Cerene® Cryotherapy Device Instructions for Use

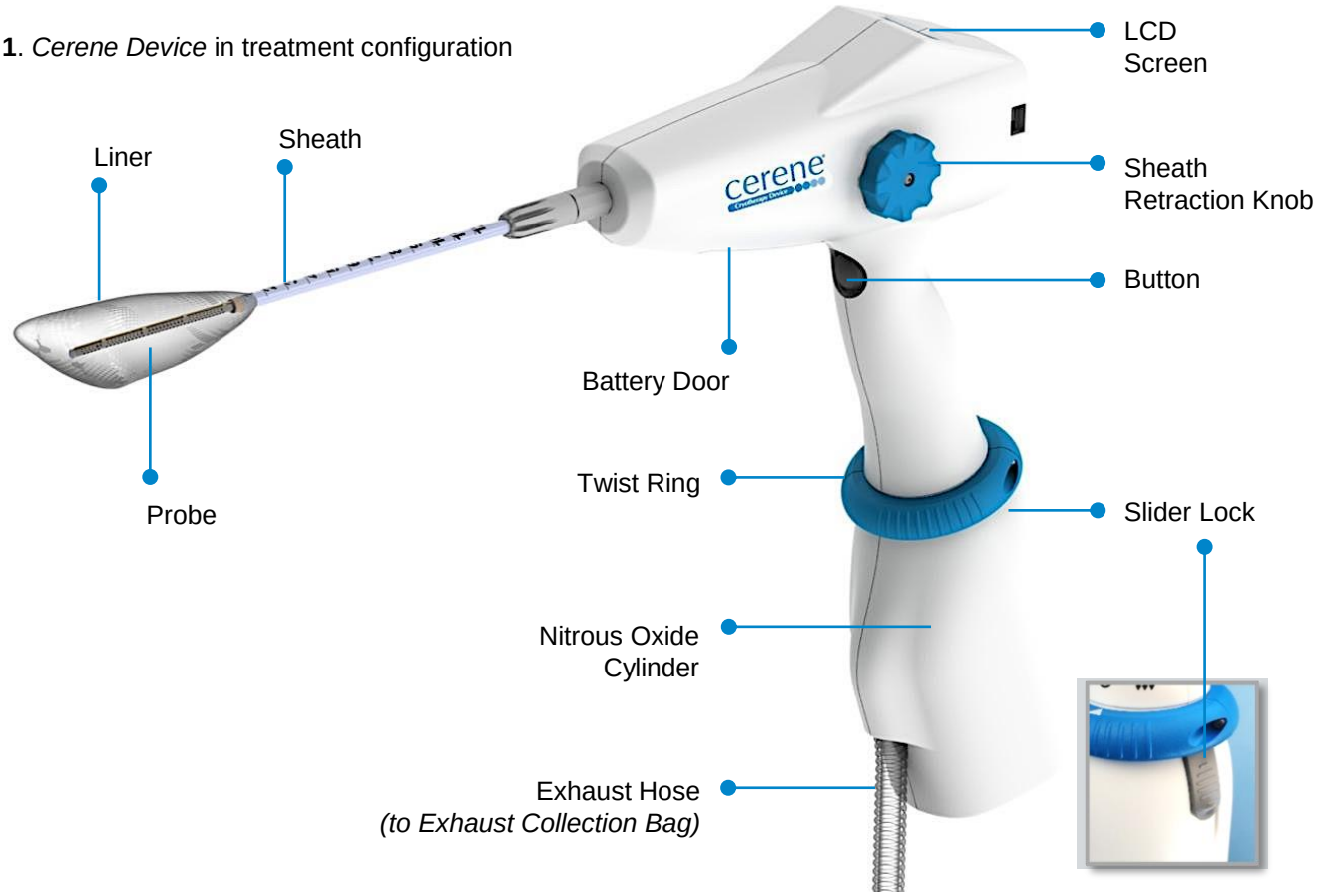
CONTENTS

CAUTION: 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 Device* in treatment configuration



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 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 adenomatous 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 Host* 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.

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.
- Uterine necrosis.
- Air or gas embolism.
- Infection or sepsis.
- Diarrhea.
- Headache.
- Complications leading to serious injury or death.

Some or all of these risks may require a need for reoperation or subsequent treatment and/or may lead to permanent disability 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	7 (2.9%)	7 (2.9%)
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
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 surgical treatment. 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

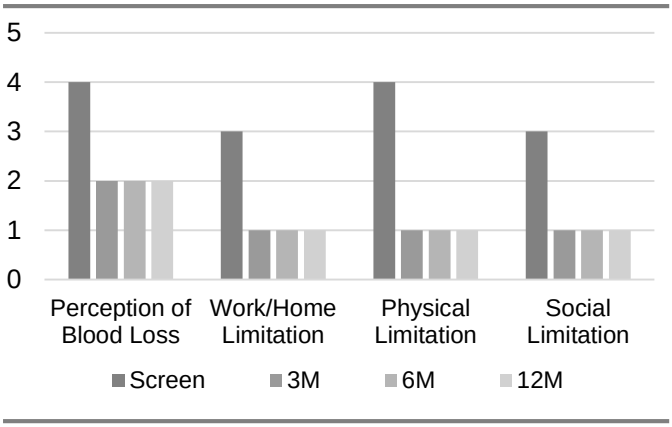
Time of Pain Rating during Treatment	N	Median Pain Score
Before Device Insertion	241*	1.0
After Device Insertion	240*	2.0
After Liner Deployment (before endometrial ablation was initiated)	240*	1.0
After 1 Minute of Ablation	240*	2.0
End of Ablation	239*	1.0
15-30 Minutes Post Procedure	242	2.0
At Time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

**Remaining 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 (93%)

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	168 (73%)
My periods are normal	25 (10.9%)
I continue to have heavy periods	22 (9.6%)

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
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 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.

GENERAL INSTRUCTIONS

- Store the *Cerene Device* at 65°F - 85°F (18.3°C – 29.5°C) for at least 4 hours prior to use.
- 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 *Slider 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 18** on page 12).

PREPARATION

1 Room Preparation

- Hang the *Exhaust Collection Bag (refer to IFU-3023)* 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.

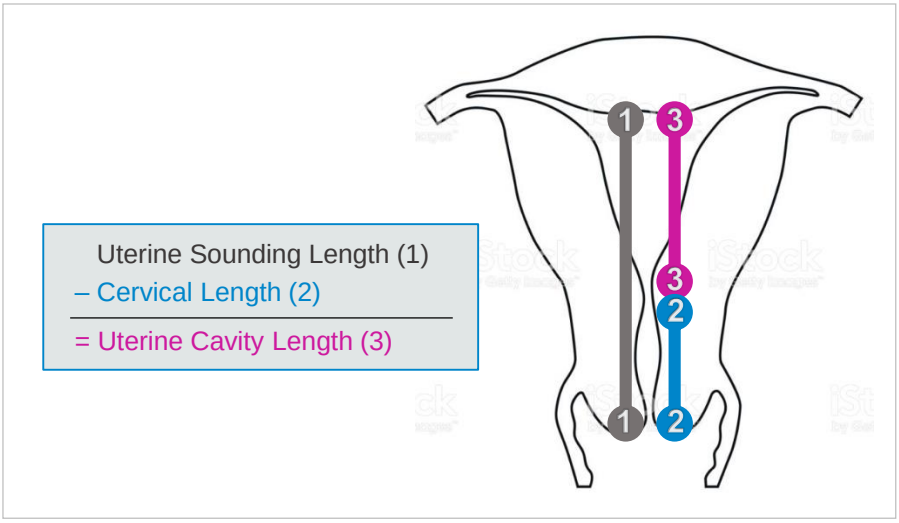


Figure 3. *Calculate the uterine cavity length*

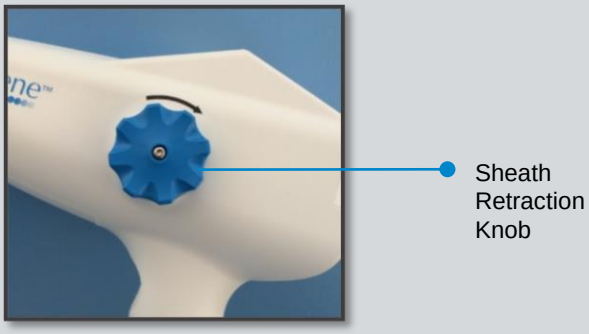


Figure 4. *Sheath Retraction Knob*

Figure 5. *Slider 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, *Twist Ring* tab, and the *Probe* tip cover.
- Connect the end of the *Exhaust* Hose to the *Exhaust Collection Bag* until you hear an audible click.

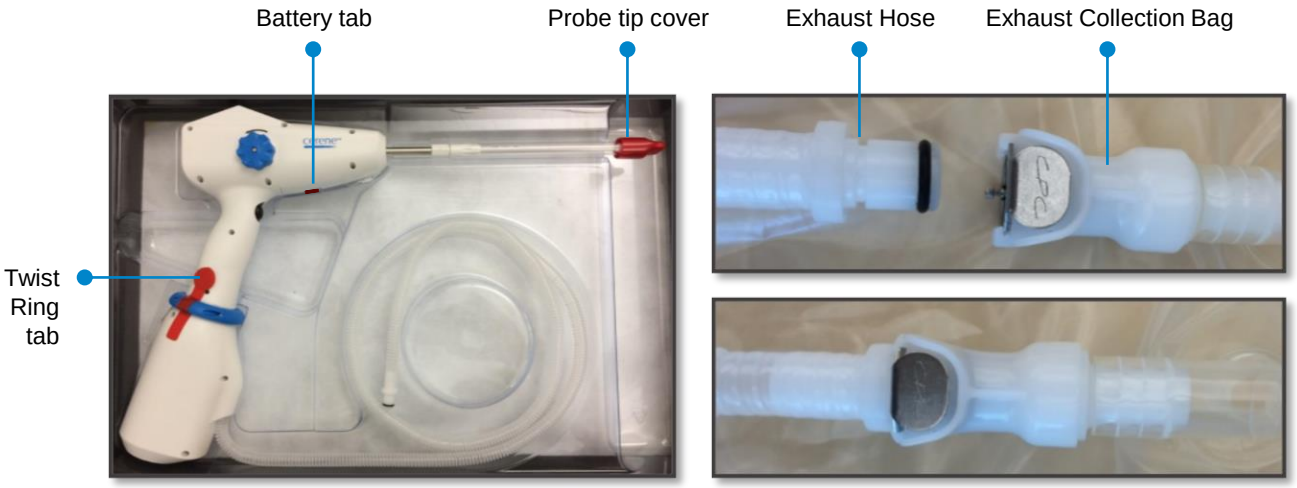


Figure 6. *Device preparation. When the Exhaust Hose and Exhaust Collection Bag are properly connected, you will hear an audible click.*

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®.

THE PROCEDURE

Turn on the device by rotating the Twist Ring counter-clockwise.

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.
- 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 8) is displayed on the *LCD Screen*.
- Reconfirm that the *Probe* tip is at the fundus.

4 TREAT THE CAVITY

- When prompted, 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, fully release the *Slider Lock,* then rotate the *Twist Ring* counter-clockwise 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 17** on page 12.

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.

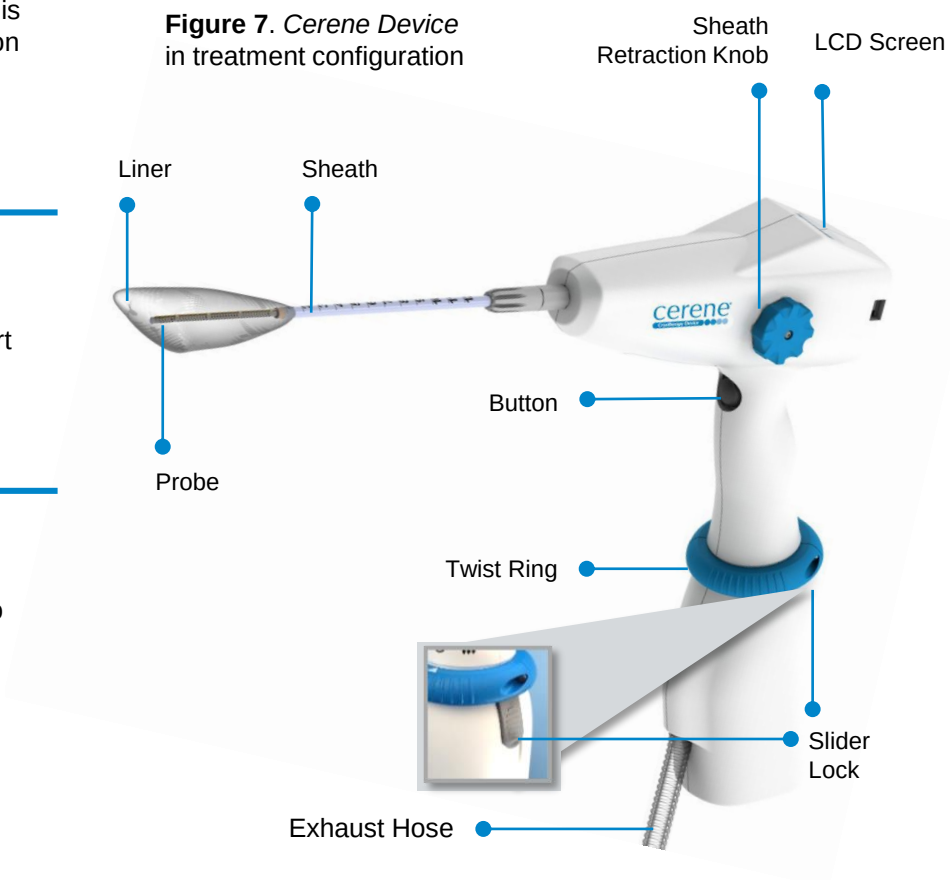
NOTE: If the calculated uterine cavity length is 2.5 cm, no additional *Sheath* retraction is required. Press and release the *Button* to confirm the 2.5 cm cavity length.

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 an additional minute for the frozen uterine tissue to thaw and release the frozen *Liner* before trying again.

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 16. 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 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 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@channelmedsystems.com).

NOTE: If local practice requires the removal of batteries prior to device disposal, loosen the screw on the side of the *Cerene Device* forward of the *Battery Door*, remove the *Battery Door*, and remove the two AAA batteries.

Empty the *Exhaust Collection Bag* and dispose per custom and practice (refer to IFU-3023, 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: Attach the wall suction adapter found in the pouch at the top of the bag to the mating fitting at the bottom of the bag. Attach the adapter to wall suction.

Figure 8. *Emptying the Exhaust Collection Bag*

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 18
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@channelmedsystems.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 17. 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)	Unlock and rotate the *Twist Ring* to vent the *Cerene Device*. Contact Channel Medsystems. Empty the *Exhaust Collection Bag* per local practice.[2]	**Uterus Not Treated** **Treat with NEW *Cerene Device***
	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** **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 65°F/18.3°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** **Continue using same device**
	Return Sheath to Starting Position	Rotate the *Sheath Retraction Know* 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, rotate the Twist Ring to vent the Cerene Device, follow instructions on the LCD screen, and treat with a new Cerene Device.

Table 17. Summary of LCD Messages and Error Codes (continued)

Error Code	LCD Message	Instructions	Treatment Status & Next Steps
001-179	Error _ _ _ ***alternating with*** Unlock and Rotate Ring to Vent	When prompted, unlock and rotate the *Twist Ring* 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**[1] **Treat with NEW *Cerene Device***
201-291	Error _ _ _ ***alternating with*** Wait _	Wait until prompted, then gently remove the *Cerene Device* and press the *Button*. When prompted, unlock and rotate the *Twist Ring* to vent the *Cerene Device*. 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 and rotate the *Twist Ring* 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** **Treat with NEW *Cerene Device* if no perforation identified**
301-391	Error _ _ _ Treated _ _ _ Sec ***alternating with*** Time Until Removal _ _ sec	When prompted, unlock and rotate the *Twist Ring* to vent the *Cerene Device*. 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 Partially Treated** **End procedure** **Do NOT re-treat**
404-468	Error _ _ _ ***alternating with*** 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** **End procedure** **Do NOT re-treat**
504-568	Error _ _ _ 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 Contact Channel Med	Call Channel Medsystems (+1-510-338-9301) for additional instructions. Do NOT dispose of *Cerene Device*.	**Uterus Treated** **Do NOT re-treat**
001-568	UNSAFE TO DISPOSE Contact Channel Med ***alternating with*** UNSAFE TO DISPOSE Error _ _ _ ***May alternate with*** 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] Ablation does not start until nitrous oxide has flowed for > 5 seconds

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.

Table 18: Electromagnetic Immunity

Immunity Test	IEC 60601-1-2 Test Levels	Compliance Level	Electromagnetic environment - guidelines
Electrostatic discharge (IESD) IEC 61000-4-2	±8 kV contact ± 2, 4, 8 & 15 kV air	±8 kV contact ± 2, 4, 8 & 15 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Electrical fast transient/burst IEC 61000-4-4	Not applicable	Not applicable	Not applicable
Surge IEC 61000-4-5	Not applicable	Not applicable	Not applicable
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	Not applicable	Not applicable	Not applicable
Power frequency (50/60Hz) magnetic field IEC 61000-4-8	50 Hz or 60 Hz; 30 A/m	60 Hz; 30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
Conducted RF IEC 61000-4-6	Not applicable	Not applicable	Not applicable
Radiated RF IEC 61000-4-3	3V/m 80% AM, 1KHz 80MHz to 2.7GHz Proximity Fields per Table 9 of IEC 60601-1-2:2014	3V/m 80% AM, 1KHz 80MHz to 2.7GHz Proximity Fields per Table 9 of IEC 60601-1-2:2014	Portable and mobile communications equipment should be separated from the Cerene Device by no less than the distances calculated/listed. See Table 4 for further information. Recommended separation distance $d = 1.2\sqrt{P}$ (150 kHz to 80 MHz) $d = 1.2\sqrt{P}$ (80MHz to 800MHz) $d = 2.3\sqrt{P}$ (800MHz to 2.7GHz) where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in metres (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, should be less than the compliance level in each frequency range. Interference may occur in the vicinity of equipment marked with the following symbol: 

Recommended separation distances between portable and mobile RF communications equipment and the *Cerene Device*. The healthcare professional or the user of the *Cerene Device* can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the *Cerene Device* as recommended in Table 4 below, according to the maximum output power of the communications equipment.

Table 19: Separation distance according to frequency of transmitter (m)

Rated maximum output power of transmitter (W)	Separation distance according to frequency of transmitter (m)		
	150kHz to 80MHz $d = 1.2\sqrt{P}$	80MHz to 800MHz $d = 1.2\sqrt{P}$	800MHz to 2.5GHz $d = 2.3\sqrt{P}$
.01	.12	0.12	0.23
.1	0.37	0.37	0.74
1	1.2	1.2	2.3
10	3.7	3.7	7.4
100	12	12	23

For transmitters rated at a maximum output power not listed above, the recommended separation distance *d* in metres (m) can be estimated using the equation applicable to the frequency of the transmitter, where *P* is the maximum power rating of the transmitter in watts (W) according to the transmitter manufacturer.

NOTE: At 80MHz and 800MHz, the separation distance for the higher frequency range applies.
NOTE: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

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 in Table 4, the user can help prevent such interference by maintaining a minimum distance 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 20: 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	

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

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

SOFTWARE ERROR CODES

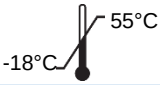
Error Code	Description
001	Ring Rotated on Power-Up
002	Low Battery
003	Previously Used
005	Voltage Fault
007	Pressure Sensor Calibration Checksum Failure
008	Startup Pressure Out of Range
009	Pressure Delta on Startup
010	Non-Volatile Offsets Validation Failure
011	Non-Volatile Device State Data Validation Failure
012	Firmware Checksum Failure
013	Thermistor Disconnected
014	Thermistor Shorted
015	Flash Communication Fault
016	Crystal Oscillator Validation Failure
101	Ring Rotated, Pre-Insertion
104	Microcontroller Fault, Pre-Insertion
105	Voltage Fault, Pre-Insertion
106	Watchdog Fault, Pre-Insertion
120	Sheath Retracted without Vacuum, Pre-Insertion
150	Pre-Treatment Timeout, Pre-Insertion
151	Vacuum Timeout, Pre-Insertion
152	Vent Liner Timeout, Pre-Insertion
162	Leaky Pump Solenoid, Pre-Insertion
168	High Pressure, Pre-Insertion

Error Code	Description
169	Max Pump-On Time Exceeded, Pre-Insertion
179	Pressure Delta - Pre-Insertion Treatment
201	Ring Rotated, Pre-Treatment
204	Microcontroller Fault, Pre-Treatment
205	Voltage Fault, Pre-Treatment
206	Watchdog 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	Dome Valve Opened During Inflation
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 Delta - Pre-Treatment

Error Code	Description
280	Low N_2O Flow
290	Initial Treatment Pause Timeout
291	Initial Treatment Pauses (3x)
300	Possible Uterus Perforation Fault
301	Ring Rotated, Treatment
304	Microcontroller Fault, Treatment
305	Voltage Fault, Treatment
306	Watchdog Fault, Treatment
340	Sheath Reposition, Treatment
368	High Pressure, Treatment Pause
377	Treatment Pressure Low
378	Treatment Pressure High
379	Pressure Delta - Treatment
380	Low N_2O Flow
389	Max Treatment Time Exceeded
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

SYMBOL DEFINITIONS

Symbol	Definition
REF	Catalog Number
	Manufacturer
LOT	Batch code
	Use by date
	Caution
	Consult Instructions for Use
	Prescription only Caution: Federal law restricts this device to sale by or on the order of a physician
IP22	Protected against fingers or objects > 12.55 mm and water spray less than 15° from the vertical
	Do not use if package is damaged

Symbol	Definition
	Do not reuse
	Do not resterilize
STERILE EO	Sterilized by ethylene oxide
	Temperature limit
	Type B Applied Part per IEC 60601-1
	Power on
	Vent
	Location of battery

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

Not made with natural latex rubber.

PACKAGING & STORAGE

The *Cerene Device* is provided sterile in a sealed package. 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 65°F - 85°F (18.3°C – 29.5°C). The *Cerene Device* must be stored at this temperature for at least four hours prior to use to ensure it is at operating temperature.

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IFU-2995 Rev 08, *Cerene® Cryotherapy Device* PMA IFU