REGENSCIENTIFIC

RENÚ® VOICE

RENÚ®CALCIUM HYDROXYLAPATITE VOCAL FOLD IMPLANT

INSTRUCTONS FOR USE

DESCRIPTION

RENÚ® Calcium Hydroxylapatite Vocal Fold Implant is a sterile, semi-solid, cohesive implant. The principle component of RENÚ® Voice is synthetic calcium hydroxylapatite, a biomaterial with over twenty years of use in orthopedics, neurosurgery, dentistry, otolaryngology and ophthalmology. The semi-sold nature is created by suspending the calcium hydroxylapatite particles in a gel. The aqueous gel carrier consists of sodium carboxymethylcellulose, glycerin, and a 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 restoration and augmentation.

Use of needles smaller than 25 gauge for the 25-45 micron product may increase the incidence of needle occlusion.

INTENDED USE / INDICATIONS

RENÚ® Calcium Hydroxylapatite Vocal Fold Implant is indicated for vocal fold medialization and vocal fold insufficiency that may be improved by injection of a soft tissue-bulking agent. RENÚ® Calcium Hydroxylapatite Vocal Fold Implant injection augments the size of the displaced or deformed vocal fold so that it may meet the opposing fold at the midline for improved phonation. Vocal fold insufficiency associated with serious aspiration difficulties may be an urgent indication.

CONTRAINDICATIONS

- Contraindicated in the presence of foreign bodies, acute inflammation, infection, inadequately controlled malignancy or rapidly advancing disease when these involve the larynx or upper respiratory tract.
- Contraindicated in bilateral laryngeal paralysis and vocal disorders of psychogenic or emotional origin.

WARNINGS

- Therapy should be delayed at least six (6) months following the onset of the paralysis and/or until an adequate trial of voice rehabilitation has been given.
- Use intended only for trained otolaryngologists or experienced head and neck surgeons.
- Not to be injected into blood vessels. Injection into blood vessels may cause platelet aggregation, vascular occlusion, infarction, embolic phenomena or hemolysis.
- Viable tissue is required for effective injection. Scar tissue and significantly compromised tissue may be suitable for injection augmentation.
- Safety and effectiveness during pregnancy has not been established.
- Airway obstruction following vocal fold injection can occur immediately or at any time up to seven (7) days following injection. Airway obstruction results from aggressive vocal fold injection, over-injection, or laryngeal edema from trauma and manipulation of the larynx. Airway obstruction can often be prevented by intraoperative and postoperative steroid treatment and by minimizing laryngeal trauma and manipulation.
- Should not be injected into the airway. Confirm placement of needle tip visually before initiating RENÚ® injection.
- Should not be injected into organs or other structures that could be damaged by a space occupying implant. Some injectable implants have been associated with hardening of the tissues at an injection site, migration of particles from an injection site to other parts of the body and/or allergic or autoimmune reactions. This has not been observed nor is it expected with RENÚ®.

PRECAUTIONS

- Do not over-inject the vocal fold. RENÚ® Calcium Hydroxylapatite Vocal Fold Implant can be easily added in subsequent injections but cannot be easily removed. In extreme cases site rupture could occur.
- In some cases, initial treatment with RENÚ® Calcium Hydroxylapatite Vocal Fold Implant may not be effective and additional injections may be indicated.
- RENÚ® Calcium Hydroxylapatite Vocal Fold Implant injection procedure and the associated instrumentation procedures have small but inherent risks of infection and/or bleeding like similar otolaryngology procedures. The patient may experience slight discomfort during and following the procedure. The usual precautions associated with otolaryngology procedures, specifically vocal fold injection, should be followed.
- Care should be taken with the injection of RENÚ® Calcium Hydroxylapatite Vocal Fold Implant, as with any surgical or implantation procedure, to avoid infection during the injection procedure.

- RENÚ® Calcium Hydroxylapatite Vocal Fold Implant is supplied sterile in a sealed foil pouch and is intended for single use only. **Do not re-sterilize.**
- The foil pouch should be carefully examined to verify that neither the pouch nor the RENÚ® Calcium Hydroxylapatite Vocal Fold Implant 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 are not in place or removed.
- Do not use a needle size smaller than recommended in the Description Section.

PHYSICIAN TRAINING

Injections of RENÚ® Calcium Hydroxylapatite Vocal Fold Implant should only be performed by physicians who have experience with diagnostic and therapeutic otolaryngology procedures including vocal fold 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® Calcium Hydroxylapatite Vocal Fold Implant. The outcome of treatment with Calcium Hydroxylapatite Vocal Fold Implant 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.

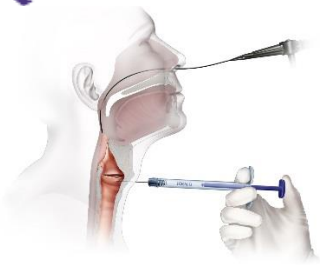
DIRECTIONS FOR USE:

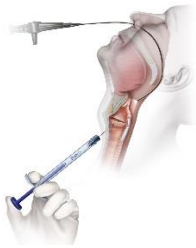
PERCUTANEOUS VOCAL FOLD INJECTION

The following is required for the vocal fold injection procedure:

- RENÚ® Calcium Hydroxylapatite Vocal Fold Implant syringe(s)
- Appropriate sized needle(s)
- Nasopharyngoscope

1. Prepare the syringe(s) of RENÚ® Calcium Hydroxylapatite Vocal Fold Implant, injection needles(s), and nasopharyngoscope equipment before the surgical injection. 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 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® Calcium Hydroxylapatite Vocal Fold Implant.**
2. Prepare nasopharyngoscope equipment using facility medical practices for a nasopharyngoscope examination.
3. Remove foil pouch from the carton. The pouch can be opened and the syringe of RENÚ® Calcium Hydroxylapatite Vocal Fold Implant placed onto the sterile field when required. *There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is not an indication of a defective product.*
4. Prepare patient for nasopharyngoscopy and anesthetize using standard methods. Local anesthesia is not required but may be utilized at the injection site.
5. Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. The injection needle can then be twisted onto the Luer lock fitting of the syringe of RENÚ®Calcium Hydroxylapatite Vocal Fold Implant.
6. **The needle must be tightened securely to the syringe and primed with RENÚ®.**
7. If excess RENÚ® Calcium Hydroxylapatite Vocal Fold Implant is on the surface of the Luer lock fittings, it will need to be wiped clean with sterile gauze. Slowly push the syringe plunger until RENÚ® Calcium Hydroxylapatite Vocal Fold Implant 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 extreme cases, replace both the syringe and the injection needle.
8. Place the nasopharyngoscope to precisely visualize the needle position and RENÚ® Calcium Hydroxylapatite Vocal Fold Implant volume during augmentation. With needle location visually confirmed through nasopharyngoscope, slowly push the plunger shaft of the syringe to start the injection.





9. RENÚ® Calcium Hydroxylapatite Vocal Fold Implant should be injected lateral to the thyroarytenoid muscle.
10. 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. Transcartilaginous injection is used unless cartilage calcification prevents it, in which case needle placement is through the cricothyroid membrane.
11. With needle location visually confirmed through nasopharyngoscope, slowly push the plunger shaft of the RENÚ® Calcium Hydroxylapatite Vocal Fold Implant syringe to start the injection.
12. After the initial injection, the patient should be asked to phonate and cough to disperse RENÚ® Calcium Hydroxylapatite Vocal Fold Implant. Additional RENÚ® Calcium Hydroxylapatite Vocal Fold Implant is injected until the vocal folds touch during phonation at a position midway between the anterior commissure and the vocal processes.
13. 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. If significant resistance continues to persist, it may be necessary to try a different injection needle.
14. If this is not successful, replace the syringe of RENÚ® Calcium Hydroxylapatite Vocal Fold Implant and injection needle. Under no circumstances should excessive force be used to overcome resistance during injection, since sudden and uncontrolled over injection may result in airway obstruction. 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.

NOTE: Do not inject into a blood vessel.

15. Used and partially used syringes and used injection needles could be biohazardous and should be handled and disposed of in accordance with facility medical practices and local, state or federal regulations.

PER ORAL VOCAL FOLD INJECTION

The following is required for the vocal fold injection procedure:

- RENÚ®Calcium Hydroxylapatite Vocal Fold Implant syringe(s)
- Appropriate sized needle(s)
- Nasopharyngoscope

1. Prepare the syringes of RENÚ® Calcium Hydroxylapatite Vocal Fold Implant, injection needles(s), and nasopharyngoscope equipment before the surgical injection. 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® Calcium Hydroxylapatite Vocal Fold Implant , 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® Calcium Hydroxylapatite Vocal Fold Implant.**
2. Prepare nasopharyngoscope equipment using facility medical practices for a nasopharyngoscope examination.
3. Remove foil pouch from the carton. The pouch can be opened and the syringe of RENÚ® Calcium Hydroxylapatite Vocal Fold Implant placed onto the sterile field when required. *There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is not an indication of a defective product.*
4. Prepare patient for nasopharyngoscopy and anesthetize using standard methods. Local anesthesia is not required but may be utilized at the RENÚ®Calcium Hydroxylapatite Vocal Fold Implant injection site.

5. Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. The injection needle can then be twisted onto the Luer lock fitting of the syringe
6. **The needle must be tightened securely to the syringe (until the squared section of the needle's Luer fitting contacts the syringe).**
7. If excess RENÚ® Calcium Hydroxylapatite Vocal Fold Implant is on the surface of the Luer lock fittings, it will need to be wiped clean with sterile gauze. Slowly push the syringe plunger until RENÚ® Calcium Hydroxylapatite Vocal Fold Implant 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 extreme cases, replace both the syringe and the injection needle.

   NOTE: The ENT needle shaft is malleable but has significant limitations. Do not place pressure on the needle tip.

8. Place the nasopharyngoscope to precisely visualize the needle position and RENÚ® Calcium Hydroxylapatite Vocal Fold Implant volume during augmentation. With needle location visually confirmed through nasopharyngoscope, slowly push the plunger shaft of the syringe to start the injection. RENÚ® Calcium Hydroxylapatite Vocal Fold Implant should be injected lateral to the thyroarytenoid muscle.
9. After the initial injection, the patient should be asked to phonate and cough to disperse RENÚ® Calcium Hydroxylapatite Vocal Fold Implant throughout the vocal fold. Additional RENÚ® Calcium Hydroxylapatite Vocal Fold Implant is injected until the vocal folds touch during respiration at a position midway between the anterior commissure and the vocal processes.
10. 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. If significant resistance continues to persist, it may be necessary to try a different injection needle.
11. If this is not successful, replace the syringe of RENÚ® Calcium Hydroxylapatite Vocal Fold Implant and injection needle. Under no circumstances should excessive force be used to overcome resistance during injection, since sudden and uncontrolled over injection may result in airway obstruction. 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.

NOTE: Do not inject into a blood vessel.

12. Used and partially used syringes and used injection needles could be biohazardous and should be handled and disposed of in accordance with facility medical practices and local, state or federal regulations.

PATIENT COUNSELING INFORMATION

- Provide an appropriate course of antibiotics as required.
- Instruct patient not to use the voice for three days. This minimizes any potential extrusion of the RENÚ® through the injection site.

RENÚ®CALCIUM HYDROXYLAPATITE VOCAL FOLD IMPLANT

General Information

HOW SUPPLIED

RENÚ® Calcium Hydroxylapatite Vocal Fold Implant is provided in an autoclaveable foil pouch that contains one sterile, 1.5 cc syringe pre-filled with sterile RENÚ® Calcium Hydroxylapatite Vocal Fold Implant. Do not use if packaging and/or syringe are damaged or if the syringe end cap or syringe plunger shaft are not intact. The contents of the syringe are intended for single patient use only and cannot be re-sterilized.

STORAGE

RENÚ® Calcium Hydroxylapatite Vocal Fold Implant should be stored at a controlled room temperature between 15° C and 32° C (59° F and 90° F). The expiration date when stored properly is two years from date of manufacture. Do not use if the expiration date has been exceeded.

Upon receipt of shipment, check the packaging to ensure that the packaging is intact and there has been no damage from shipment.

WARRANTY

REGENSCIENTIFIC, 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 REGENSCIENTIFIC's control directly affect the product and the results obtained from its use. REGENSCIENTIFIC's obligation under this warranty is limited to the replacement of this product and REGENSCIENTIFIC shall not be liable for any incidental or consequential loss, damage, or expense, directly or indirectly arising from the use of this product. REGENSCIENTIFIC neither assumes, nor authorizes any person to assume for REGENSCIENTIFIC, any other or additional liability or responsibility in connection with this product.

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Temperature limitations


Do not reuse

Sterilized using steam or dry heat


CAUTION: Consult accompanying documents

Catalog number


Manufacturer

Batch number


Use before