Prolaryn® Plus

Injectable Implant

INSTRUCTIONS FOR USE

DESCRIPTION

Prolaryn® Plus injectable implant is a sterile, latex-free, non-pyrogenic, semi-solid, cohesive implant. The principal component of Prolaryn® Plus is synthetic calcium hydroxylapatite, a biomaterial with over twenty years of use in orthopedics, neurosurgery, dentistry, otolaryngology and ophthalmology. Calcium hydroxylapatite is the primary mineral constituent of bone and teeth. The semi-solid nature of Prolaryn® Plus is created by suspending calcium hydroxylapatite in a gel carrier that consists primarily of water (sterile water for injection USP) and glycerin (USP). The gel structure is formed by the addition of a small amount of sodium carboxymethylcellulose (USP). The gel is dissipated *in vivo* and replaced with soft tissue growth, while the calcium hydroxylapatite remains at the site of injection. The result is long-term restoration and augmentation.

Prolaryn® Plus 1cc has a particle size range of 25-45 microns and can be injected with a 26 gauge or larger diameter thin-wall needle with a standard Luer fitting. **Use of needles smaller than 26 gauge may increase the incidence of needle occlusion.**

INTENDED USE/INDICATIONS

Prolaryn® Plus is indicated for vocal fold medialization and vocal fold insufficiency that may be improved by injection of a soft tissue bulking agent. Prolaryn® Plus 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 laryngeal or upper respiratory tract.
- Contraindicated in bilateral laryngeal paralysis and vocal disorders of psychogenic or emotional origin.

WARNINGS

- Should not be injected into blood vessels. Injection into blood vessels may cause platelet aggregation, vascular occlusion, infarction, embolic phenomena or hemolysis.
- 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 Prolaryn® Plus 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.
- Safety and effectiveness during pregnancy has not been established.

PRECAUTIONS

- Prolaryn® Plus therapy should be delayed at least six months following the onset of the paralysis and/or until an adequate trial of voice rehabilitation has been made.
- Prolaryn® Plus requires viable tissue for effectiveness. Scar tissue and significantly compromised tissue may not coapt appropriately. Patients who have had multiple surgeries may not be appropriate candidates for bulking injection treatment.
- Do not over-inject the vocal fold. Prolaryn® Plus can be easily added in subsequent injections but cannot be easily removed. In extreme cases site rupture could occur.
- The Prolaryn® Plus 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 Prolaryn® Plus, as with any surgical or implantation procedure, to avoid infection during the injection procedure. If infection occurs and cannot be corrected, it may be necessary to remove the implant.
- **Do not re-sterilize or store partially used syringes for later use.** Prolaryn® Plus is supplied sterile and non-pyrogenic in a sealed foil pouch and is intended for single patient use only.
- The foil pouch should be carefully examined to verify that neither the pouch nor the Prolaryn® Plus 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 is not in place.
- Use of needles smaller in diameter than 26 gauge may increase the incidence of needle occlusion.

POST MARKET SURVEILLANCE

The following adverse events have been identified during post-approval use of Prolaryn® Plus. Because they are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal connection to Prolaryn® Plus. These events have been chosen for inclusion due to a combination of their seriousness, frequency in reporting, or causal connection to Prolaryn® Plus: infection, over injection/under injection, ineffective treatment, tissue displacement, exposed material, superficial injection, edema, pain, stiffness at injection site, extraction of material, voice changes, dyspnea, airway obstruction, nodule, cough, hypersensitivity reactions including anaphylaxis, urticaria, erythema, facial edema, pruritus and hives.

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 Prolaryn® Plus. The outcome of treatment will vary between patients. In some patients additional treatments may be necessary to improve and/or maintain the level of resolution. 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 percutaneous vocal fold injection procedure:

- Prolaryn® Plus syringe(s)
- Appropriate size needle(s) {Provided}
- Nasopharyngoscope

1. Prepare patient for nasopharyngoscopy and anesthetize using standard methods. Local anesthesia is not required but may be utilized at the Prolaryn® Plus injection site.

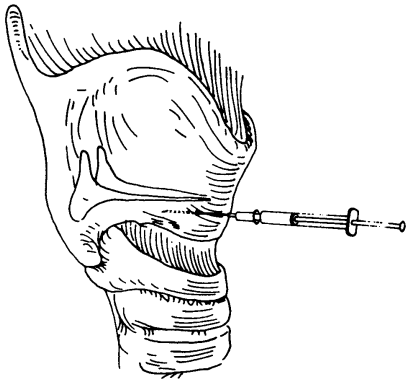
2. Prepare the syringe(s) of Prolaryn® Plus, injection needle(s) and nasopharyngoscopic equipment before the surgical injection. A new injection needle may be used for each syringe, or the same injection needle may be connected to each new syringe.

3. Remove foil pouch from the carton. The pouch can be opened and the syringe of Prolaryn® Plus dropped onto the sterile field when required. *There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is <u>not</u> an indication of a defective product.*

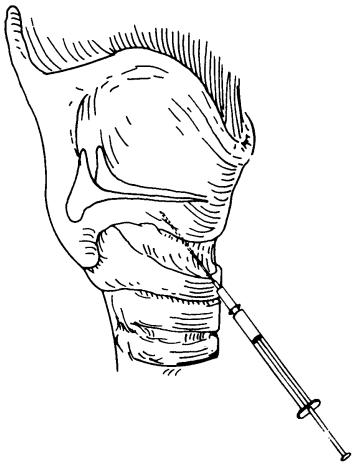
4. Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. The syringe of Prolaryn® Plus can then be twisted onto the Luer lock fitting of the needle. **The needle <u>must</u> be tightened securely to the syringe and primed with Prolaryn® Plus.** If excess Prolaryn® Plus 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 Prolaryn® Plus 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.

5. Place the nasopharyngoscope to precisely visualize the needle position and Prolaryn® Plus volume during augmentation.

LOCATION AND DIRECTION OF NEEDLE PLACEMENT FOR TRANSCUTANEOUS INJECTION



[A] Through thyroid cartilage.



[B] Through cricothyroid membrane.

6. Extend the patient's neck if possible and identify by 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 such injections, in which case needle placement is through the cricothyroid membrane.

NOTE: Do not inject into a blood vessel.

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

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. 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. If this is not successful, replace the syringe of Prolaryn® Plus and injection needle.

ORAL VOCAL FOLD INJECTION

The following is required for the vocal fold injection procedure:

- Prolaryn® Plus syringe(s)
- Appropriate size needle(s) {Provided}
- Nasopharyngoscope

1. Prepare patient for nasopharyngoscopy and anesthetize using standard methods. Local anesthesia is not required but may be utilized at the Prolaryn® Plus injection site.

2. Prepare the syringe(s) of Prolaryn® Plus, injection needle(s) and nasopharyngoscopic 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.

3. Remove foil pouch from the carton. The pouch can be opened and the syringe of Prolaryn® Plus dropped onto the sterile field when required. *There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is <u>not</u> an indication of a defective product.*

4. Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. The syringe of Prolaryn® Plus can then be twisted onto the Luer lock fitting of the needle. **The needle <u>must</u> be tightened securely to the syringe and primed with Prolaryn® Plus.** If excess Prolaryn® Plus 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 Prolaryn® Plus 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.

5. Place the nasopharyngoscope to precisely visualize the needle position and Prolaryn® Plus volume during augmentation.

6. Position injection needle for oral vocal fold injection. Prolaryn® Plus should be injected lateral to the thyroarytenoid muscle.

NOTE: Do not inject into a blood vessel.

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

8. Some tissue planes may be difficult to inject. If significant resistance is encountered when pushing the plunger, the injection needle should be pulled back 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. If this is not successful, replace the syringe of Prolaryn® Plus and injection needle.

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 Prolaryn® Plus through the injection site.

HOW SUPPLIED

Prolaryn® Plus is provided sterile and non-pyrogenic in a pre-filled syringe containing 1.0cc of Prolaryn® Plus packaged in a foil pouch. The individual pouched unit is packaged in a kit configuration (contains more than one part number) with appropriate size needle(s).

The contents of the syringe are intended for single patient, single treatment use only and cannot be re-sterilized.

STORAGE

Prolaryn® Plus should be stored in its unopened, sealed package at a controlled room temperature between 15°C and 32°C (59°F and 90°F). Do not use if packaging and/or syringe are damaged or if the syringe end cap or syringe plunger is not intact. Do not use if the expiration date has been exceeded. The expiration date is printed on the product labels and is based on storing the product as described above.

DISPOSAL

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

WARRANTY

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

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