# Patient Labeling
# for the
# Cerene® Cryotherapy Device

**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**

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# 1. Glossary

**Anesthesia:** Medical treatment with drugs to reduce and/or stop pain, usually used to prevent pain during surgery.

**Cerene Cryotherapy Device:** A handheld device that is used to treat heavy menstrual bleeding.

**Cervix:** Part of the uterus that contains the cervical canal and connects the uterus to the vagina.

**Clinical Study:** A carefully planned test in people to find out if a new medical product or treatment is safe and if it works.

**Diagnostic:** A test or procedure to identify a disease or problem.

**Dilation and Curettage ("D & C"):** A surgical procedure your doctor uses to go through your vagina and cervical canal to gently remove the lining of the uterus (endometrium).

**Endometrial Ablation:** A surgical treatment to eliminate the endometrium, the tissue lining of the uterus, and the source of excessive menstrual bleeding.

**Effectiveness:** The measure of how well a medical treatment works.

**Endometrium:** The tissue lining of the uterus and the source of excessive menstrual bleeding.

**Tubal Occlusion Device (e.g., Essure® or Adiana®):** A small device implanted into the Fallopian tubes to provide blockage and permanent birth control for women who do not desire more children.

**Estrogen:** A hormone made by your body. Estrogen plays a very important role in your menstrual cycle, becoming pregnant, and many other body functions.

**FDA:** The United States Food and Drug Administration is the government agency whose mission is to protect and promote public health by giving the public access to safe and effective medical products.

**Fibroid tumors or fibroids:** Noncancerous tumors of the uterine muscle that can alter the shape of the uterine cavity and be the cause of excessive menstrual bleeding.

**General Anesthesia:** Under general anesthesia, you are completely unconscious and unable to feel pain during medical procedures. General anesthesia usually uses a combination of intravenous drugs and inhaled gases.

**Gynecologist:** A doctor who specializes in treating the female reproductive system.

**Hormone:** A chemical made in your body. Your body makes hundreds of hormones and uses hormones to control a large number of body functions.

**Hysterectomy:** A surgical procedure to remove the uterus.

**Hysteroscopy:** A procedure completed using a hysteroscope, a thin, lighted telescope that is inserted into the vagina to examine the cervix and inside of the uterus.

**Intrauterine Device ("IUD"):** A birth control device prescribed by your doctor to prevent pregnancy. Your doctor places the small device inside the uterus to prevent pregnancy.

**Menopause:** The natural biological process of gradually ending your monthly period (menstruation). Menopause also ends fertility. The average age of menopause is 51 years old in the United States. Women in menopause can have physical symptoms such as hot flashes or night sweats. Other symptoms of menopause may include changes in sleep patterns, decreased energy, or changes in mood.

**Progesterone or progestin:** A hormone made by your body. Progesterone has a very important role in your menstrual cycle, becoming pregnant, and many other body functions. A progestin is the form of progesterone found in medical treatments.

**Tubal Ligation:** A surgical method of permanent birth control that closes a woman's Fallopian tubes.

**Ultrasound:** Images of internal organs, like the uterus, that are made by a machine using sound waves.

**Uterus:** Also known as the womb, the uterus is the part of the female reproductive system that is responsible for the development of a fetus during pregnancy.

## 2. What is the Cerene Cryotherapy Device (Cerene Device) for Endometrial Ablation?

Heavy periods can have a significant impact on your life. If you are experiencing heavy periods, treatment with the Cerene procedure may be a good option for you. The Cerene procedure is a safe and effective procedure that can reduce heavy menstrual bleeding. The Cerene Device is used for endometrial cryoablation in premenopausal women with heavy menstrual bleeding due to benign causes for whom child bearing is complete. The treatment does not require sedation or general anesthesia. It can be performed at your gynecologist's office.

## 3. What is Heavy or Excessive Menstrual Bleeding?

A period with bleeding totaling over 1/3 cup (80ml) is considered heavy or excessive. If you have to change your sanitary protection (pads or tampons) frequently (for example, more than twice an hour), your bleeding may be excessive. You may also feel weak, tired, and have no energy. Many women also say that excessive menstrual bleeding makes it difficult to work, exercise, and to be socially and sexually active.

## 4. How common is this problem?

Heavy menstrual bleeding is a very common problem that affects about 1 in 5 women. The signs of heavy menstrual bleeding are most likely to start between the ages of 30 and 40, but some women experience heavy menstrual bleeding from an earlier age.

## 5. How does the Cerene Device Work?

The Cerene Device is an endometrial ablation device. It works by using a freezing agent to destroy the endometrium, the tissue lining the inner cavity of the uterus (or womb). Monthly shedding of the

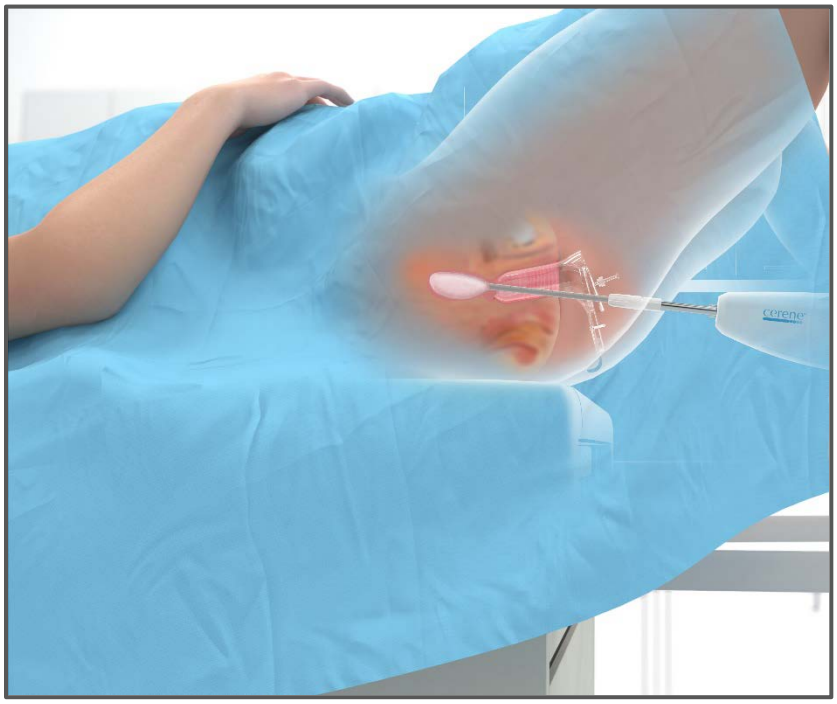
endometrium causes menstrual blood flow. During an endometrial ablation procedure, the endometrial lining of the uterine cavity is destroyed, which reduces the monthly endometrial shedding. If the shedding is reduced, your menstrual bleeding may be reduced or it may even stop. Not all of the endometrium needs to be destroyed for a woman to see an improvement in her menstrual bleeding. Treatment with the Cerene procedure is only for women who no longer want to have children.

Figure 1. The Cerene Device


## 6. Description of the Cerene Device

The Cerene Device is used to support a safe and effective, office-based endometrial ablation. The Cerene Device is self-contained and handheld. At the end of the Cerene Device is a slim probe that is inserted through the cervix and into the uterus. This Probe is less than 6mm in diameter, thinner than a drinking straw. The Cerene Device uses a freezing agent to freeze and destroy the endometrium. The freezing agent is released within a thin yet durable liner (balloon) that fits the shape of each woman's unique uterine cavity. The instructions on the device screen guide the gynecologist through each step of the procedure.

Figure 2. The Cerene Device in the Uterine Cavity



## 7. Who cannot have endometrial ablation with the Cerene Device?

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

The Cerene Device should not be used in women who have, or had, the following conditions:

- 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 abdominal, pelvic or gynecological cancer.
- A patient with any anatomic condition (e.g., history of prior classical cesarean section) or other condition that could weaken the muscular layer of the uterus.
- 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, pelvic, or urinary tract infection at the time of treatment.
- A patient with an intrauterine device (IUD) currently in place.
- A patient with undiagnosed vaginal bleeding.

## 8. What are the risks of treatment with the Cerene Device?

With any procedure, there are risks related to the treatment and to the medications used during the treatment. Your doctor will talk to you about the risks of treatment with the Cerene Device and will give you details about your individual situation. It is important for you to know the risks of treatment with the Cerene Device. Following extensive research, laboratory testing, and a smaller, early clinical study, the Cerene Device was tested in the CLARITY Pivotal Clinical Study, with a total of 242 women treated. These women were treated with the Cerene Device and then followed for 12 months to determine the safety and effectiveness of the Cerene procedure. The risks observed in the study are listed in **Table 1** and cover the entire 12 months following treatment with the Cerene Device. It is also important to know how often these risks may happen. In the table, this information is shown using the actual number of cases and as a percent (%). The percent (%) shows how many women had this event when 100 women were treated. You can discuss these risks with your doctor for more information.

The risks listed in the tables below are for the group tested in the CLARITY Study. Please see section 13 for more information about how the CLARITY Study group was evaluated.

### Table 1. Number of Related Adverse Events and Percentage of Women by Time of Occurrence

| Adverse Event Term | Number of Events | Number and Percent of Women (n=242) | | | |
|---|---|---|---|---|---|
| | | Day of Treatment | Day 1 | Day 2 to Week 2 | > Week 2 to Month 12 |
| Vomiting | 1 | | | 1 (0.4%) | |
| Fever | 1 | | 1 (0.4%) | | |
| Vaginal infection | 7 | | | 7 (2.9%) | |
| Infection of the endometrium | 1 | | | 1 (0.4%) | |
| Infection of the vulva and vagina | 1 | | | | 1 (0.4%) |
| Groin pain | 1 | | | | 1 (0.4%) |
| Lightheadedness** | 4 | 3 (1.2%) | | | |
| Urinary incontinence | 2 | | | 2 (0.8%) | |
| Painful intercourse | 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%) |
| High blood pressure | 2 | 2 (0.8%) | | | |

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

Table 2. Number and Percentage of Women that Experienced a Gynecologic Adverse Event after Month 12 through Month 36 after Treatment

| Adverse Event Term | Number and Percent of Women (N=232*) |
|---|---|
| Adenomyosis (a thickening of the lining of the uterus that occurs when endometrial tissue grows into the muscular wall of the uterus) | 1 (0.43%) |
| Dysmenorrhea (painful menstrual cramping) | 2 (0.86%) |
| Dyspareunia (painful sexual intercourse) | 1 (0. 43%) |
| Endometritis (inflammation or irritation of the lining of the uterus) | 1 (0.43%) |
| Intermenstrual bleeding | 2 (0.86%) |
| Menorrhagia; continuing, worsening, irregular menses | 15 (6.5%) |
| Pelvic cramping | 2 (0.86%) |
| Pelvic Pain | 4 (1.7%) |
| Polycystic ovarian disease | 1 (0.43%) |
| Post coital bleeding (bleeding after sexual intercourse) | 1 (0.43%) |
| Pregnancy; uterine continuing | 1 (0.43%) |
| Pregnancy; uterine terminated | 1 (0.43%) |
| Right breast mass | 1 (0.43%) |
| Uterine fibroids | 2 (0.86%) |
| Uterine Prolapse Stage 2 | 1 (0.43%) |
| Vaginal infection and/or discharge | 11 (4.7%) |
| Vaginal/vulvar pruritus (itching) | 2 (0.86%) |

*Number of women continuing in the post approval study after the 12-month follow-up visit.

Over the course of the 3 year study, ten women (4.1%) underwent a hysterectomy. Four were due to heavy menstrual bleeding, three were due to pelvic pain, 2 were due to uterine fibroids, and one was due to uterine prolapse. There were five pregnancies reported; one ectopic and four uterine pregnancies. The ectopic pregnancy was surgically removed, three uterine pregnancies resulted in pre-term (35-36 weeks) live births, and one uterine pregnancy was terminated. None of these subjects were using contraception despite the counseling they and all subjects received. It is very important for you to follow your doctor's instructions regarding the use of contraception following endometrial ablation, even if you no longer have menstrual bleeding.

## Additional Risk-Related Information

As with all endometrial ablation procedures, serious injury or death can occur. The following events have been reported with the use of other endometrial ablation techniques and are also possible risks during or after endometrial ablation when the Cerene Device is used. Another surgery may be required in the case of certain complications.

1. Difficulty with bowel movements or urination.
2. Injury to organs in the abdomen (e.g., bowel or bladder).

3. Bleeding from injury to the uterus or other organs.
4. Excessive tissue death involving the uterine wall.
5. Any insertion of instruments through the cervix and into the uterus can push air into the blood system, which is rare but can be serious.
6. Inserting instruments into the vagina, cervix or uterus can cause a tear in the tissue.
7. Contact of freezing instruments with the skin outside of the uterus can cause a thermal injury.
8. The doctor may notice a temporary change to the appearance of the surface of the cervix following endometrial ablation.
9. Diarrhea that is temporary.
10. Headache that is temporary.
11. Potential complication (e.g., new pain during menstrual cycles) in women who have previously had a tubal ligation.
12. Serious pregnancy complications for both mother and unborn baby. Endometrial ablation with the Cerene Device does not protect women from future pregnancy. Women will still need to use contraception until menopause or undergo a permanent sterilization procedure.
13. Life-threatening infection. Women should contact their doctor if they develop any of the following:
    a. Fever higher than 100.4 °F
    b. Abdominal pain that becomes worse and does not get better by pain medication given by the doctor
    c. Nausea
    d. Vomiting
    e. Bowel or bladder problems
    f. Vaginal discharge that has a foul smell
    g. Increased vaginal bleeding
14. Other risks and complications leading to serious injury or death.

## 9. Benefits of Endometrial Ablation with the Cerene Device

The Cerene Device has been shown in clinical trials to effectively reduce heavy menstrual bleeding. The following results were seen in women who were treated with the Cerene Device in the CLARITY Study:

- 76.9% of women had their heavy menstrual bleeding reduced to a normal level or less at one year after treatment, per their menstrual diary record
- 10% of women had no menstrual bleeding at one year after treatment, per their menstrual diary record
- 88.6% of women had no or normal or lighter than normal menstrual bleeding at three years after treatment, per their report of their last menstrual period
- 14.4% of women had no menstrual bleeding at three years after treatment, per their report of their last menstrual period

## Patient Experience of Pain and Pain Management

In the CLARITY Study, women were asked to rate their acceptable pain level on a numeric rating scale of 0-10. The median (middle number in a list of numbers from smallest to largest) acceptable level score was six out of ten. At several points before, during, and after the procedure, women were asked to rank their level of pain on the 0-10 scale. At all time points measured, the median pain score was less than or equal to 2. **Table 3** provides additional information about the womens' report of pain before, during and after treatment with the Cerene Device.

### Table 3. Patient Rating of Pain During Treatment and Day 1 Post Treatment

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

Women received a local anesthetic with medication for pain and/or relaxation for the procedure as needed. Twenty women (8.3%) received only a local anesthetic with no other medication. Forty eight women (19.8%) received a local anesthetic with a non-steroidal anti-inflammatory medication (such as Motrin or Toradol) for pain. The majority of women (167 women or 69%) received an oral narcotic for pain and/or a medication for relaxation. Only 7 women (2.9%) received intravenous sedation for pain management, but none of these women required breathing support. None of the women treated with the Cerene Device received general anesthesia.

## Procedure Time and Location

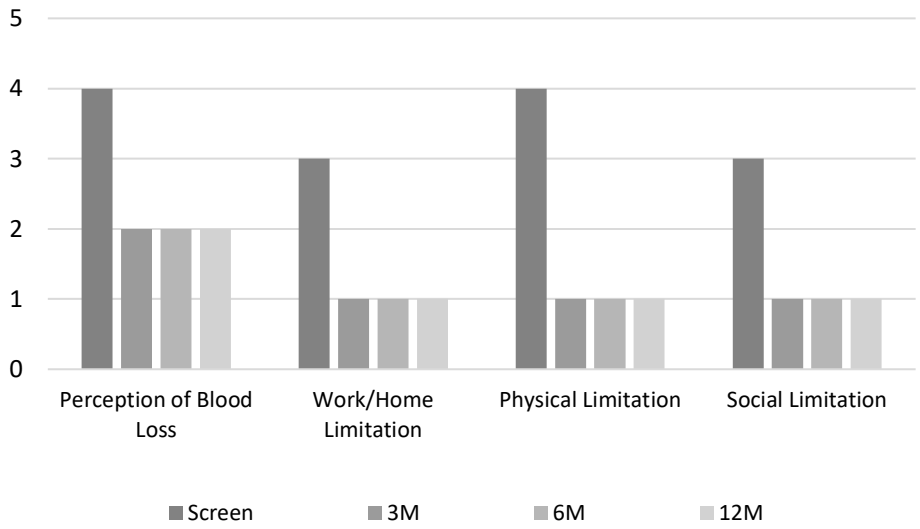
The procedure time from insertion of the Cerene Device to removal of the Cerene Device is about seven minutes, which includes multiple safety checks completed before the 2.5 minutes of active treatment. The procedure can be done in an office or clinic without general anesthesia or intravenous (IV) medications. Your endometrial lining should be thin prior to endometrial ablation with the Cerene Device. Your physician may choose to perform the procedure just after your menstrual period has ended or may give you a course of medication to produce a thinning of the endometrium prior to the procedure.

## Quality of Life

Using a questionnaire that asks about how heavy periods can affect a woman's life (the Menstrual Impact Questionnaire, or MIQ), women reported an improvement in quality of life following the Cerene procedure. An improvement in quality of life is noted when the MIQ score decreases. All women in the CLARITY Study reported an improvement in quality of life from before the treatment through Month 12

after treatment. **Table 4** provides additional information on the change in women's MIQ score from screening (prior to treatment) through Month 12 after treatment.

### Table 4. Change in Women's Response to MIQ




*Note: 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.*

Limitations in activities can also be presented as a composite of symptoms. At screening, 84% of subjects reported that they experienced moderate, quite a bit, or extreme limitations in their social-leisure and/or physical activities and/or their ability to work. Only 9.5 % reported the same symptoms in their MIQ survey at the Month 36 follow-up visit.

## Reduction in Premenstrual Symptoms

Using a questionnaire that measures the impact of premenstrual symptoms on life activities (the Premenstrual Symptoms Impact Survey™, or PMSIS), women reported a 68.6% reduction in the combined PMSIS score, from an average (typical) score of 53.8 prior to treatment to a score of 16.9 at Month 12 after treatment. These scores indicate an improvement in premenstrual symptoms following treatment with the Cerene Device.

Premenstrual symptoms (PMS) 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. Similar to MIQ, PMS can also be presented as a composite of symptoms and severity. At screening, 74.8% of subjects reported PMS symptoms at a frequency of often, very often, or most or all of the time. Only 14.9% reported the same symptoms in their PMSIS at the Month 36 follow-up visit.

### Reduction in Painful Periods

Prior to receiving treatment with the Cerene Device, over 40% of women reported dysmenorrhea as 'severe' or 'very severe' and at Month 12 after treatment, only 6% of women reported the same intensity of symptoms.

### Satisfaction with the Cerene Procedure

Women reported high level of satisfaction with the Cerene procedure. One year after the treatment in the CLARITY Study, 90% of women were satisfied or very satisfied with their outcome following treatment with the Cerene Device and 95% of women would definitely recommend or consider recommending the Cerene procedure to a friend or family member. Three years after the treatment, 84.5% of women were satisfied or very satisfied with their outcome following treatment with the Cerene Device and 90.7% of women would definitely recommend or consider recommending the Cerene procedure to a friend/family member.

### Return to Normal Daily Activities

Women reported a rapid return to normal daily activities following the Cerene procedure. On average, women in the CLARITY Study returned to normal daily activities within two days. Over half (57%) of the women returned to normal daily activities in one day or did not require any recovery time.

### Post-Ablation Scarring in the Uterus

Whenever a doctor performs a procedure in the uterus, there is a risk of scarring and adhesions (i.e., parts of the uterine cavity that stick together). In some cases, this complication may lead to pain following the endometrial ablation. Scarring may also prevent the doctor's ability to access and evaluate the uterine cavity. Scarring and the related problems may lead to hysterectomy (surgical removal of the uterus).

Women in the CLARITY Study were evaluated for post-ablation scarring at 12 months after the procedure. The doctors performing the study were able to enter the uterine cavity with a hysteroscope (a thin, lighted telescope that is inserted into the vagina to examine the cervix and inside of the uterus) in 98.7% of the women and felt satisfied that they could see and fully evaluate the uterine cavity in 89% of these women.

### Treatment in Women with Prior C-Section

The Cerene Device can be performed if you have had a low transverse c-section, which is the most common type in the United States. You should ask your physician about the type of c-section you had.

## 10. How is the Cerene Procedure Performed?

Prior to coming into the treatment room, you may be asked to take specific medications at the direction of your physician. A nurse or medical assistant will take your blood pressure, temperature, and other important information. Once you are in the procedure room, you will lie down on a table and be placed in the same position as if you were having a gynecological exam. Your feet will be placed in stirrups. At the time of the procedure, the doctor will insert a speculum (a medical tool that opens your vagina) so

that he or she can see inside your vagina to gain access to your cervix. The doctor may inject a medication into your cervix to make your cervix numb and help reduce discomfort during insertion of the Cerene Device. You may also be given some medication to help you relax and feel more comfortable. Your vagina and cervix will be cleaned with a special solution that kills germs. The doctor will measure the length of your uterus before performing the ablation procedure. Measurements are taken by inserting a thin probe and advancing it until your doctor can feel the probe touching the top of your uterus. The probe is then removed.

The doctor will then insert the Cerene Device through your vagina and cervix and into your uterus. Prior to initiating the treatment, a small, plastic liner (balloon) on the end of the Cerene Device inflates with filtered air to prepare for the ablation and to ensure there is no leak in the liner. You may feel mild to moderate menstrual-like cramping at this time. This step in the procedure will conduct safety tests to verify that there are no leaks within the uterine cavity.

Once the doctor confirms that the treatment can begin, the liner (balloon) on the end of the Cerene Device will be filled with a substance called nitrous oxide. Nitrous oxide freezes the lining of your uterus. During the Cerene Device placement, the procedure may be monitored by ultrasound, which would be placed on your abdomen. The Cerene Device will remain inserted in your uterus for approximately seven minutes. The freezing treatment will last for 2.5 minutes.

After the treatment is finished, you will remain to recover until the doctor determines that you return home (usually within 30 minutes). You may need to arrange for another adult to drive you home after the procedure.

You will experience vaginal discharge during the first few days following treatment that may last as long as six weeks. It is generally described as bloody during the first few days, a mixture of blood and fluid for another week, and then heavy, watery discharge that diminishes over time until stopping. This vaginal discharge is a normal part of the healing process and is expected to last for two to four weeks, so you will need to wear a sanitary pad during this time.

Your doctor's office will likely call to check on you after your Cerene procedure. However, if after the procedure you are experiencing increasing abdominal or pelvic pain, increased vaginal bleeding, vaginal discharge that is greenish or has a foul odor, or a fever greater than 100.4°F, immediately call your doctor's office. In rare cases, endometrial ablation can cause a serious injury that, if not treated promptly, can lead to death. If you call your doctor at night or on a weekend, your doctor's office will likely have an answering service that will put you in touch with your doctor or the doctor on call. If you are not able to talk with your doctor, call 911 or go to the nearest Emergency Room.

## 11. What are some other treatments for heavy menstrual bleeding?

The following practices and procedures are currently available to treat heavy menstrual bleeding if it is not caused by growths in the uterus such as a fibroid or polyp. Your doctor will tell you if you have any of these causes of heavy periods, and which therapy may be beneficial for you. The therapies for heavy periods are:

## Hormone Therapy

Hormone therapy is conveniently available as oral contraceptive pills, patches, or injection. Hormone therapy is frequently prescribed first, before trying surgical treatments. There are also several types of hormonal intrauterine devices that are inserted by a healthcare professional into the uterine cavity for contraception and control of bleeding. Hormone therapies require long-term use to maintain their effect and may have unpleasant side effects. There is no permanent effect on a woman's fertility (ability to have children).

## Dilatation and Curettage (D&C)

D&C was previously used more frequently to treat heavy menstrual bleeding and provide useful information through testing of the uterine lining removed. It requires sedation or general anesthesia to perform, because the cervix is dilated and the uterine contents are mechanically removed or suctioned away. There is no long-term effect on your period, and the procedure may need to be repeated. A D&C is best used to obtain uterine lining samples for testing when necessary. If performed frequently, a woman's fertility may be impacted by the formation of scarring in the uterus.

## Heat-Based Endometrial Ablation

Heat-based endometrial ablation uses heated saline, steam, or electrical energy to destroy the endometrium. The treatment is delivered by a variety of methods, but always through the vagina and cervix. The procedures may be performed under local or general anesthesia, and dilation of the cervix may be required. This treatment is only for women who do not wish to preserve fertility.

## Cold-Based Endometrial Ablation

Cold-based endometrial ablation uses a cryogen, or cooling agent, to freeze and destroy the endometrium. The treatment is delivered by two methods, but always through the vagina and cervix. Because cold provides natural pain relief, cold-based endometrial ablation procedures are typically performed in the physician's office without the need for general anesthesia or intravenous sedation. The Cerene Device provides endometrial ablation using a freezing agent that is released within a thin, flexible liner (balloon). This treatment is only for women who do not wish to preserve fertility.

## Hysterectomy

Hysterectomy is the most invasive therapy, with more risk; but it completely stops bleeding because the uterus is removed. It is performed in a hospital setting under general anesthesia and is associated with risks and complications of major surgery. Recovery is longer than the previously described methods, and there is no chance of pregnancy afterward because the uterus is removed.

Table 5 below outlines the advantages and disadvantages of other treatments for excessive menstrual bleeding.

Table 5. Advantages and Disadvantages of Other Treatments for Excessive Menstrual Bleeding

| Treatment | Endometrial Ablation | Progestin IUD[1] | Hormonal Therapy | D&C | Hysterectomy |
|---|---|---|---|---|---|
| **Description** | Device inserted into uterus that destroys the uterine lining with heat or cold. | Drug-covered device that the doctor inserts into the uterine cavity. The IUD gradually releases a steady amount of hormone which can help control bleeding. | Hormone that can be provided in a patch or injection that works for a given amount of time, or a pill that is taken daily. | Surgical procedure in which the doctor scrapes the inside of the uterus to remove the lining of the uterus. | Surgical removal of the uterus. |
| **Advantages** | For most women, menstrual bleeding is reduced to normal levels or less. For some women, menstrual bleeding completely stopped. Can usually be performed in a few minutes. Can be done in your doctor's office with minimal anesthesia. Rapid recovery. | Results in a lighter period in most women. Provides contraception for 3-7 years. Does not affect future childbearing potential. | Reduces bleeding in about half of the patients. Provides contraception. Does not affect future childbearing potential. | Diagnostic tool that can provide tissue samples to test for cancer or pre-cancerous conditions of the lining of the uterus. Does not likely affect future childbearing potential. | Permanently eliminates bleeding. One-time procedure. |

[1] "IUD - Birth Control Method." Besider, 2020, https://www.bedsider.org/methods/iud.

| Treatment | Endometrial Ablation | Progestin IUD[1] | Hormonal Therapy | D&C | Hysterectomy |
|---|---|---|---|---|---|
| **Disadvantages** | Procedure only for women who have completed childbearing.<br><br>Requires anesthesia.<br><br>Side effects include:<br>• Pain/ cramping<br>• Vaginal discharge<br>• Infection<br>• Bleeding or spotting | Must be removed and replaced every 3-7 years.<br><br>Side effects may include:<br>• Bleeding/spotting for the first few months<br>• IUD falling out<br>• IUD pushing through the walls of the uterus<br>• Infection | Results may vary depending on hormone used.<br>Not suitable for smokers.<br><br>Side effects may include:<br>• Nausea<br>• Headache<br>• Weight gain | No longer considered a long-term solution for treatment of excessive bleeding.<br>Requires anesthesia.<br>Reduction in bleeding is temporary.<br><br>Side effects include:<br>• Uterine wall perforation<br>• Abdominal pain<br>• Infection | Major surgical procedure, requires general anesthesia.<br>2-8 week recovery time.<br><br>Irreversible and permanent loss of fertility.<br><br>Side effects may include:<br>• Bleeding (which, if excessive, can require transfusion)<br>• Wound infection<br>• Injury to bladder or another organ<br>•Hospitalization (1-3 days) |

## 12. How do I know if the Cerene Procedure for endometrial ablation is right for me?

The first step is to talk to your doctor about your heavy menstrual bleeding problem. Your doctor will do a series of tests to find the cause of your heavy menstrual bleeding. Heavy menstrual bleeding by itself is not a disease. It can be a sign or symptom of a number of possible medical conditions. Using ultrasound and/or hysteroscopy (methods used by doctors to look at the inside and/or outside of your uterus), and some other medical tests, your doctor should find the cause of your bleeding. Your doctor will then help you select the right treatment. Depending on the reason for your heavy menstrual bleeding, your doctor may suggest that you first try medications. If medications do not work, or you are not allowed to take them for other medical reasons, your doctor may suggest endometrial ablation using the Cerene Device. Tell your doctor if you have a tubal occlusion device (e.g., Essure® or Adiana®) or an intrauterine device (IUD) in place. The Cerene Procedure has not been tested in women with tubal occlusion devices in place and cannot be used when an IUD is in place.

## 13. How were the Cerene Clinical Studies performed?

The CLARITY Study of the Cerene Device for endometrial ablation was tested in 11 centers. The 14 doctors who performed this study were gynecologists who routinely treat women with heavy menstrual bleeding. The women treated with the Cerene Device were between 25 and 50 years old, had heavy menstrual bleeding, and did not want to have more children. All of the women were examined to determine the cause of their heavy menstrual bleeding and to make sure they were otherwise healthy and had no infection. In addition, they had to qualify for treatment by recording their menstrual bleeding, in a special diary, which had to exceed a certain amount.

The 242 women who were treated with the Cerene Device as part of the CLARITY Study attended follow-up visits for up to 36 months to identify any complications and to determine their menstrual bleeding status. They recorded their menstrual bleeding using the same type of menstrual bleeding diary before and after treatment through the time of their 12-month follow-up visit. Each diary was collected to determine the amount of menstrual bleeding. The Cerene treatment was considered successful if the woman achieved a certain reduction in bleeding at 12 months following the treatment (bleeding diary score of 75 or less). Women also reported on their experience of pain during treatment and at 1 day, their ability to return to normal activities of daily living, their quality of life, their satisfaction with the treatment, and if they had any procedure because of their menstrual bleeding.

Women had follow-up visits with the study investigator by telephone or in person at 24-months and 36-months after treatment to answer questions about any gynecologic complications they experienced, their menstrual bleeding, their quality of life, their satisfaction with the Cerene treatment, and if they had any procedure because of their menstrual bleeding.

## 14. What Were the Results of the Clinical Study?

Twelve months after the Cerene procedure, 77% of women treated with the Cerene Device successfully met the study goal for reduced bleeding, and 10% of women had no menstrual bleeding. Over 95% of women reported that their improvement in monthly blood loss was meaningful. 84% of women reported that their painful periods decreased following the Cerene procedure. The overall patient satisfaction was 90%. Women tolerated the Cerene procedure well with minimal pain. General anesthesia was not used in the study. The vast majority (97.1%) of women received only a local anesthetic along with oral medication for pain and/or relaxation while tolerating the treatment with minimal pain.

Over the course of the 3 year study, ten women (4.1%) underwent a hysterectomy.

At 36-months, the vast majority of women reported sustained improvements in many aspects of their lives. Menstrual status improvements and satisfaction continued. 88.6% of women reported that they had no menstrual period or had a lighter than normal or normal period and 84.5% of women reported they were satisfied or very satisfied. Quality of life improvements also continued. 5% of women experienced a moderate or greater amount of limitation in their social-leisure and/or physical activities and/or their ability to work compared to 84% at screening and 14.8% of women reported PMS symptoms often or a greater amount of time compared to 74.8% at screening.

## 15. Places to Find Out More About Your Condition

To find out more about heavy menstrual bleeding and the Cerene Device, please visit the Cerene Website at: www.cerene.com.

### Other sources of information are the following:

1. American College of Obstetricians and Gynecologists. Heavy Menstrual Bleeding. https://www.acog.org/Patients/FAQs/Heavy-Menstrual-Bleeding
2. Mayo Clinic. Heavy Menstrual Bleeding. https://www.mayoclinic.org/diseases-conditions/menorrhagia/symptoms-causes/syc-20352829
3. Clue. Heavy Periods: How to tell if your heavy periods are normal. https://helloclue.com/articles/cycle-a-z/heavy-periods-how-to-tell-if-your-heavy-periods-are-normal