ClariFix® Instructions For Use

CAUTION: Federal (USA) law restricts this device to sale by, or on the order of a physician.

PRODUCT DESCRIPTION

The ClariFix device is a handheld cryotherapy device, which provides focal, controlled freezing to the target tissue. A nitrous oxide canister is loaded into the cryoprobe as a source of cryogen. The balloon is placed in contact with the target tissue, under direct visualization. The low profile semi-flexible cannula allows the user to maintain visibility of the balloon and apply pressure to target tissue with the cryoprobe to ensure contact throughout the treatment. Once the balloon is in the desired position, the physician manually initiates the flow of cryogen using the valve on/off button and ablates unwanted tissue. The nitrous oxide gas is contained within the cryoprobe and exits out of the exhaust ports at the bottom of the handle.

The ClariFix device is designed for single patient use. The cryoprobe is provided sterile. The cryogen canisters (10 mL) are provided non-sterile and contain enough cryogen for 60 seconds of treatment. Sterile caps are provided to load and unload the cryogen canisters for use in a sterile field. The cryoprobe and caps are sterilized using irradiation.

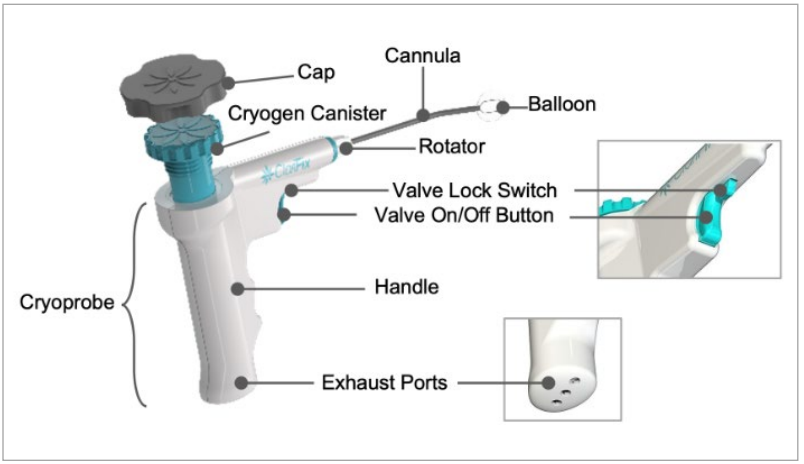

Figure 1: ClariFix Device

CONTENTS

The ClariFix device consists of:
1 Cryoprobe (provided sterile)
2 Caps (provided sterile)
2 Cryogen canisters (provided nonsterile)

NOTE: The ClariFix device, components and packaging are not made with natural rubber latex.

INDICATIONS FOR USE

The ClariFix device is intended to be used as a cryosurgical tool for the destruction of unwanted tissue, including in adults with chronic rhinitis.

CONTRAINDICATIONS

The ClariFix device is contraindicated in patients with the following conditions:

- Cryoglobulinemia
- Paroxysmal cold hemoglobinuria
- Cold urticaria
- Raynaud's disease
- Open and/or infected wounds or other skin conditions at or near the target tissue
- Patients with diabetes, sensitivity to cold, neuropathic disorders, bleeding disorders, or impaired peripheral circulation in the area to be treated should be treated with caution

POTENTIAL ADVERSE EFFECTS

Patients may experience one or more of the following adverse effects related to cryosurgery and/or local anesthesia. Adverse effects may be mild or transient in nature and self-resolving:

- Bleeding
- Crusting and/or tissue sloughing
- Pain/discomfort and/or facial pain
- Swelling
- Intranasal scarring/nasal obstruction
- Sensory alterations (numbness, tingling) in the face/mouth
- Headache
- Septal perforation
- Vasovagal reaction
- Infection
- Dry eyes, optical changes or orbital damage
- Frost-bite and/or cryolysis to surrounding area
- Delayed diagnosis due to change in pain perception or presentation on clinical or imaging assessment
- For chronic rhinitis patients, transient increase in nasal congestion, dry nose and/or ear blockage/hearing loss
- Continued or worsening symptoms

Care should be exercised when treating thin tissue structures, as excessive freezing may cause tissue damage.

Nosebleed is rare, but a potential side effect, and may be increased if patient has clotting disorder, uncontrolled high blood pressure, or uses anticoagulants or blood thinners.

SAFETY INFORMATION

WARNINGS

- This product is intended solely for use by medical professionals (physicians) trained in ENT procedures and navigating the nasal anatomy.
- Carefully inspect the sterile package seal and device for any signs of damage prior to use. Do not use a device with a breached sterile seal as it could be contaminated. Do not use a damaged device as it could malfunction.
- DO NOT REUSE or RESTERILIZE. Reuse of the device may result in device malfunction. The device is intended for single patient use only.
- After the cryogen canister is loaded, the device is under high pressure.
- Any change to the construction of the device may cause a device malfunction leading to a potential injury to the user and/or the patient.
- Never block the exhaust ports at the bottom of the cryoprobe handle.
- When replacing the cryogen canister, it is important to remove the cryogen canister slowly and to wait for at least one minute before loading another cryogen canister. This will allow the excess nitrous oxide to completely vent from the handle and be released safely.
- Do not discard pressurized cryogen canisters. Disposing of pressurized cryogen canisters could injure personnel if the canister is not emptied prior to incineration or other disposal methods. A pressurized cryogen canister can explode at temperatures above 50°C (122°F).
- The device is not intended for use in a Magnetic Resonance Environment.

PRECAUTIONS

- The cryogen canisters are provided non-sterile, attached to the bottom of the sterile cryoprobe tray. Use the sterile caps provided inside the tray with the cryoprobe to handle the non-sterile cryogen canisters in a sterile field.
- Always advance the ClariFix device under direct visualization. If desired, a rigid endoscope may be used to augment visualization in the nasal passageway.
- Avoid moving the cryoprobe during treatment to ensure good contact with the target tissue is maintained and optimum treatment is achieved.
- Allow the balloon to thaw before removing it from the target tissue to avoid unwanted tissue injury. Thawing is indicated by ice melting from the balloon and the distal tip of the cannula. Minimal to no resistance should be felt when moving the balloon from tissue.
- Keep orientation of the device within the range shown in Figure 5 to ensure proper nitrous oxide flow.
- Avoid nasal packing or debridement for up to 90 days postprocedure as this may increase risk of nosebleeds.
- In accordance with the European REACH regulation and other environmental regulatory requirements, the ClariFix device contains internal brass components with lead.

STORAGE CONDITIONS

Store the device in a cool, dry place. Store the cryogen canisters in a controlled room temperature environment that does not exceed 50°C. The cryogen canisters can explode at temperatures above 50°C (122°F).

DIRECTIONS FOR USE

Preparation

1. Remove the non-sterile cryogen canisters and place in a non-sterile/clean field.
2. Peel open the sterile packaging lid to remove the ClariFix cryoprobe & sterile caps. Place in the sterile field, as appropriate.
3. Before beginning treatment, the target tissue should be thoroughly inspected to ensure appropriateness for treatment. When applied to the target tissue, the balloon of the ClariFix device freezes a circular area of tissue approximately 15-20 mm (0.6-0.8 inches) in diameter. Freezing depth depends upon the time of treatment (i.e./ how long the valve is in the "open" position).

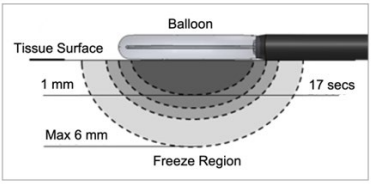

Figure 2: Freeze area is restricted to the surrounding tissue in contact with the balloon.

NOTE: Because both sides of the balloon will freeze during treatment, user discretion is required to ensure appropriateness of the treatment area, including hollow structures. Freeze penetration is on average 1 mm for every 17 seconds up to a maximum depth of 6 mm (see Figure 2). Variability in tissue thickness may impact penetration of the treatment; thinner tissues may require shorter treatment times.

4. Visualize the target treatment area and apply anesthetic. When placing the device in the nasal passageway, endoscopic guidance is recommended.
5. Load a cryogen canister into the cryoprobe handle and puncture it by screwing the cryogen canister all the way down, ensuring the threads are fully tightened.

   NOTE: If using ClariFix in a sterile field, use one of the sterile caps to grasp the non-sterile cryogen canister and load it into the device.

Figure 3: Cap & canister loading

Balloon Placement

1. Rotate the cannula to the desired position by turning the rotator until the cannula locks into place.
2. Place the balloon on target tissue. When using for chronic rhinitis symptoms, insert the balloon and cannula into the nasal cavity and advance until the

balloon is located on the target tissue over the branches of the posterior nasal nerve.
3. Ensure the balloon is in firm contact with the target tissue.

Treatment

1. Depress the valve on/off button to open the valve and activate the flow of cryogen. Maintain the cryoprobe position on the target tissue.
   - Depress the valve on/off button all the way to engage the valve lock switch, locking the valve open. To release, push the valve lock switch up.

NOTE: During treatment, cryogen gas will exit from the bottom of the cryoprobe handle from the exhaust ports as shown in Figure 4.

Figure 4: Cryogen gas exits from the exhaust ports on the bottom of the cryoprobe.

NOTE: Throughout treatment, the cryoprobe orientation should be maintained within the range depicted in Figure 5 to ensure proper flow of cryogen from the canister. The flow of cryogen from the canister to the balloon during treatment may be reduced if the cryoprobe is not oriented correctly, thus reducing freezing at the balloon.

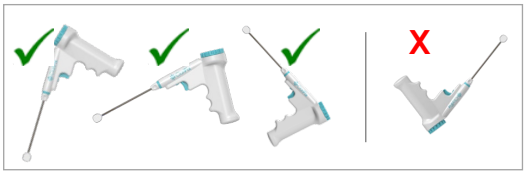

Figure 5: Orientation of the ClariFix device to ensure proper flow of cryogen from the canister.

2. As nitrous oxide flows into the balloon, the flow of cryogen can be seen through the formation of ice and the balloon surface changing from translucent to white. Ice crystals should be observed on the balloon and distal end of the cannula, and the visible portion of the target tissue will turn white.
3. Keep the valve open as long as treatment is desired, using Figure 2 to estimate the depth of the treatment over time.
4. Depending on the length of treatment, it is normal for the balloon to adhere to the tissue.
5. Close the valve and stop treatment by pushing the valve lock switch up and releasing the on/off button to stop the flow of nitrous oxide at any time. If the valve is not closed, the treatment will continue for approximately 60 seconds until the canister is empty. When used for chronic rhinitis symptoms, deliver approximately 30 to 60 seconds of treatment.

NOTE: To ensure good contact with the target tissue and optimum treatment, avoid moving the cryoprobe during treatment.

NOTE: To avoid unwanted tissue injury, always allow the balloon to thaw prior to removing it from the target tissue, as indicated visually by ice melting from the balloon and target tissue. Minimal to no resistance should be felt when removing the balloon from the tissue.

6. Once the flow of nitrous oxide has been stopped, ice crystals on the balloon will melt. It is generally safe to move the cryoprobe away from the target tissue, as indicated by no adherence of the balloon to tissue. In the event resistance is felt, wait for at least 30 seconds and try again.
7. Remove the balloon from the target tissue.
8. If a second treatment is desired, re-treat the target tissue or nearby area after the tissue is thawed, approximately 2 minutes after the first application.

   NOTE: Tissue may freeze faster during the second treatment if the tissue is still cold. The “freeze-thaw-freeze” technique may be desirable for maximum destruction of the target tissue.

9. Once the cryogen canister is empty, it can be replaced following the directions below.

Canister Replacement

1. To remove a canister, hold the device with the cryogen canister pointing up and the exhaust port pointing away from the user and patient. Grasp the handle of the cryoprobe with one hand and use the other hand to loosen the top of the cryogen canister. Do not cover the exhaust ports at the bottom of the cryoprobe handle to allow for optimal venting. Do not depress the valve on/off button as you remove the cryogen canister.

   NOTE: If using ClariFix in a sterile field with one of the provided sterile caps, grasp the sterile cap to loosen, and replace the non-sterile cryogen canister.

2. Loosening the cryogen canister will exhaust excess nitrous oxide.
3. Unscrew and remove the empty cryogen canister from the cryoprobe and discard.
4. If desired, load a new cryogen canister into the handle, turning to ensure the threads are fully tightened. Do not overtighten. When loading the cryogen canister in a sterile field, use the additional sterile cap to grasp the non-sterile cryogen canister. Refer to Figure 3.

Figure 6: Cryogen canister removal and/or replacement

Disposal

1. At the completion of the treatment, dispose of the ClariFix cryoprobe, caps, and all empty canisters according to federal, state, or local regulations, and appropriate environmental health safety guidelines for standard medical waste.

Medical waste should be considered infectious and requires special management/treatment.

WARNING: Do not discard pressurized cryogen canisters. Disposing of pressurized cryogen canisters could injure personnel if the canister is not emptied prior to incineration or other disposal methods. The cryogen canisters can explode at temperatures above 50°C (122°F).

NOTE: In accordance with the European REACH regulation and other environmental regulatory requirements, the ClariFix device contains internal brass components with lead.

INCIDENT REPORTING

Any serious incident that has occurred in relation to the device should be reported to Entellus Medical by calling Customer Service at (866) 620-7615.

CLINICAL STUDIES

A prospective, multicenter clinical study was performed at 3 sites in the United States to evaluate the feasibility of cryoablation in the nasal cavity, using the ClariFix device, in adults with chronic rhinitis. Twenty seven participants with chronic allergic or nonallergic rhinitis were treated bilaterally with the ClariFix device (n=54 treatments) using local anesthesia. Participants were followed at 7, 30, 90, 180 and 365 days after treatment. Cryosurgery was well-tolerated and participants reported an average pain rating of 1.19 on the Wong-Baker FACES pain scale (0=minimum score, 5=maximum score).

The primary efficacy outcome was the change in reflective Total Nasal Symptom Score (rTNSS) and Visual Analog Scale (VAS). Nasal symptoms scores were significantly improved at all follow-up time points through the 365-day follow-up. The mean rTNSS score was 6.2 ± 0.5 (scale of 0 to 12) at baseline and was decreased to 4.3 ± 0.4 (n=27, $p<0.005$) at 7 days, 2.6 ± 0.3 (n=27, $p<0.001$) at 30 days, 2.7 ± 0.4 (n=27, $p<0.001$) at 90 days, 2.3 ± 0.5 (n=21, $p<0.001$) at 180 days, and 1.9 ± 0.3 (n=15, $p<0.001$) at 365 days. Rhinorrhea and nasal congestion were the symptoms with the greatest improvements. The average total VAS scores demonstrated a reduction from 7.6 at baseline to 5.5 at the 7 days (0=minimum score, 10=maximum score), with further reductions at longer follow-ups: 3.8 at 30 days, 3.6 at 90 days, 4.4 at 180 days, and 2.7 at 365 days ($p<0.001$ at all timepoints).

The primary safety endpoint was the frequency of device and procedure related serious adverse events (SAEs). No device or procedure related SAEs were reported throughout the 90 day follow up duration. The secondary safety endpoint was the frequency of device and procedure-related adverse events (AEs). One participant reported moderate nasal bleeding at day 27 that was controlled

with standard nasal packing and cautery. The investigator deemed it to be remotely related to the device as the target treatment location was completely healed during endoscopic examination at day 7. Other adverse events commonly associated with healing after cryosurgery in the nasal passageways (pain/discomfort, headache, facial pain, bleeding, dry nose and ear blockage) were observed and by day 90, they had either self-resolved or the remaining events were rated as mild with a probable cause relating to pre-existing conditions.

Another multicenter, prospective, nonrandomized, single-arm interventional clinical trial was conducted at 6 centers in the US to assess the safety and effectiveness of the ClariFix device in patients with chronic rhinitis (allergic and nonallergic). The primary efficacy endpoint was the change from baseline to 90-day follow-up in rTNSS. The primary safety endpoint was the incidence of treatment-related adverse events.

Ninety-eight participants underwent bilateral treatment with ClariFix in the office under local anesthesia. The mean 90-day rTNSS score was significantly improved over baseline (6.1 ± 1.9 vs 3.0 ± 2.3, $p<0.001$) and remained improved through 9-month follow-up (3.0 ± 2.4, $p<0.001$).

One treatment-related serious adverse event was reported: a case of epistaxis that occurred 19 days after treatment during retrieval of a pledget that had been inadvertently left in the nasal cavity on the day of treatment. Bleeding was controlled with suction cautery in the operating room. Nonserious adverse events included headache, sinus infections, epistaxis, eye dryness, and nasal synechia.

SYMBOL DEFINITIONS

	Manufacturer (ISO 15223-1, 5.1.1)		Do Not Use if the Product Sterile Barrier System or Its Package is Compromised (ISO 15223-1, 5.2.8)
	Date of Manufacture (ISO 15223-1, 5.1.3)		Keep Dry (ISO 15223-1, 5.3.4)
	Use-by Date (ISO 15223-1, 5.1.4)		Upper Limit of Temperature 50°C (ISO 15223-1,5.3.6)
	Batch Code (ISO 15223-1, 5.1.5)		Consult Instructions for Use (ISO 15223-1,)
	Catalogue Number (ISO 15223-1, 5.1.6)		Risk of Explosion (ISO 7000, W002)
	Non-sterile (ISO 15223-1, 5.2.7)		Do Not Re-use (ISO 15223-1, 5.4.2)
	Sterilized Using Irradiation (ISO 15223-1, 5.2.4)		Prescription Use Only
	MR Unsafe (Unsafe for Use in a Magnetic Resonance Environment)		Caution (ISO 15223-1, 5.4.4)
	Sterile Barrier System		Quantity Per Box

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