **In all cases, when the injection needle is attached to the syringe of RENÚ®, the needle must be tightened securely to the syringe (the needle must be tightened until the squared section of the needle's Luer fittings contacts the syringe) and be primed with RENÚ®.**

CAUTION: The foil pouch should be carefully examined to verify that neither the pouch nor the RENÚ syringe has been damaged during shipment. Do not use if the foil pouch is compromised or the syringe has been damaged. Do not use if the syringe end cap or syringe plunger have been displaced.

CAUTION: RENÚ is supplied sterile in a sealed foil pouch and is intended for **single use only**. Do not store partially used syringes for later use. Reuse of a syringe or needle at a later time, or on multiple patients, could be biohazardous and pose a risk of contamination and infection.

CAUTION: Do not re-sterilize; re-sterilized device safety and performance has not been validated.

2. Remove foil pouch from the carton. The pouch can be opened and the syringe of RENÚ® placed onto the sterile field when required. **NOTE**: ***There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is not an indication of a product issue.***

CAUTION: Health care practitioners are encouraged to discuss all potential risks of soft tissue injection with each patient prior to treatment to ensure that patients are aware of signs and symptoms of potential complications.

3. Prepare patient for nasopharyngoscopy and anesthetize using standard methods. Local anesthesia is not required but may be utilized at the RENÚ® injection site.
4. Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. If excess RENÚ® is on the surface of the Luer-loc fittings, it will need to be wiped clean with sterile gauze. The injection needle can then be twisted onto the Luer-loc fitting of the syringe.

CAUTION: Use of needles with a nominal inner diameter smaller than 0.26mm and/or longer than 1.5" (38.1mm) increase the incidence of needle occlusion.

CAUTION: Do not bend or attempt to straighten a bent 24 gauge needle; discard it and replace with a new needle. Renú Transoral Needles have a malleable 16G cannula, however care should be taken to avoid placing undue pressure upon or bending any portion of the 24G needle to avoid needle breakage.

5. **The needle must be tightened securely to the syringe (until the squared section of the needle's Luer fitting contacts the syringe) and primed with Renú.** Slowly push the syringe plunger until RENÚ® extrudes from the end of the injection needle. If leakage is noted at the Luer fitting, it may be necessary to remove the needle and clean the surfaces of the Luer fitting or, in some cases, replace both the syringe and the injection needle.

WARNING: RENÚ should not be injected into the airway. Confirm placement of needle tip visually before initiating the injection.

WARNING: Special care should be taken when injecting soft tissue fillers to avoid injection into blood vessels/vasculature. Rare but serious adverse events associated with intravascular injection of soft tissue fillers have been reported. Associated complications can be serious and may be permanent. Complications can include vision abnormalities/impairment, blindness, stroke, temporary scabs, platelet aggregation, vascular occlusion, infarction, hemolysis, embolization, embolic phenomena, necrosis, ischemia, cerebral ischemia or cerebral hemorrhage leading to stroke, permanent scarring of the skin, and damage to underlying facial structures. Immediately stop the injection if a patient exhibits any of the following: changes in 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 (blanching) of the skin, or unusual pain during or shortly after treatment. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care practitioner should an intravascular injection occur.

WARNING: Do not overcorrect (overfill) a deficiency because the depression should gradually improve within several weeks as the treatment effect of RENÚ occurs (see INDIVIDUALIZATION OF TREATMENT). Inject the product slowly and apply the least amount of pressure necessary.

CAUTION: Do not over-inject the RENÚ into the tissue. RENÚ can be easily added in subsequent injections but cannot be easily removed. Inject the product slowly and apply the least amount of pressure necessary.

WARNING: Viable tissue is required for effective injection. Scar tissue, cartilage, and significantly compromised tissue may not respond to treatment. If possible, avoid passing through these tissue types when advancing the injection needle.

6. Place the nasopharyngoscope to precisely visualize the needle position and RENÚ® injection volume during augmentation. With needle location visually confirmed through nasopharyngoscope, slowly push the plunger shaft of the syringe to start the injection. RENÚ® should be injected lateral to the thyroarytenoid muscle.
7. After the initial injection, the patient should be asked to phonate and cough to disperse RENÚ® throughout the vocal fold. Additional RENÚ® is injected until the vocal folds touch during phonation at a position midway between the anterior commissure and the vocal processes.

WARNING: Airway obstruction may result from aggressive vocal fold injection, over-injection, or laryngeal edema from trauma and manipulation of the larynx. Under no circumstance should excessive force be used to overcome resistance during injection, since sudden and uncontrolled over injection may occur. Airway obstruction following vocal fold injection can occur immediately, or at any time up to seven (7) days following injection. Airway obstruction can often be prevented by minimizing laryngeal trauma and manipulation during the injection and can be treated by administering intraoperative and postoperative steroid treatment.

CAUTION: If significant resistance is encountered when pushing the plunger, under no circumstance should excessive force be used to overcome resistance since the injection needle may disconnect from the Renú syringe. It may be necessary to try a different needle or replace both the syringe and needle.

8. Some tissue planes may be difficult to inject. If significant resistance is encountered when pushing the plunger, pull back the injection needle about one (1) to three (3) millimeters (with the needle still in the vocal fold tissue) and push the plunger slowly again. If significant resistance is still encountered, it may be necessary to pull the needle entirely out of the injection site and try again in a new position.
9. The number of injection attempts is at the discretion of the treating physician and must take into account the patient's tolerance of the procedure and discomfort.

CAUTION: After use, treatment syringes and needles may be potential biohazards. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal requirements.

10. Dispose of the opened syringes, as well as used injection needles.
11. Instruct the patient to not use his/her voice for three days so as to minimize any potential extrusion of the RENÚ through the injection site.

CAUTION: The RENÚ vocal fold injection procedure has a small but inherent risk of infection. Post injection infections which do not respond to standard medical treatment are uncommon. However, if an infection is unresponsive to treatment and removal of the implant is determined to be required; partial or total removal of the implant can be performed following standard surgical techniques including through phonomicrosurgery operative techniques.

12. A course of antibiotics maybe prescribed, as appropriate.

TISSUE INJECTION

(RENÚ SOFT TISSUE VOLUMIZING FILLER, RENÚ COSMETIC, RENÚ LIPOATROPHY AESTHETIC CORRECTION, RENÚ VOLUME FILLER)

The following is required for the sub dermal tissue injection procedure:

- RENÚ implant syringe(s)
- Needle(s) with Luer-loc fittings, ≤ 1.5" (38.1mm) in length, and a nominal inner diameter ≥ 0.26mm (e.g., 27G thin wall, 26G, or 25G)

CAUTION: Safety and effectiveness in the periorbital area has not been established.

WARNING: There have been published reports of nodules associated with the use of CaHA based injectable implant injected into the lips. The safety and effectiveness for use in the lips has not been established.

CAUTION: Universal precautions must be observed during the injection procedure.

CAUTION: The injection session must be conducted with aseptic technique.

CAUTION: Health care practitioners are encouraged to discuss all potential risks of soft tissue injection with each patient prior to treatment to ensure that patients are aware of signs and symptoms of potential complications.
CAUTION: The RENÚ aesthetics injection procedure has a small but inherent risk of infection. Post injection infections which do not respond to standard medical treatment are uncommon. However, if an infection is unresponsive to treatment and removal of the implant is determined to be required; partial or total removal of the implant can be performed following standard surgical techniques.

1. Prepare the patient injection site using standard antiseptic methods. The treatment injection site should be marked. Local or topical anesthesia should be used at the discretion of the physician.
2. Immediately before the injection, prepare the RENÚ and the injection needle(s). A new injection needle should be used for each syringe.

CAUTION: The foil pouch should be carefully examined to verify that neither the pouch nor the RENÚ syringe has been damaged during shipment. Do not use if the foil pouch is compromised or the syringe has been damaged. Do not use if the syringe end cap or syringe plunger has been displaced.
CAUTION: RENÚ is supplied sterile in a sealed foil pouch and is intended for **single use only**. Do not store partially used syringes for later use. Reuse of a syringe or needle at a later time, or on multiple patients, could be biohazardous and pose a risk of contamination and infection.
CAUTION: Do not re-sterilize; re-sterilized device safety and performance has not been validated.

3. Remove foil pouch from the carton. Open the foil pouch by tearing at the notches. Remove the syringe from the foil pouch. **NOTE:** ***There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is not an indication of a product issue.***

CAUTION: Safety and efficacy of Renú has not been evaluated when an anesthetic is mixed into the product prior to injection.

4. Remove the Luer syringe cap from the distal end of the syringe. If excess RENÚ is on the surface of the Luer-loc fittings, it will need to be wiped clean with sterile gauze. The RENÚ syringe can then be twisted onto the Luer-loc fitting of the needle.

CAUTION: Use of needles with a nominal inner diameter smaller than 0.26mm and/or longer than 1.5" (38.1mm) increase the incidence of needle occlusion.

5. **The needle must be tightened securely to the syringe and primed with RENÚ.** Slowly load the needle by pushing the syringe plunger until RENÚ extrudes from the end of the needle. If leakage is noted, it may be necessary to tighten the needle, or to remove the needle and clean the surfaces of the Luer fitting or, in some cases, replace both the syringe and the needle.
6. RENÚ should be injected into accepting soft tissue. The amount injected will vary depending on the site, extent of the restoration or augmentation desired and is at the discretion of the treating physician.

WARNING: Do not overcorrect (overfill) a deficiency because the depression should gradually improve within several weeks as the treatment effect of RENÚ occurs (see INDIVIDUALIZATION OF TREATMENT). Inject the product slowly and apply the least amount of pressure necessary.
CAUTION: Do not over-inject the RENÚ into the tissue. RENÚ can be easily added in subsequent injections but cannot be easily removed. Inject the product slowly and apply the least amount of pressure necessary.

7. No overcorrection is needed. A nominal 1:1 correction factor is expected.

WARNING: Special care should be taken when injecting soft tissue fillers to avoid injection into blood vessels/vasculature. Rare but serious adverse events associated with intravascular injection of soft tissue fillers have been reported. Associated complications can be serious and may be permanent. Complications can include vision abnormalities/impairment, blindness, stroke, temporary scabs, platelet aggregation, vascular occlusion, infarction, hemolysis, embolization, embolic phenomena, necrosis, ischemia, cerebral ischemia or cerebral hemorrhage leading to stroke, permanent scarring of the skin, and damage to underlying facial structures. Immediately stop the injection if a patient exhibits any of the following: changes in 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 (blanching) of the skin, or unusual pain during or shortly after treatment. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care practitioner should an intravascular injection occur.
WARNING: Viable tissue is required for effective injection. Scar tissue, cartilage, and significantly compromised tissue may not respond to treatment. If possible, avoid passing through these tissue types when advancing the injection needle.

8. Insert needle with bevel down at approximately a 30° angle to the tissue. Identify the point you wish to begin the injection. This should be easily palpable with the non-dominant hand.

CAUTION: If significant resistance is encountered when pushing the plunger, under no circumstance should excessive force be used to overcome resistance since the injection needle may disconnect from the Renú syringe. It may be necessary to try a different needle or replace both the syringe and needle.

9. Some tissue planes may be difficult to inject. If significant resistance is encountered when pushing the plunger, pull back the injection needle about one (1) to three (3) millimeters (with the needle still in the tissue) and push the plunger slowly again. If significant resistance is still encountered, the injection needle may be moved slightly to allow easier placement of the material or it may be necessary to change the injection needle. Needle jams are more likely with use of needles with a nominal inner diameter smaller than 0.26mm and/or longer than 1.5" (38.1mm).
10. Advance the needle to the starting location. Carefully push the plunger of the RENÚ syringe to start the injection and slowly inject the implant material while withdrawing the needle. Continue placing additional material until the desired level of correction is achieved.
11. Apply slow continuous even pressure to the syringe plunger to inject the implant as you withdraw the needle without leaving globular deposits. Based on the procedure and effect required, the injection area may be messaged as needed to achieve even distribution of the implant.

CAUTION: After use, treatment syringes and needles may be potential biohazards. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal requirements.

12. Dispose of the opened syringes, as well as used injection needles.

RENÚ® Calcium Hydroxylapatite (CaHA) Soft Tissue Filler Implant
General Information

HOW SUPPLIED
RENÚ is provided in a foil pouch that contains one sterile, 1.5 cc syringe pre-filled RENÚ Implant. Upon receipt of shipment, check the packaging to ensure that the packaging is intact and there has been no damage from shipment. Do not use if packaging and/or syringe are damaged or if the syringe end cap or syringe plunger has been displaced. The contents of the syringe are intended for single patient use only and cannot be re-sterilized.

STORAGE & EXPIRATION
RENÚ should be stored at a controlled room temperature between 15° C and 30° C (59° F and 86° F). The expiration date when stored properly is two years from date of manufacture. Do not use if the expiration date has been exceeded.

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

THIS WARRANTY IS IN LIEU OF AND EXCLUDES ALL OTHER WARRANTIES NOT EXPRESSLY SET FORTH HEREIN, WHETHER EXPRESSED OR IMPLIED BY OPERATION OF LAW OR OTHERWISE, INCLUDING BUT NOT LIMITED TO, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR ITS PARTICULAR PURPOSE.

Handling and storage of this product, as well as factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond Cytophil's control, directly affect the product and the results obtained from its use. Cytophil, Inc.'s obligation under this warranty is limited to the replacement of this product and Cytophil, Inc. shall not be liable for any incidental or consequential loss, damage, or expense, directly or indirectly arising from the use of this product. Cytophil neither assumes, nor authorizes any person to assume for Cytophil, Inc., any other or additional liability or responsibility in connection with this product.

Cytophil, Inc
2485 Corporate Circle, Suite 2
East Troy, WI 53120 U.S.A.
Telephone: 262-642-2765
Fax: 262-642-2745
Email: info@cytophil.com
Website: www.cytophil.com

EC REP
Emergo Europe
Prinsessegracht 20
2514 AP The Hague
The Netherlands
CE 2797

	Manufacturer
REF	Catalog number
LOT	Batch code
EC REP	Authorized representative in the European community
	Use by date
	Temperature limitations
MR	MR Safe

2 STERILIZE	Do not resterilize
2	Do not reuse
	Do not use if package is damaged
	CAUTION: Consult accompanying documents
	Consult instructions for use
STERILE	Sterilized using steam or dry heat