# Cerene® Cryotherapy Device Instructions for Use

## CONTENTS



**CAUTION: UNITED STATES FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN TRAINED IN THE USE OF THE CERENE CRYOTHERAPY DEVICE**

## INDICATIONS FOR USE

The *Cerene Cryotherapy Device (Cerene Device)* is indicated for endometrial cryoablation in premenopausal women with heavy menstrual bleeding due to benign causes for whom child bearing is complete.

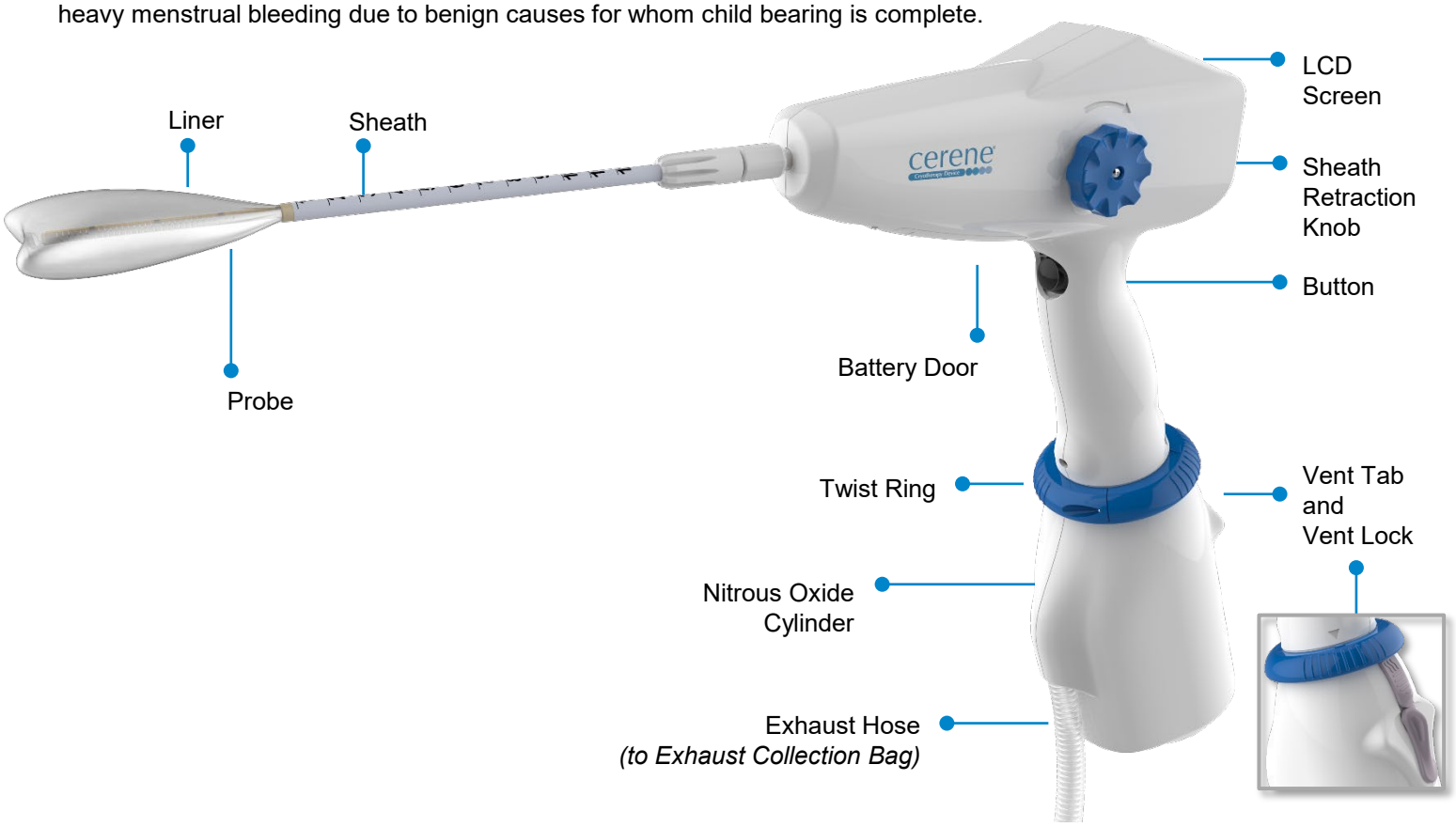



**Figure 1**. *Cerene Cryotherapy Device*

## CONTRAINDICATIONS

The *Cerene Device* is contraindicated for use in the following:

- A patient who is pregnant or who wants to become pregnant in the future. PREGNANCIES FOLLOWING ENDOMETRIAL ABLATION CAN BE DANGEROUS FOR BOTH MOTHER AND FETUS.
- A patient with known or suspected uterine cancer or pre-malignant conditions of the endometrium, such as unresolved endometrial hyperplasia.
- A patient with any anatomic condition (e.g., history of previous classical cesarean section or transmural myomectomy, including hysteroscopic and/or laparoscopic myomectomy performed immediately prior to the Cerene procedure) or pathologic condition (e.g., requiring long-term medical therapy) that could lead to weakening of the myometrium.
- A patient with a history of endometrial ablation and/or resection (including endometrial ablation/resection performed immediately prior to the Cerene procedure), regardless of the modality by which it was performed. REPEAT ABLATION MAY RESULT IN SERIOUS PATIENT INJURY.
- A patient with active genital or urinary tract infection (e.g., cervicitis, vaginitis, endometritis, salpingitis, cystitis, pelvic inflammatory disease, or tubo-ovarian abscess) at the time of treatment.
- A patient with an intrauterine device (IUD) currently in place.
- A patient with undiagnosed vaginal bleeding.

## WARNINGS

- Special care should be taken during instrumentation of a highly flexed uterus (i.e., acutely retroverted or anteverted) to ensure correct device placement and avoid uterine perforation.
- The *Exhaust Hose* must not be occluded during treatment. *Exhaust Hose* occlusion will cause the *Cerene Device* to shut down to avoid excessive intrauterine pressures and may result in early termination of the procedure.
- Always connect the *Exhaust Hose* to the *Exhaust Collection Bag* prior to turning on the *Cerene Device*. Connecting the *Exhaust Hose* to the *Exhaust Collection Bag* during the procedure could result in a temporary occlusion and could cause the *Cerene Device* to shut down to avoid excessive uterine pressure and may result in early termination of the procedure.
- Modification of the *Cerene Device* may result in serious patient injury.

## PRECAUTIONS

- Only healthcare professionals who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects, and hazards commonly associated with endometrial ablation should use the *Cerene Device*.
- Contents under pressure; do not disassemble. Follow storage instructions.
- Dropping the *Cerene Device* may affect sterility or cause damage. Do not use the *Cerene Device* if it has been dropped.
- Ensure all nitrous oxide is vented before disposing of the *Cerene Device*.
- Inhalation of nitrous oxide ($N_2O$) gas (exhaust gas) can cause short-term effects such as breathing difficulty, drowsiness, headache, and asphyxia. Use of the *Exhaust Collection Bag* accessory is required.
- Chronic exposure to nitrous oxide gas (exhaust gas) can lead to adverse reproductive, neurological, and hematological effects. Use of the *Exhaust Collection Bag* accessory is required.
- Since the *Exhaust Hose* may become very cold, avoid contact between the *Exhaust Hose* and the user or the patient (e.g., ensure the *Exhaust Hose* is not draped across the patient's leg).
- Use of carbon dioxide ($CO_2$) hysteroscopy is not indicated immediately prior to ablation.
- When performing saline hysteroscopy immediately prior to the ablation, take care to minimize the introduction of air and/or bubbles, which could interfere with the subsequent ablation procedure.
- Hysteroscopy should not be routinely performed post-ablation, as introduction of fluid or gas post-ablation could speed the thawing of the frozen uterine tissue and negatively impact the effectiveness of the cryotherapy.
- The safety and effectiveness of the Cerene Cryotherapy Device has not been fully evaluated in patients with
  - a permanent intratubal contraceptive device (e.g. Essure® or Adiana®).
  - sounded uterine length greater than 10 cm;
  - uterine cavity length that is less than 2.5 cm or greater than 6.5 cm;
  - myometrial thickness of less than 10 mm in any area of the uterus; or
  - structural abnormalities including septate, bicornuate, or other congenital malformation of the uterus; any endometrial polyp larger than 1 cm; any submucous fibroid; and any intramural fibroid(s) that distort(s) the uterine cavity.

## ADVERSE EVENTS

A total of 242 subjects were evaluated for safety. **Table 1** shows the number and percentage of subjects who reported device- or procedure-related adverse events. **There were no reported serious adverse device effects (SADEs) nor any reported serious adverse events (SAEs) that were procedure related.**

**Table 1 .** Number of Related Adverse Events and Number and Percentage of Subjects with One or More Related Adverse Events by Time of Occurrence

| Adverse Event | Number of Events | Number and Percent of Subjects (n=242) | | | |
|---|---|---|---|---|---|
| | | Day of Treatment | Day 1 | Day 2 to Week 2 | > Week 2 to Month 12 |
| Emesis | 1 | | | 1 (0.4%) | |
| Fever | 1 | | 1 (0.4%) | | |
| Bacterial vaginosis | 7 | | | 7 (2.9%) | |
| Endometritis | 1 | | | 1 (0.4%) | |
| Vulvovaginitis | 1 | | | | 1 (0.4%) |
| Groin pain | 1 | | | | 1 (0.4%) |
| Presyncope** | 4 | 3 (1.2%) | | | |
| Urinary incontinence | 2 | | | 2 (0.8%) | |
| Dyspareunia | 1 | | | | 1 (0.4%) |
| Menstrual cramps | 2 | | | | 2 (0.8%) |
| Pelvic pain | 2 | | | | 2 (0.8%) |
| Uterine cramps | 8 | 4 (1.7%) | 2 (0.8%) | 1 (0.4%) | 1 (0.4%) |
| Uterine tenderness | 1 | | | | 1 (0.4%) |
| Vaginal discharge | 2 | | | 1 (0.4%) | 1 (0.4%) |
| Hypertension | 2 | 2 (0.8%) | | | |

***Subjects with more than one occurrence of same event are only counted once.*

**Anticipated Post-Procedural Symptoms.**
For **any** endometrial ablation procedure, commonly reported postoperative symptoms include the following:

- Postoperative cramping can range from mild to severe. This cramping will typically last a few hours and significantly decreases by the first day following the procedure.
- When present, nausea and vomiting typically occur immediately following the procedure, are associated with anesthesia, and can be managed with medication.
- Vaginal discharge.
- Vaginal bleeding/spotting.

NOTE: Pregnancy following endometrial ablation is very dangerous for both the mother and the fetus.

Some or all of these risks may require a need for reoperation or subsequent treatment and/or may lead to permanent disability or death.

**Other Adverse Events.**
As with **all** endometrial ablation procedures, serious injury or death can occur. The following adverse events could occur or have been reported in association with the use of other endometrial ablation systems and may occur when the *Cerene Device i*s used:

- Post-ablation tubal sterilization syndrome.
- Pregnancy-related complications.
- Thermal injury to adjacent tissue, including bowel, bladder, cervix, vagina, vulva and/or perineum.
- Thermal injury to extremity.
- Perforation of the uterine wall.
- Mechanical bowel injury.
- Cervical or vaginal laceration.
- Transient change in the appearance of the cervical epithelium
- Hemorrhage.
- Hematometra.
- Difficulty with defecation or micturition.
- Abdominal pain and/or bloating
- Uterine necrosis.
- Air or gas embolism.
- Infection or sepsis.
- Diarrhea.
- Headache.
- Complications leading to serious injury or death.

## CLINICAL STUDY

**Purpose.** The objective of the study was to evaluate the safety and effectiveness of the *Cerene Device* in premenopausal women with heavy menstrual bleeding due to benign causes for whom childbearing was complete.

**Pretreatment.** Prior to undergoing the ablation procedure, the subject's endometrial lining was thinned using medications or the procedure was scheduled in the early proliferative phase. Dilatation and curettage (D&C) was not permitted prior to the ablation procedure, with the exception of a light suctioning with a cannula to remove residual clots or loose intracavitary debris. The Investigator could reschedule the procedure if there was any concern that endometrial thinning was not properly accomplished.

**Study Endpoints.** The primary safety endpoint was incidence of serious adverse events and serious device-related adverse effects at 12 months. The primary effectiveness endpoint was reduction in menstrual bleeding at 12 months; success was defined as a Pictorial Blood Loss Assessment Chart (PBLAC) score of ≤ 75.[1,2] Additional evaluations included amenorrhea rate at Month 12, subject-reported peri-procedural pain experience, evaluation of dysmenorrhea at Month 12, Quality of Life outcomes at Month 3, 6, and 12 using the Menorrhagia Impact Questionnaire (MIQ) and the Premenstrual Symptoms Impact Survey (PMSIS™), evaluation of uterine access and healing at twelve months post-procedure, and additional medical or surgical interventions for continued heavy menstrual bleeding through Month 36.

**Methods.** A prospective, multi-center, single-arm, open-label, non-randomized study was conducted at 11 sites by Investigators experienced with endometrial ablation. Subjects were required to meet a set of entry criteria.

**Patient Population.** A total of 242 subjects were treated in this study and comprise the Intent-to-Treat (ITT) population. The demographics of the ITT cohort are typical for an endometrial ablation study performed in the United States. **Table 2** provides the baseline demographic and gynecological history parameters. An evaluation of these data confirmed the data could be pooled across sites and countries.

**Key Inclusion Criteria**

- Refractory heavy menstrual bleeding with no definable organic cause
- Women aged 25 to 50 years
- Uterine length ≤ 10cm
- Endometrial cavity length ≥2.5 cm and ≤6.5 cm
- Myometrial thickness ≥10 mm
- Menstrual blood loss with a PBLAC score of ≥150
- Premenopausal
- Willing to use reliable contraception
- Predictable, cyclic menstrual cycles

[1] The PBLAC is a self-administered instrument that allows the subject to record the number of menstrual products she used during her menstrual period. A PBLAC score is calculated from the number, type, and saturation level of menstrual products recorded on the diary.

[2] The effectiveness of the *Cerene Device* was compared to an FDA established objective performance criterion (OPC) and therefore did not have an active Control Group in the study. The OPC was developed by FDA with input from industry and members of the Obstetrics and Gynecology Devices Panel.

**Table 2.** Demographics and Gynecological History

| | **Patient number = 242** |
|---|---|
| **Age** | |
| Mean ± SD (median) | 40.1 ± 5.1 (41.0) |
| Range (min, max) | (25, 50) |
| N Age 25-40 | 116 (47.9%) |
| N Age >40 | 126 (52.1%) |
| **Ethnicity** | |
| Hispanic or Latino | 42 (17.4%) |
| Not Hispanic or Latino | 200 (82.6%) |
| **Race** | |
| White | 190 (78.5%) |
| Black or African American | 6 (2.5%) |
| Asian | 0 (0.0%) |
| American Indian or Alaska Native | 3 (1.2%) |
| Native Hawaiian or Other Pacific Islander | 0 (0.0%) |
| Other | 43 (17.8%) |
| **BMI, kg/m2** | |
| Mean ±SD (median) | 29.8 ± 6.9 (28.5) |
| Range (min, max) | (16.7, 50.5) |
| **Gravida** | |
| Mean ± SD (median) | 3.0 ± 1.5 (3.0) |
| Range (min, max) | (0, 8) |
| **Para** | |
| Mean ± SD (median) | 2.4 ± 1.1 (2.0) |
| Range (min, max) | (0, 6) |
| **C-Section (Low Transverse)** | |
| Number of subjects | 86 (35.5%) |
| **Dysmenorrhea** | |
| No symptom | 27 (11.2%) |
| Very Mild | 16 (6.6%) |
| Mild | 23 (9.5%) |
| Moderate | 74 (30.6%) |
| Severe | 69 (28.5%) |
| Very Severe | 33 (13.6%) |
| **PBLAC Score at Baseline** | |
| Mean ± SD (median) | 360.6 ± 332.1 (290.5) |
| Range (min, max) | (150.0, 4506.5) |
| **FSH (IU/L)** | **N=126*** |
| Mean ± SD (median) | 7.8 ± 5.3 (6.3) |
| Range (min, max) | (0.2, 29.1) |

**Only those subjects > 40 years old at screening received an FSH test.*

**Key Exclusion Criteria**

- Pregnant or has a desire to conceive
- Endometrial hyperplasia
- Active endometritis
- Active pelvic inflammatory disease
- Active sexually transmitted disease
- Bacteremia, sepsis, or other active systemic infection
- Active infection of the genitals, vagina, cervix, or uterus
- Gynecological malignancy
- Known clotting defects or bleeding disorders
- Prior uterine surgery that interrupts the integrity of the uterine wall
- Previous low transverse cesarean section with myometrial thickness <10 mm
- Previous endometrial ablation procedure
- Clinically significant adenomyosis
- Presence of an implantable contraceptive device
- Currently on medications that could thin the myometrial muscle
- Currently on anticoagulants
- Abnormal or obstructed cavity
- Presence of an IUD
- Postpartum ≤6 months

**Subject Accountability.** Of the 242 subjects who were treated in the study, 230 (95%) were available for evaluation of safety or effectiveness at the 12-month post-operative visit.

**Table 3:** Subject Disposition at Month 12

| Disposition Category | Safety N (%) | Effectiveness N (%) |
|---|---|---|
| **ITT: Treated** | **242 (100%)** | **242 (100%)** |
| **Not evaluable at Month 12** | **12 (5.0%)** | **12 (5.0%)** |
| Lost to follow-up | 6 (2.5%) | 6 (2.5%) |
| Secondary intervention for menstrual bleeding | 4 (1.7%) | 4 (1.7%) |
| Other: No menstrual diary | N/A | 1 (0.4%) |
| Other: Safety evaluation not available | 1 (0.4%) | N/A |
| Missed Visit | 1 (0.4%) | 1 (0.4%) |
| **Subjects with known Month 12 outcome** | **230 (95.0%)** | **230 (95.0%)** |

## RESULTS

***Safety Endpoint.*** There were no reported serious adverse device effects (SADEs) nor any reported serious adverse events (SAEs) that were procedure related. Adverse event information is described in the Adverse Events Section.

**Primary Effectiveness Results.** Patient success at 12 months post procedure is defined as a reduction in Pictorial Blood Loss Assessment Chart (PBLAC) score from ≥150 before the procedure to ≤ 75 after the procedure. **Table 4** includes the clinical results based on the 242 subjects (ITT group) in the study.

**Table 4.** Primary Endpoint Response Rate at Month 12

| Month 12 Response Rate | ITT analysis cohort (N=242) |
|---|---|
| Number of successes (PBLAC ≤75) | 186 |
| Study success rate | 76.9% |

**Secondary Effectiveness Results**

***Need for Medical or Surgical Intervention.*** Four subjects (1.7%) had interventions for continued heavy menstrual bleeding and were exited from the study. Two subjects (0.83%) elected to proceed to hysterectomy. One subject (0.41%) required medication for frequent, prolonged heavy menses. One subject (0.41%) resumed treatment with Lysteda and voluntarily withdrew at Month 3.

***Pain Management and Peri-Procedural Pain Experience.*** All treatments were performed under local anesthesia using paracervical or parametrial block (PCB) per standard of care. A combination of other medications was administered per investigator discretion. **Table 5** presents the anesthesia and medications administered at the time of Cerene treatment. A subject is counted only once in each category, according to the highest level of medication administered.

**Table 5.** Anesthesia and Pain Medications at Treatment

| Anesthesia & Medications Used During Treatment (N=242) | N (%) |
|---|---|
| PCB only | 20 (8.3%) |
| PCB with NSAIDs | 48 (19.8%) |
| PCB with oral narcotics and/or anxiolytics | 167 (69.0%) |
| PCB with IV sedation | 7 (2.9%) |
| General anesthesia | 0 (0.0%) |

Prior to the procedure, subjects were asked to rate their acceptable pain threshold on a numeric rating scale of 0-10. The median acceptable pain score was six (6). At several points before, during, and after the procedure, subjects were asked to rank their level of pain on the 0-10 scale. After one minute of ablation, 92.1% of subjects described their pain level at or below the median acceptable pain score.

**Table 6.** Subject Rating of Pain during Treatment & Day One Post Treatment

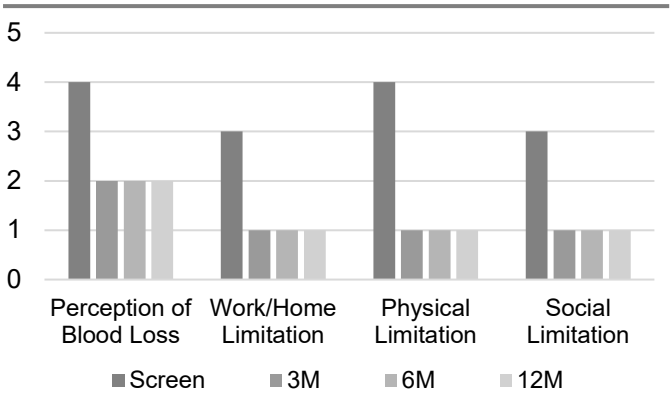
| Pain Rating during Treatment | N | Median Pain Score |
|---|---|---|
| Before Device Insertion | 241* | 1.0 |
| After Device Insertion | 240* | 2.0 |
| After Liner Deployment (before endometrial ablation was initiated) | 240* | 1.0 |
| After 1 Minute of Ablation | 240* | 2.0 |
| End of Ablation | 239* | 1.0 |
| 15-30 Minutes Post Procedure | 242 | 2.0 |
| At Time of Discharge | 242 | 2.0 |
| Day One | 241 | 0.0 |

**Subjects unable to provide pain score rating due to sedation.*

***Quality of Life.*** The Menorrhagia Impact Questionnaire (MIQ) and the Premenstrual Symptoms Impact Survey (PMSIS) were used at baseline and follow up to assess quality of life.

**Menstrual Impact Questionnaire.** Subjects' responses to the MIQ demonstrate a reduction in perceived blood loss and limitations due to menstrual bleeding between Screening and Month 12.

**Table 7.** Change in Median Response to MIQ




*For Perception of Blood Loss, 1= light, 2= moderate, 3= heavy, 4= very heavy. For other metrics, 1= not at all, 2= slightly, 3= moderately, 4= quite a bit, 5= extremely.*

**Premenstrual Symptoms Impact Survey.** The tabulation demonstrates a 68.6% reduction in the subjects' combined PMSIS score, from a mean screening score of 53.8 to 16.9 at Month 12. These scores indicate an improvement in premenstrual syndromes following treatment.

**Table 8.** Combined PMSIS Score

| Combined Score | Screening (N=242) | Month 12 (N=230) |
|---|---|---|
| Mean | 53.8 | 16.9 |
| Median | 58.3 | 8.3 |

**Dysmenorrhea.** At screening, over 40% of subjects reported dysmenorrhea as 'severe' or 'very severe' and at Month 12, 6% of subjects reported the same intensity of symptoms.

**Table 9.** Dysmenorrhea at Screening and Month 12

| Subject report of Dysmenorrhea | Screening (N=242) | Month 12 (N=230) |
|---|---|---|
| 0-No symptom | 11.2% | 32.2% |
| 1-Very Mild | 6.6% | 30.4% |
| 2-Mild | 9.5% | 17.4% |
| 3-Moderate | 30.6% | 14.3% |
| 4-Severe | 28.5% | 4.3% |
| 5-Very Severe | 13.6% | 1.3% |
| Missing | 0% | 0% |

***Subject Satisfaction.*** Of 214 subjects that reported their level of satisfaction, 192 (89.7%) were satisfied or very satisfied with their outcome following treatment with the *Cerene Device*. Of 225 subjects that reported their level of recommendation to a friend/family, 213 subjects (94.7%) would definitely recommend or consider recommending the *Cerene* procedure.

***Uterine Access and Intrauterine Adhesions.*** The Month 12 follow-up assessment included a hysteroscopic evaluation of the uterine cavity to determine if physical access and the ability to systematically assess the post-ablation uterine cavity were preserved. Of 230 available subjects, 223 (97%) underwent a hysteroscopy at Month 12. Uterine cavity entry was not possible in three subjects (1.8%) due to pain intolerance (2) and cervical stenosis (1).

**Table 10.** Investigator Evaluation of Uterine Cavity

| Assessment (N=223) | Yes (%) |
|---|---|
| Uterine cavity entry with a hysteroscope | 220 (98.7%) |
| Full visualization of the uterine cavity | 204 (91%) |

**Table 11.** Investigator Assessment of Cavity Findings

| Assessment (N=204)* | Yes (%) |
|---|---|
| Would the Investigator be able to direct a biopsy anywhere within the uterine cavity? | 178 (87.3%) |
| Overall, was the Investigator satisfied that he/she was able to adequately visualize the endometrium to evaluate the uterine cavity for pathologic change? | 195 (95.6%) |

**Uterine cavities that could be fully visualized*

***Additional Bleeding Outcome.*** In addition to the primary success criterion of PBLAC ≤75, analysis was completed to evaluate amenorrhea (PBLAC=0).

**Table 12**. Amenorrhea at Month 12

| Month 12 Amenorrhea Rate | ITT analysis cohort (N=242) |
|---|---|
| Number of subjects with amenorrhea (PBLAC=0) | 25 |
| Amenorrhea rate | 10% |

**Additional Evaluations**

***Procedure Time.*** Procedure time for each subject was determined by recording the time of device insertion and device removal. Treatment time is fixed at 2.5 minutes for each subject.

**Table 13.** Procedure and Treatment Times

| | ITT analysis cohort (N=242) |
|---|---|
| Mean procedure time (device insertion to device removal) | 6.9 minutes |
| Treatment time | 2.5 minutes |

***Subjects' Report of Their Last Menstrual Period.*** Subjects were asked to describe their last menstrual period prior to the Month 12 follow-up visit. Over 90% of subjects reported that they no longer get their period or have a normal or lighter-than-normal period.

**Table 14.** Subjects' Report of Last Menstrual Period

| Description of Last Menstrual Period | N=230 N (%) |
|---|---|
| I no longer get my period | 15 (6.5%) |
| My periods are lighter than normal | 160 (69.6%) |
| My periods are normal | 34 (14.8%) |
| I continue to have heavy periods | 21 (9.1%) |

***Return to Work and Normal Daily Activities.*** At the two week follow-up visit, subjects were asked to report when they returned to normal daily activities, including work and home responsibilities.

**Table 15.** Return to Normal Daily Activities

| 2 Week Follow-up | Return to Normal Daily Activities (N=242) |
|---|---|
| Mean ±SD (median) | 2.0 ± 2.3 (1) |
| Range (min, max) | (0, 21) |
| No recovery time needed | 19 (7.8%) |
| Returned in 1 Day | 118 (48.8%) |
| Returned in 2 Days | 46 (19.0%) |
| Returned in 3 Days | 26 (10.7%) |

**PATIENT SELECTION**

Abnormal uterine bleeding can be caused by a variety of underlying problems including, but not limited to: endometrial cancer, myomas, polyps, drugs and endometrial ovulatory dysfunction.[3] Patients always should be screened and evaluated to determine the cause of excessive uterine bleeding before any treatment is initiated. Consult medical literature relative to various endometrial ablation techniques, indications, contraindications, complications and hazards prior to the performance of any endometrial ablation procedure.

**PATIENT COUNSELING**

As with any procedure, the physician needs to discuss with the patient the risks, benefits and alternatives to endometrial ablation. Patients should read the Patient Information Booklet (PIB). While the PIB is not intended to replace appropriate physician counseling, each patient should receive the PIB during their initial visit/consultation to allow her sufficient time prior to the procedure to read and adequately understand the important information on the risks and benefits associated with the Cerene Device. Patients should also be informed that pregnancy is not likely after endometrial ablation, but it can happen. If it does, the risk of miscarriage and other problems are greatly increased. If a woman still wants to become pregnant, she should not have this procedure. Women who have endometrial ablation should use birth control until after menopause.[4]

Vaginal discharge is typically experienced during the first few weeks following ablation and may last as long as several weeks. Generally, the discharge is described as bloody during the first few days; serosanguinous (thin, watery discharge, yellow to red in color) by approximately one week; then profuse and watery thereafter. Any unusual or foul-smelling discharge should be reported to the physician immediately. Other post-procedural complications include cramping/pelvic pain, nausea and vomiting.

**Uterine perforation should be considered in the differential diagnosis of any post-operative patient complaining of acute abdominal pain, fever, shortness of breath, dizziness, hypotension or any other symptom that may be associated with uterine perforation with or without damage to the adjacent organs of the abdominal cavity. Patients should be counseled that any such symptoms should be immediately reported to their physician.**

**Endometrial Thinning.** The lining of the uterus should be thin prior to endometrial ablation with the *Cerene Device*. This can be accomplished by performing the procedure during the early proliferative phase or after administration of an appropriate medication (e.g., oral contraceptives or a progestin). The safety and effectiveness of the Cerene procedure following mechanical pretreatment has not been evaluated.

[3] American College of Obstetrics and Gynecology. Practice Bulletin No. 128. Diagnosis of Abnormal Uterine Bleeding in Reproductive-Age Women. July 2012.

[4] American College of Obstetrics and Gynecology. Frequently Asked Questions Special Procedures: Endometrial Ablation. July 2017.

## POST APPROVAL STUDY OVERVIEW AND RESULTS

Purpose: The objective of the post-approval study (PAS) was to provide long term safety and effectiveness data on subjects treated with the Cerene device.

Study Endpoints. Subject long term outcomes, assessed at the Month 24 and Month 36 follow-up visit, included medical and/or surgical intervention for heavy menstrual bleeding (HMB), menstrual status, gynecologic adverse events, pregnancy status, contraception status, QoL using the MIQ and PMSIS, and satisfaction.

Methods. All available subjects from the pivotal clinical study were enrolled in the PAS.

Patient Population. 232 of the 242 subjects treated in the pivotal study were enrolled in the PAS.

**Subject Accountability.** Of the 242 subjects who were treated in the study, 232 continued in the PAS. **Table 16** provides the subject disposition details during the PAS.

**Table 16.** Subject Disposition During the PAS

| Subject Disposition | Month 24 | Month 36 |
|---|---|---|
| **Subject Visit Expected** | **N=232** | **N=213** |
| **Subject Visit Performed** | **210** | **201** |
| *Visit Missed* | *3* | *0* |
| **Exited: Visit Not Performed** | **19** | **12** |
| *Endometrial Ablation* | *1* | *0* |
| *Endometrial Ablation and Mirena IUD* | *1* | *0* |
| *Hormonal medication for menstrual bleeding* | *1* | *3* |
| *Hysterectomy for menstrual bleeding* | *2* | *2* |
| *Hysterectomy for pelvic pain* | *2* | *1* |
| *Hysterectomy for uterine fibroids* | *1* | *1* |
| *Hysterectomy for uterine prolapse* | *0* | *1* |
| *IUD: Mirena* | *1* | *0* |
| *Lost to follow-up* | *4* | *3* |
| *Uterine Pregnancy* | *2* | *1* |
| *Withdrew Voluntarily* | *4* | *0* |

**Subjects' Report of Their Last Menstrual Period.** **Table 17** provides subject's description of their LMP at the Month 24 and Month 36 follow-up visit. At their final study visit, 88.6% of subjects reported that they no longer get their period or have a normal or lighter-than-normal period; 14.4% had no menstrual bleeding.

**Table 17.** Subject's Description of LMP

| Description of LMP | Month 24* N = 162 | Month 36 N = 201 |
|---|---|---|
| I no longer get my period | 5 (3.1%) | 29 (14.4%) |
| My periods are lighter than normal | 98 (60.5%) | 99 (49.3%) |
| My periods are normal | 35 (21.6%) | 50 (24.9%) |
| I continue to have heavy periods | 24 (14.8%) | 23 (11.4%) |

**Gynecologic Adverse Event Reports.** Only gynecologic AEs were reported after the Month 12 follow-up visit. **Table 18** provides the AEs that were reported in the PAS. There were no unanticipated adverse device effects. One event, postcoital bleeding, was recorded as related to the procedure. There were 5 pregnancies reported between 1 and 3 years of follow-up. One ectopic and two uterine pregnancies were reported prior to and two uterine pregnancies were reported during the PAS. The ectopic pregnancy was surgically removed, three uterine pregnancies resulted in pre-term (35-36 weeks) live births, and one uterine pregnancy was terminated and the subject continued in the PAS. None of these subjects were using contraception despite the counseling they and all subjects received.

**Table 18.** Gynecologic Adverse Events During the PAS

| Adverse Event | N |
|---|---|
| Adenomyosis | 1 |
| Dysmenorrhea | 2 |
| Dyspareunia | 1 |
| Endometritis | 1 |
| Intermenstrual bleeding | 2 |
| Menorrhagia; continuing, worsening, irregular menses | 15 |
| Pelvic cramping | 2 |
| Pelvic Pain | 4 |
| Polycystic ovarian disease | 1 |
| Post coital bleeding | 1 |
| Pregnancy; uterine | 1 |
| Pregnancy; uterine terminated | 1 |
| Right breast mass | 1 |
| Uterine fibroids | 2 |
| Uterine Prolapse Stage 2 | 1 |
| Vaginal infection and/or discharge | 11 |
| Vaginal/vulvar pruritus | 2 |

**Menstrual Impact Questionnaire.** Subjects' responses to the MIQ demonstrate a sustained reduction in limitations in work/home, physical, and social/leisure activities, due to menstrual bleeding. 90.5% of subjects were free of moderate to significant limitations at the final study visit. **Table 19** provides subjects responses to the MIQ at Month 24 and 36.

**Table 19.** MIQ; Subjects' Report of Activity Limitations

| MIQ: Limitations in Activities | Month 24* N = 162 | Month 36 N =201 |
|---|---|---|
| Free of limitation in activity at moderate or higher level | 155 (95.1%) | 182 (90.5%) |
| Limitation in activity is present at moderate or higher level | 8 (4.9%) | 19 (9.5%) |

*IRB/EC approval had not been obtained at all sites, therefore the full cohort of available subjects was not queried.

## POST APPROVAL STUDY RESULTS

**Premenstrual Symptoms Impact Survey.** Subjects' responses to the PMSIS demonstrate a sustained reduction in pre-menstrual symptoms (PMS), which include frustration, mood swings, limited concentration, feelings of tension and tiredness, and an inability to socialize. PMS generally occurs 5-7 days before the onset of the menstrual period and go away after it begins or shortly thereafter. **Table 20** provides subjects' responses to the PMSIS at Month 24 and 36.

**Table 20.** PMSIS; Subjects' Report of PMS

| PMSIS: PMS Prior to Menses | Month 24* N=163 | Month 36 N=201 |
|---|---|---|
| Free of PMS often, most often, very often, or all of the time | 133 (81.6%) | 171 (85.1%) |
| PMS occur often, most often, very often, or all of the time | 30 (18.4%) | 30 (14.9%) |

*IRB/EC approval had not been obtained at all sites, therefore the full cohort of available subjects was not queried.

**Subject Satisfaction.** Of 181 subjects that reported their level of satisfaction at the final study visit, 153 (84.5%) were satisfied or very satisfied with their outcome following treatment with the *Cerene Device*. Also at the final study visit, 175 (90.7%) of 193 subjects reported they would definitely recommend or consider recommending the *Cerene* procedure to a friend/family member.

**Study Limitations.** The limitations of our study include the underrepresentation of African American women, which is present in studies of all endometrial ablation devices. Additionally, the trial was not randomized with a specific comparator ablation technique. However, the primary outcome is measured against the standard (FDA's OPC taken from historic data of other NREA techniques), thereby negating the need for a comparative technique.

## CLINICAL BENEFITS

The probable benefits of the Cerene Cryotherapy Device are based on data collected in clinical studies as described above. The main benefit of the Cerene Cryotherapy Device is a reduction in menstrual blood loss. In addition, improvement in subjective quality of life scores and high patient satisfaction provide further evidence of probable benefit. The clinical study demonstrated that treatment with the Cerene Cryotherapy Device does not necessarily require the use of IV sedation or general anesthesia and can be performed in an office setting. Following treatment with the Cerene Cryotherapy Device, it should be possible to adequately evaluate the endometrial cavity in most patients to diagnose and treat intrauterine conditions.

## GENERAL INSTRUCTIONS

- Device is to be used at standard atmospheric pressure.
- Follow all instructions on the *LCD Screen* during the entire procedure.
- The *LCD Screen* will illuminate for at least 15 seconds whenever new information is displayed and will flash to attract attention when necessary.
- Do not rotate the *Sheath Retraction Knob* at any time unless prompted.
- Do not release the *Vent Lock* before being prompted.
- Pressing the *Button* before being prompted will pause the device.
- The *Cerene Device* may be paused and the procedure interrupted to accommodate patient comfort or clinical need (see **Table 21** on page 14).

## PACKAGING & STORAGE

- The *Cerene Device* is provided sterile in a sealed package (sterilization method is ethylene oxide). Do not use the *Cerene Device* if the package appears damaged in any way.
- Do not re-sterilize or reuse the *Cerene Device*. Re-sterilization or re-use will damage the *Cerene Device* and could harm the patient.
- Each *Cerene Device* contains enough nitrous oxide for only one treatment.
- Store the Cerene Device in a dry place at 55°F - 85°F (12.8°C – 29.5°C). The Cerene Device must be stored at this temperature for at least four (4) hours prior to use to ensure it is at operating temperature.

## PREPARATION

### 1 Room Preparation

- Hang the *Exhaust Collection Bag (refer to IFU-3244)* on an IV pole.
- Prepare ultrasound equipment, if necessary.

**Figure 2**. *Exhaust Collection Bag*

### 2 Patient Preparation

- Prepare and drape patient for an intrauterine procedure per custom and practice.
- Administer any medications for anesthesia, sedation, anxiolysis, and/or pain management per custom and practice (including a paracervical block, if administering).
- Use a speculum and/or retractors and sufficient illumination to adequately visualize the vagina and cervix.
- Sound the uterus and cervix, and calculate the uterine cavity length by subtracting the cervical length from the uterine sounding length.
- Note if the patient has an acutely retroverted or anteverted uterus.
- Ensure the cervix is dilated to 6 mm.

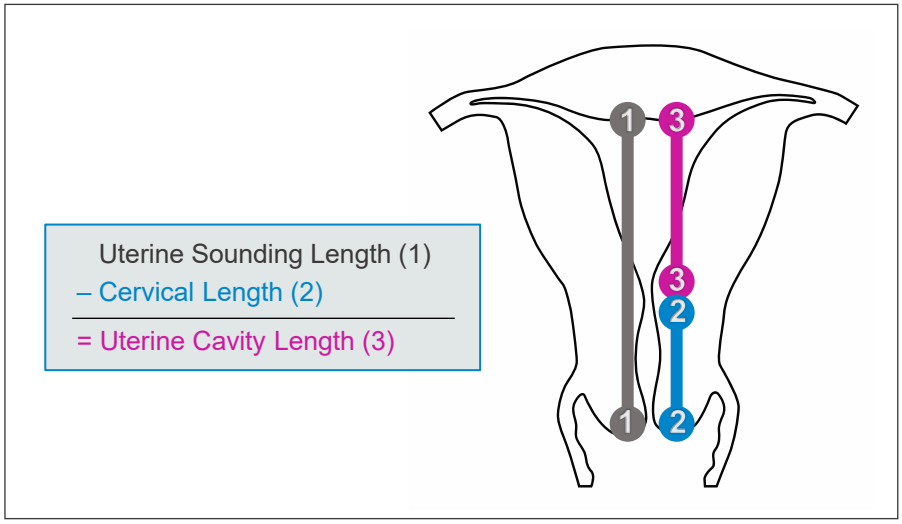



**Figure 3**. *Calculate the uterine cavity length*

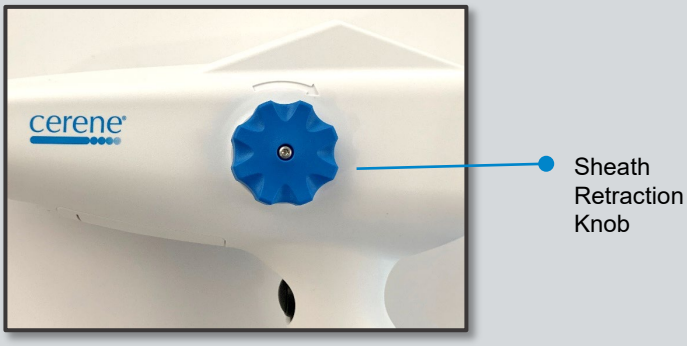



**Figure 4**. *Sheath Retraction Knob*

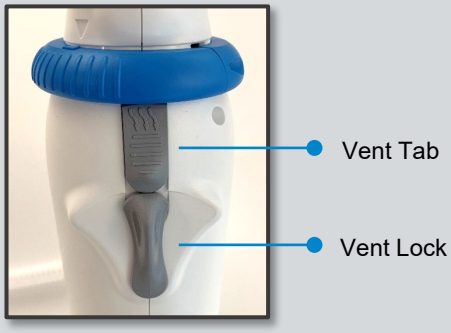



**Figure 5**. *Vent Tab and Vent Lock*

## 3 Device Preparation

- Peel off the Tyvek® lid and remove the plastic retainer.
- Remove the *Cerene Device* from the plastic tray, keeping the inside of the tray sterile.
- Remove the *Battery* tab and the *Probe* tip cover.
- Connect the end of the *Exhaust* Hose to the *Exhaust Collection Bag* until you hear an audible click.

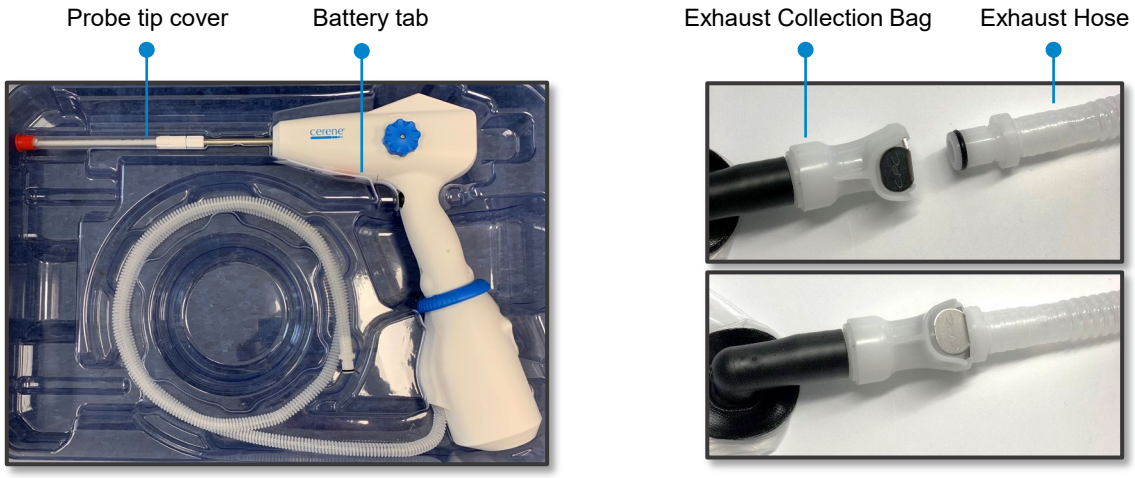



**Figure 6.** *Device preparation. When the Exhaust Hose and Exhaust Collection Bag are properly connected, you will hear an audible click.*

NOTE: Ensure that the *Exhaust Hose* is not kinked or obstructed at any time.

NOTE: Do not connect the *Exhaust Hose* to a scavenging system or to wall suction directly, or to any other collection system other than the *Exhaust Collection Bag* accessory manufactured by Channel Medsystems®.

**Turn on the device by rotating the Twist Ring counter-clockwise until the triangle on the device handle and the triangle on the Twist Ring are aligned.**

**Confirm that the Exhaust Collection Bag is attached.**

## 1 INSERT THE CERENE DEVICE

- When prompted, press and release the *Button* to start.
- When prompted to insert the *Cerene Device*, grasp the anterior cervical lip with a tenaculum, apply traction to the tenaculum, and gradually insert the *Probe* to the fundus, taking care not to damage the *Liner* on the tenaculum.
- Ensure the number on the *Sheath* at the external os corresponds to the uterine sounding length and/or confirm proper placement using ultrasound to view the location of the probe.

## 2 INITIATE LINER DEPLOYMENT & SAFETY CHECKS

- Turn the *Sheath Retraction Knob* toward you until the *LCD Screen* displays 2.5 cm.
- Confirm that the *Probe* tip is placed at the fundus.
- When prompted, press and release the *Button* to initiate the *Liner* inflation and safety checks.

## 3 SET CAVITY LENGTH

- When prompted, turn the *Sheath Retraction Knob* toward you until the calculated uterine cavity length (see “Patient Preparation”, page 10) is displayed on the *LCD Screen*.

## 4 TREAT THE CAVITY

- When prompted, confirm that the *Probe* tip is placed at the fundus.
- Press and release the *Button* to initiate the final inflations and safety checks and start treatment.
- Maintain the *Cerene Device* position for the duration of this step.

## 5 REMOVE THE DEVICE

- When prompted, unlock the *Vent Lock,* then slide the *Vent Tab* to vent excess nitrous oxide and initiate vacuum.
- Once the device removal countdown is complete, gently withdraw the *Cerene Device* from the patient.
- Once removed, press and release the *Button*. Set the *Cerene Device* aside to complete venting.

To pause the *Cerene Device* press and release the *Button*. To resume, press and release the *Button*.

For additional information, see **Table 21** on page 14.

NOTE: Maintain the same angle of insertion throughout the procedure. Do not exceed 30° from horizontal (anterior or posterior).

NOTE: If insertion is difficult, remove the *Cerene Device*, reassess the cervico-uterine axis, further dilate the cervix as needed, and then reinsert the *Probe*. Do not apply excessive force to insert the *Probe*.

⚠ If the uterus is acutely retroverted or anteverted, take extra care during insertion to ensure correct device placement and avoid uterine perforation.

NOTE: If the *LCD Screen* indicates that the *Sheath* has been retracted beyond 2.5cm, turn the *Sheath Retraction Knob* away from you until the *LCD screen* displays 2.5cm.

NOTE: If the *Cerene Device* is removed from the patient after the *Sheath Retraction Knob* has been turned, do not re-insert. Continue treatment with a new *Cerene Device* to ensure proper *Liner* deployment.

NOTE: Once the *Sheath Retraction Knob* has been turned and the *Sheath* has been retracted, *Sheath* markings can no longer be used to confirm device position.

⚠ Attempting to advance the device so the *Sheath* markings match the uterine sounding length at this point in the procedure could cause a uterine perforation.

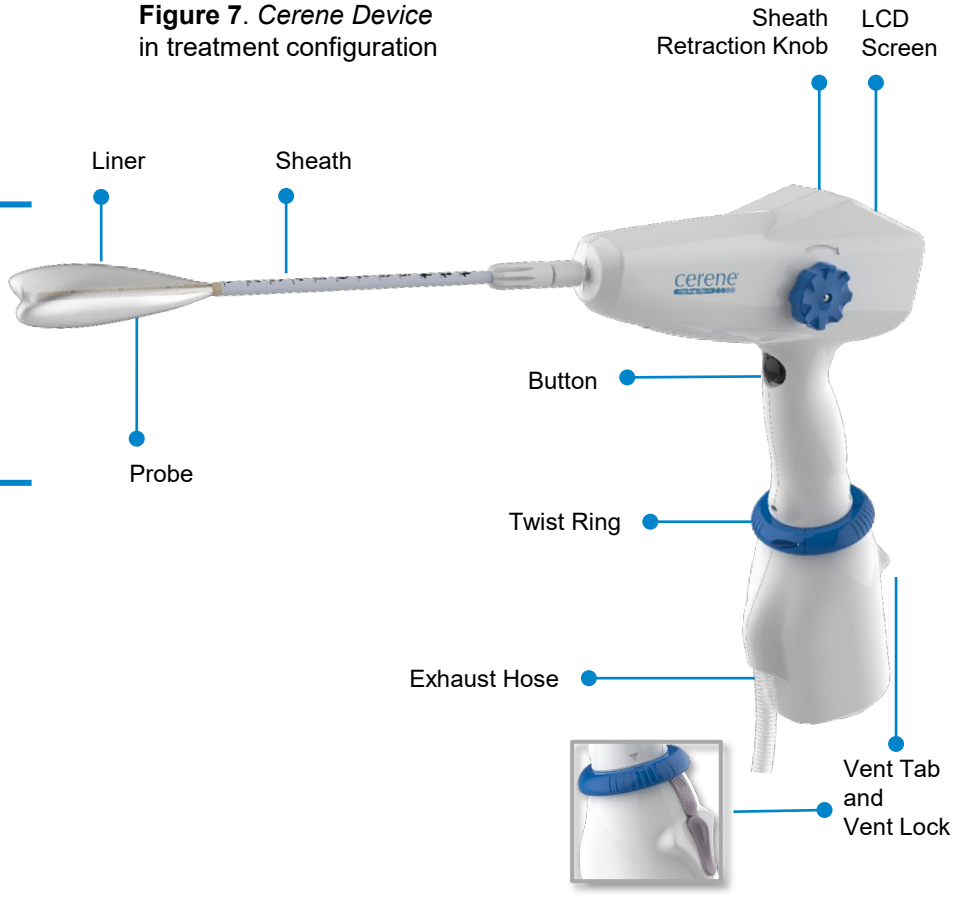
NOTE: If the calculated uterine cavity length is 2.5 cm, no additional *Sheath* retraction is required. Press and release the *Button* to confirm the 2.5 cm cavity length.

NOTE: Do not move the *Sheath Retraction Knob* after pressing the *Button* to start treatment.

NOTE: If you cannot easily remove the *Cerene Device*, wait for the frozen uterine tissue to thaw and release the *Liner* before trying again. This could take several minutes.

NOTE: To avoid detaching the *Liner*, do not use excessive force when removing the *Cerene Device*.

**Figure 7**. *Cerene Device* in treatment configuration



## PAUSING THE CERENE DEVICE

The *Cerene Device* may be paused to accommodate patient comfort or clinical need. Pausing the *Cerene Device* deflates the *Liner* and relieves intrauterine pressure.

**Table 21**. Information on Pausing the *Cerene Device*

| | BEFORE Treating the Cavity | DURING Treatment of the Cavity |
|---|---|---|
| **To PAUSE:** | Press and release the *Button* | Press and release the *Button* |
| **Number and length of pauses allowed** | No limit on the number or length of pauses<br><br>NOTE: Treatment must begin within 25 minutes of powering on the *Cerene Device* | When "treating" is displayed on the *LCD screen*, the user may pause the *Cerene Device* up to two times, for up to 15 seconds each time<br><br>NOTE: *LCD screen* will display a 15-second countdown |
| **To RESUME:** | Press and release the *Button* | Press and release the *Button* |

## DISPOSAL

Once the *LCD Screen* indicates the *Cerene Device* is safe for disposal, disconnect the *Exhaust Collection Bag* from the *Cerene Device* and dispose of the *Cerene Device* per local procedure.

NOTE: If the *LCD Screen* indicates that it is unsafe to dispose of the *Cerene Device*, contact Channel Medsystems (+1-510-338-9301, support@cerene.com).

NOTE: If local practice requires the removal of batteries prior to device disposal, locate the battery compartment on the underside of the device, remove the Battery Door, and remove the two AAA batteries.

Empty the *Exhaust Collection Bag* and dispose per custom and practice (refer to IFU-3244, IFU for *Cerene Exhaust Collection Bag*).

- Outdoors: Open the plug, hold the bag below waist level, and roll the bag from the top down.
- Via wall suction: The Exhaust Collection Bag can be emptied via wall suction using an adapter that can be requested when ordering the device. Attach the barbed end of the adapter to wall suction. Then, connect the adapter to the mating fitting at the bottom of the bag.

**Figure 8.** *Emptying the Exhaust Collection Bag outdoors*

## TROUBLESHOOTING

In the event that an error code or message is displayed on the *LCD Screen* or the *Cerene Device* stops functioning:

1. Identify the error code and *LCD message* in Table 22
2. Follow the "Next Steps" to safely end the procedure
3. Write down the error code or message and contact Channel Medsystems (+1-510-338-9301 or support@cerene.com)

In the event of an error, nitrous oxide flow is stopped, *Liner* pressure is relieved and the user is prompted to remove and dispose of the *Cerene Device*. The *Cerene Device* is disabled and cannot be re-used after an error has been detected. If the *Cerene Device LCD Screen* displays "Unsafe to Dispose," do not dispose of the device and call Channel Medsystems at +1-510-338-9301.

**Table 22**. Summary of LCD Messages and Error Codes

| Error Code | LCD Message[1] | Instructions | Treatment Status & Next Steps |
|---|---|---|---|
| | *Screen is blank* (Device does not Power ON or before insertion) | Unlock the *Vent Lock* and slide the *Vent Tab* to vent the *Cerene Device.* Contact Channel Medsystems. Empty the *Exhaust Collection Bag* per local practice.[2] | **Uterus Not Treated**<br>**Treat with NEW *Cerene Device*** |
| | *Screen goes blank (after insertion, before nitrous oxide flow)* | Unlock the *Vent Lock* and slide the *Vent Tab* to vent the *Cerene Device* and stop the procedure. Gently remove the *Cerene Device* and press the *Button*. Contact Channel Medsystems. Empty the *Exhaust Collection Bag* per local practice.[2] | |
| | *Screen goes blank (after nitrous oxide flow)* | Unlock the *Vent Lock* and slide the *Vent Tab* to vent the *Cerene Device* and stop the procedure. Gently remove the *Cerene Device* and press the *Button*. Contact Channel Medsystems. Empty the *Exhaust Collection Bag* per local practice.[2] | **Uterus Partially Treated**<br>**End procedure**<br>**Do NOT re-treat** |
| | Allow Device to Cool Down | Place *Cerene Device* back in sterile tray and move to a cool area. *Cerene Device* will resume normal function when device temperature reaches 85°F/29.5°C. Treatment must begin within 25 minutes of powering on the *Cerene Device*; otherwise, replace *Cerene Device*. | **Uterus Not Treated**<br>**Continue using same device, or replace if 25 minutes elapses** |
| | Allow Device to Warm Up | Place *Cerene Device* back in sterile tray and move to a warm area. *Cerene Device* will resume normal function when device temperature reaches 55°F/12.8°C. Treatment must begin within 25 minutes of powering on the *Cerene Device*; otherwise, replace *Cerene Device*. | |
| | Release Button | Release pressure on the *Button*.[3] | **Uterus Not Treated**<br>**Continue using same device** |
| | Return Sheath to Starting Position | Rotate the *Sheath Retraction Knob* clockwise to the starting position and continue the procedure. | |
| | Sheath Moved Press to Continue | Press *Button* to continue the procedure. | |
| | Out of Range Retract Sheath | Rotate the *Sheath Retraction Knob* counterclockwise to a cavity length of at least 2.5cm and continue the procedure. | |

[1] *No error code associated with these LCD messages*

[2] *During the venting process, the Exhaust Collection Bag will fill to near capacity. If the Exhaust Collection Bag does not appear to be filling or if the Exhaust Collection Bag is not near capacity after 15 minutes of venting, do not dispose of the Cerene Device. Call Channel Medsystems at +1-510-338-9301.*

[3] *Note: If pressure on the Button is released and this message continues, unlock the Vent Lock and slide the Vent Tab to vent the Cerene Device, follow instructions on the LCD screen, and treat with a new Cerene Device.*

**Table 22**. Summary of LCD Messages and Error Codes (continued)

| Error Code | LCD Message | Instructions | Treatment Status & Next Steps |
|---|---|---|---|
| 001-179 | Error _ _ _<br>***alternating with***<br>Unlock and Rotate Ring to Vent | When prompted, unlock the *Vent Lock* and slide the *Vent Tab* to vent the *Cerene Device.*[1] Wait for the *LCD Screen* to display "Safe for Disposal." Empty the *Exhaust Collection Bag* per local practice. | **Uterus Not Treated**[2]<br>**Treat with NEW *Cerene Device*** |
| 201-291 | Error _ _ _<br>***alternating with***<br>Wait _ | Wait until prompted, then gently remove the *Cerene Device* and press the *Button*. When prompted, unlock the *Vent Lock* and slide the *Vent Tab* to vent the *Cerene Device.*[1] Wait for the *LCD Screen* to display "Safe for Disposal." Empty the *Exhaust Collection Bag* per local practice. | |
| 300 | Possible Perforation Abort Procedure | Wait until prompted, then gently remove the *Cerene Device* and press the *Button*. When prompted, unlock the *Vent Lock* and slide the *Vent Tab* to vent the *Cerene Device.* Wait for the *LCD Screen* to display "Safe for Disposal." Empty *the Exhaust Collection Bag* per local practice. | **Uterus Not Treated**<br>**Treat with NEW *Cerene Device* if no perforation identified** |
| 003[3] | | | |
| 301-391 | Error _ _ _<br>Treated _ _ _ Sec<br>***alternating with***<br>Time Until Removal _ _ sec | Wait until prompted, then gently remove the *Cerene Device* and press the *Button*. When prompted, unlock the *Vent Lock* and slide the *Vent Tab* to vent the *Cerene Device.*[1] Wait for the *LCD Screen* to display "Safe for Disposal." Empty the *Exhaust Collection Bag* per local practice. | **Uterus Partially Treated**<br>**End procedure**<br>**Do NOT re-treat** |
| 404-468 | Error _ _ _<br>***alternating with***<br>Time Until Removal _ _ sec | Wait until prompted, then gently remove the *Cerene Device* and press the *Button*. Wait for the *LCD Screen* to display "Safe for Disposal." Empty the *Exhaust Collection Bag* per local practice. | **Uterus Treated**<br>**End procedure**<br>**Do NOT re-treat** |
| 504-589 | Error _ _ _<br>Venting _ _ min | Wait for the *LCD Screen* to display "Safe for Disposal." Empty the *Exhaust Collection Bag* per local practice. | |
| **For the following errors, Call Channel Medsystems.** | | | |
| none | UNSAFE TO DISPOSE<br>Contact Channel Med | Call Channel Medsystems (+1-510-338-9301) for additional instructions. Do NOT dispose of the *Cerene Device*. | **Uterus Treated**<br>**Do NOT re-treat** |
| 001-589 | UNSAFE TO DISPOSE<br>Contact Channel Med<br>***alternating with***<br>UNSAFE TO DISPOSE Error _ _ _<br>***May alternate with***<br>UNSAFE TO DISPOSE Treated _ _ _ sec | Call Channel Medsystems (+1-510-338-9301) for additional instructions. Do NOT dispose of the *Cerene Device*. | **Refer to specific error code above** |

[1] For Error Codes 001, 101, 201, and 301, the LCD will not prompt the operator to unlock the *Vent Lock* and slide the *Vent Tab*. The error is due to the *Vent Tab* having been positioned prematurely to vent the *Cerene Device*.
[2] Ablation does not start until nitrous oxide has flowed for > 5 seconds.
[3] Error Code 003 can occur prior to, during, or after treatment. Follow instructions on LCD and refer to "Treatment Status & Next Steps" in Table 22 that corresponds to the LCD message shown.

## GUIDANCE AND MANUFACTURER'S DECLARATION – ELECTROMAGNETIC EMMISSIONS AND IMMUNITY

**Immunity**

The *Cerene Device* has been tested and found to comply with the limits for medical devices to IEC 60601-1-2:2014. The *Cerene Device* is intended for use in the electromagnetic environment specified below. The user of the *Cerene Device* should assure that it is used in such an environment.

**WARNING**: Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.

**Table 23**: Electromagnetic Immunity

<table>
<tr><th>Immunity Test</th><th>IEC 60601-1-2 Test Levels</th><th>Compliance Level</th><th>Electromagnetic environment - guidelines</th></tr>
<tr><td>Electrostatic discharge (IESD) IEC 61000-4-2</td><td>±8 kV contact<br>± 2, 4, 8 & 15 kV air</td><td>±8 kV contact<br>± 2, 4, 8 & 15 kV air</td><td>Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.</td></tr>
<tr><td>Electrical fast transient/burst<br>IEC 61000-4-4</td><td>Not applicable</td><td>Not applicable</td><td>Not applicable</td></tr>
<tr><td>Surge IEC 61000-4-5</td><td>Not applicable</td><td>Not applicable</td><td>Not applicable</td></tr>
<tr><td>Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11</td><td>Not applicable</td><td>Not applicable</td><td>Not applicable</td></tr>
<tr><td>Power frequency (50/60Hz) magnetic field IEC 61000-4-8</td><td>50 Hz or 60 Hz;<br>30 A/m</td><td>60 Hz;<br>30 A/m</td><td>Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.</td></tr>
<tr><td>Conducted RF<br>IEC 61000-4-6</td><td>Not applicable</td><td>Not applicable</td><td>Not applicable</td></tr>
<tr><td>Radiated RF<br>IEC 61000-4-3</td><td>3V/m 80% AM, 1KHz<br>80MHz to 2.7GHz</td><td>3V/m 80% AM, 1KHz<br>80MHz to 2.7GHz</td><td rowspan="2">WARNING: Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the Cerene Device. Otherwise, degradation of the performance of this equipment could result.<br><br>Interference may occur in the vicinity of equipment marked with the following symbol:<br><br>  </td></tr>
<tr><td>Proximity fields from RF wireless communications equipment<br>Table 9 of IEC 60601-1-2:2014</td><td colspan="2">
<table>
<tr><th>Frequency (MHz)</th><th>Field Strength (V/m)</th><th>Distance (m)</th><th>Modulation<br>PM = pulse modulation</th><th>Polarization</th></tr>
<tr><td>385</td><td>27</td><td>1</td><td>PM 18 Hz</td><td rowspan="6">Horizontal and vertical</td></tr>
<tr><td>450</td><td>28</td><td>1</td><td>PM 18 Hz</td></tr>
<tr><td>710<br>745<br>780</td><td>9</td><td>1</td><td>PM 217 Hz</td></tr>
<tr><td>810<br>870<br>930</td><td>28</td><td>1</td><td>PM 18 Hz</td></tr>
<tr><td>1720<br>1845<br>1970<br>2450</td><td>28</td><td>1</td><td>PM 217 Hz</td></tr>
<tr><td>5240<br>5500<br>5785</td><td>9</td><td>1</td><td>PM 217 Hz</td></tr>
</table>
</td></tr>
</table>

**Essential Performance**

The performance of the Cerene Device determined to be Essential Performance is: a) Correct and legible display of the device operating information and b) Correct response to user input to stop the procedure.

If the LCD screen on the Cerene Device is not legible or the device does not respond to user input to stop the procedure, the performance of the device may be lost or degraded due to electromagnetic disturbances. As noted above, the user can help prevent such interference by maintaining a minimum distance of 30 cm (12 inches) between equipment and the device.

**Emissions**

The *Cerene Device* is intended for use in the electromagnetic environment specified below. The user of the *Cerene Device* should assure that it is used in such an environment.

**Table 24**: Electromagnetic Emissions

| Emissions Test | CISPR 11 Emissions Limits | Electromagnetic environment - guidelines |
|---|---|---|
| RF emissions CISPR 11 | CLASS B | The *Cerene Device* uses electronic circuitry that generates low level RF emissions (below required CISPR 11 Class B limits) in its operation. |
| RF emissions CISPR 11 | Not applicable | Not applicable |
| Harmonic emissions IEC 61000-3-2. | Not applicable | |
| Voltage fluctuations/flicker emissions. IEC 61000-3-3. | Not applicable | |

**WARNING:** The *Cerene Device* should be observed to verify normal operation before use.

The electromagnetic interference from the device is under limits approved by the Federal Communications Commission

**Limits of Accuracy**

All measurements having centimeter (cm) units have a tolerance of +/- 2 millimeters (mm).

**Performance Characteristics**

The *Cerene Device* delivers liquid nitrous oxide at -86 ºC for 2.5 minutes within the *Liner* to uniformly ablate the uterine cavity walls to depths of 5-9 mm. Uterine cavity pressure is controlled and limited to a maximum of 165 mmHg, to deploy the *Liner* with filtered air, prior to the flow of nitrous oxide.

The temperature of the applied part (*Liner*) reaches -86°C.

**Serious Incident Reporting**

Contact Channel Medsystems (+1-510-338-9301 or support@cerene.com) for any incident. In the EU, any serious incident that has occurred in relation to the device should be reported to the competent authority of the Member State in which the user is established. To report a product complaint or adverse event in the United States, please contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. In the UK, report to the Yellow Card scheme in England and Wales, to the Northern Ireland Adverse Incident Centre in Northern Ireland, and to Health Facilities Scotland online incident reporting system in Scotland.

## SOFTWARE ERROR CODES

| Error Code | Description |
|---|---|
| 001 | Cylinder Venting Activated on Power-Up |
| 002 | Low Battery |
| 003 | Previously Used |
| 005 | Voltage Fault |
| 007 | Sheath Encoder Fault |
| 008 | Startup Pressure Out of Range |
| 009 | Pressure Agreement on Startup |
| 010 | Non-Volatile Offsets Validation Failure |
| 011 | Non-Volatile Device State Data Validation Failure |
| 012 | Firmware CRC Test Failure |
| 013 | Thermistor Disconnected |
| 014 | Thermistor Shorted |
| 015 | Flash Communication Fault |
| 016 | Timer Failure |
| 017 | Pressure Sensor Calibration CRC Test Failure |
| 018 | Microcontroller Calibration Data Integrity Test Failure |
| 101 | Cylinder Venting Activated, Pre-Insertion |
| 104 | Microcontroller Fault, Pre-Insertion |
| 105 | Voltage Fault, Pre-Insertion |
| 106 | Watchdog Fault, Pre-Insertion |
| 107 | Sheath Encoder Fault, Pre-Insertion |
| 120 | Sheath Retracted without Vacuum, Pre-Insertion |
| 150 | Pre-Treatment Timeout, Pre-Insertion |
| 151 | Vacuum Fail, Pre-Insertion |
| 152 | Vent Liner Timeout, Pre-Insertion |
| 162 | Leaky Pump Solenoid, Pre-Insertion |
| 168 | High Pressure, Pre-Insertion |
| 169 | Max Pump-On Time Exceeded, Pre-Insertion |
| 179 | Pressure Agreement, Pre-Insertion |
| 201 | Cylinder Venting Activated, Pre-Treatment |
| 204 | Microcontroller Fault, Pre-Treatment |
| 205 | Voltage Fault, Pre-Treatment |
| 206 | Watchdog Fault, Pre-Treatment |
| 207 | Sheath Encoder Fault, Pre-Treatment |
| 220 | Sheath Retracted without Vacuum, Pre-Treatment |
| 230 | Sheath Reposition (3x) During Liner Predeployment |
| 240 | Sheath Reposition (3x), Pre-Substantive Treatment |
| 250 | Pre-Treatment Timeout |
| 251 | Vacuum Fail, Pre-Treatment |
| 252 | Vent Timeout, Pre-Treatment |
| 260 | Puff Fault |
| 261 | Puff Timeout |
| 262 | Leaky Pump Solenoid, Pre-Treatment |
| 263 | Puff Dome Valve Failure |
| 264 | Leaky Liner |
| 265 | Leak Detected |
| 268 | High Pressure, Pre-Treatment |
| 269 | Max Pump-On Time Exceeded, Pre-Treatment |
| 277 | Treat Delivery Failure |
| 278 | Initial Treatment Pressure High |
| 279 | Pressure Agreement - Pre-Treatment |
| 280 | Low $N_2O$ Flow |
| 290 | Initial Treatment Pause Timeout |
| 291 | Initial Treatment Pauses (3x) |
| 300 | Possible Uterus Perforation Fault |
| 301 | Cylinder Venting Activated, Treatment |
| 304 | Microcontroller Fault, Treatment |
| 305 | Voltage Fault, Treatment |
| 306 | Watchdog Fault, Treatment |
| 307 | Sheath Encoder Fault, Treatment |
| 340 | Sheath Reposition, Treatment |
| 368 | High Pressure, Treatment Pause |
| 377 | Treatment Pressure Low |
| 378 | Treatment Pressure High |
| 379 | Pressure Agreement - Treatment |
| 380 | Low $N_2O$ Flow |
| 389 | Max Inflow Solenoid Activation Time Exceeded, Treatment |
| 390 | Treatment Pause Timeout |
| 391 | Treatment Pauses (3x) |
| 404 | Microcontroller Fault, Suction |
| 406 | Watchdog Fault, Suction |
| 468 | High Pressure, Suction |
| 504 | Microcontroller Fault, Venting |
| 506 | Watchdog Fault, Venting |
| 568 | High Pressure, Venting |
| 589 | Max Inflow Solenoid Activation Time Exceeded, Venting |

## SYMBOLS GLOSSARY

| Symbol | Standard/Symbol Reference Number | Title of Symbol | Definition |
|---|---|---|---|
| REF | ISO 15223-1, Clause 5.1.6 | Catalog number | Indicates the manufacturer's catalog number so that the medical device can be identified. |
| | ISO 15223-1, Clause 5.1.1 | Manufacturer | Indicates the medical device manufacturer. |
| LOT | ISO 15223-1, Clause 5.1.5 | Batch code | Indicates the manufacturer's batch code so that the batch or lot can be identified. |
| | ISO 15223-1, Clause 5.1.4 | Use by date | Indicates the date after which the medical device is not to be used. |
| US | ISO 15223-1, Clause 5.1.11 | Country of manufacture (with date of manufacture adjacent) | Identifies the country of manufacture of products and indicates the date when the medical device was manufactured. |
| | IEC 60601-1, Table D.2, Symbol 2 | General warning sign | Indicates that caution is necessary when operating the device; the current situation needs operator awareness or operator action in order to avoid undesirable consequences. |
| | IEC 60601-1, Table D.2, Symbol 10 | Refer to instruction manual/booklet | To signify that the instruction manual/booklet must be read |
| | ISO 15223-1, Clause 5.4.3 | Consult Instructions for Use | Indicates the need for the user to consult the instructions for use. |
| IP22 | IEC 60529 / Degrees of protection provided by enclosures (IP Code) | n/a | Protected against fingers or objects > 12.55 mm and water spray less than 15° from the vertical. |
| | ISO 15223-1, Clause 5.2.8 | Do not use if package is damaged and consult *instructions for use* | Indicates a *medical device* that should not be used if the package has been damaged or opened and that the user should consult the *instructions for use* for additional information |
| | ISO 15223-1, Clause 5.4.2 | Do not reuse | Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure. |
| STERILIZE | ISO 15223-1, Clause 5.2.6 | Do not resterilize | Indicates a medical device that is not to be resterilized. |
| STERILE EO | ISO 15223-1, Clause 5.2.3 | Sterilized by ethylene oxide | Indicates a medical device that has been sterilized using ethylene oxide. |
| STERILE EO | ISO 15223-1, Clause 5.2.11 | Single sterile barrier system | Indicates a single sterile barrier system |
| 55°C -18°C | ISO 15223-1, Clause 5.3.7 | Temperature limit | Indicates the temperature limits to which the medical device can be safely exposed. |
| | IEC 60417, Reference No. 5840 | Type B Applied Part | To identify a type B applied part complying with IEC 60601-1. |
| MD | ISO 15223-1, Clause 5.7.7 | *Medical device* | Indicates the item is a *medical device* |
| EC REP | ISO 15223-1, Clause 5.1.2 | Authorized representative in the European Community | Indicates the authorized representative in the European Community. |
| CE | Medical Device Regulation 2017/745 | CE marking | Indicates that a device is in conformity with MDR 2017/745 and other applicable Union harmonisation legislation |
| | ISO 15223-1, Clause 5.1.8 | Importer | Indicates the entity importing the medical device into the locale |
| ℞Only | 21 CFR 801.109 | Prescription only | Requires a prescription in the United States. |
| UK CA | UK MDR 2002 | UK Conformity Assessed Marking | Indicates that a device is in conformity with UK MDR 2002 |


Channel Medsystems, Inc.
2919 7th Street
Berkeley, CA 94710, USA
www.cerene.com
support@cerene.com
+1-510-338-9301

**Kalms Consulting GmbH**
Rheinstr. 45-46
12161 Berlin
Germany
cs@kalmsoperations.com
+49 30 405 045 320

EC REP
**MedEnvoy Global B.V.**
Prinses Margrietplantsoen 33 - Suite 123
2595 AM The Hague
The Netherlands
CE 2797

**UK Responsible Person**
**MedEnvoy UK Limited**
85, Great Portland Street, First Floor
London, W1W 7LT
United Kingdom
UK CA 0086


**Not made with natural latex rubber.**