Mara®

Patient Labeling for the Mara® Water Vapor Ablation System

Prescription Only

CAUTION: FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN TRAINED IN THE USE OF THE MARA WATER VAPOR ABLATION SYSTEM.

CooperSurgical®

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1. GLOSSARY

Adenomyosis
Occurs when endometrial tissue, which normally lines the uterus, exists within and grows into the muscular wall of the uterus.

Mara Console
The part of the system that creates water vapor (steam). It also contains the control system that monitors the water vapor treatment to provide a safe, effective therapy.

Mara Water Vapor Probe
The hand-held part of the Mara system that is used by physicians to treat the uterus and is inserted through the vagina and cervix.

Mara Water Vapor Ablation System
The combination of the Mara Console and Mara Water Vapor Probe used together to treat heavy menstrual bleeding.

Amenorrhea
No menstrual bleeding

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

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 (also called a 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).

Dysfunction
The change of a body or organ function from normal to not normal. Another word for dysfunction is abnormal.

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.

Endometritis
Irritation of the lining of the uterus.

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

Essure® Permanent Birth Control
A small device implanted in the Fallopian tubes to provide blockage and permanent birth control for women who do not desire more children.

Estrogen
A chemical substance 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 protecting the safety of the food supply and 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.

Hematometra

An accumulation of blood within the uterus.

Hormone

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

Hydrosalpinx

A condition of the Fallopian Tube caused when previous infection causes the end of the tube to be damaged and sealed.

Hyperplasia

Overgrowth of a tissue, which in the endometrium can be pre-cancerous.

Hysterectomy

A surgical procedure to remove the uterus.

Hysteroscopy

A procedure completed using a hysteroscope, a thin, lighted tube with a camera that is inserted into the vagina to examine the cervix and inside of the uterus.

IUD (Intra-uterine Device)

A birth control device prescribed by your doctor to prevent pregnancy. Your doctor places the small device inside the uterus to prevent pregnancy.

Local Anesthesia

Uses medicine to block sensations of pain from a specific area of the body. Local anesthetics are usually given by injection into the body area that needs to be numb or anesthetized.

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 having menopause can have physical symptoms such as hot flashes, and emotional symptoms of menopause that may disrupt sleep, lower energy, or make them feel anxious or sad.

Minimally Invasive Procedure

A procedure that can be done through the body's natural openings or through one or more small incisions to avoid large incisions (cuts).

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.

Success Rate

The percent (%) of patients who are expected to have their excessive bleeding reduced to a normal level or less than normal levels after endometrial ablation treatment.

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.

Uterine Structural Abnormalities

Fibroids, benign tumors or polyps that can alter the shape of the uterine cavity. These abnormalities can sometimes cause excessive menstrual bleeding, or make the treatment of the bleeding more difficult.

2. What is the Mara Water Vapor Treatment?

If heavy periods are making it difficult for you to live a normal life, Mara may be a solution for you. Mara is a safe, effective and quick endometrial ablation treatment that uses natural water vapor to reduce your heavy menstrual bleeding. The treatment is designed to be conveniently performed in your doctor's office or clinic without making incisions or using general anesthesia that puts you to sleep.

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. Are Heavy Periods Common?

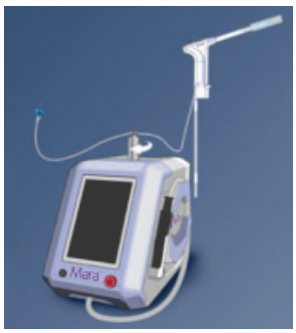
Heavy periods are a very common problem that affects about 1 in 5 women. The signs of heavy menstrual bleeding are most likely to start between the ages of 30 and 40.

5. How does the Mara Water Vapor Treatment Work?

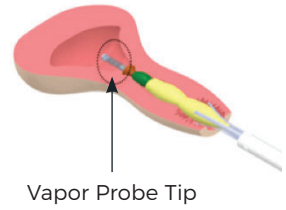
Mara uses natural water vapor to gently eliminate the lining of the uterus, known as the endometrium. The endometrium is the source of heavy menstrual bleeding in women who have not yet reached menopause. When the endometrium is destroyed, it can no longer re-grow to cause monthly bleeding. Not all of the endometrium needs to be destroyed for a woman to see an improvement in her menstrual bleeding. **Mara is only for women who no longer want to have children in the future.**

6. DESCRIPTION OF THE MARA WATER VAPOR ABLATION SYSTEM

The Mara Water Vapor Ablation System has two parts: the Mara Water Vapor Probe and the Mara Console. First, the doctor will gently insert the slender, soft tip of the Water Vapor Probe into your uterus through your vagina and cervix. Second, the Console and Water Vapor Probe heat natural water to make the water vapor inside the Water Vapor Probe. The water vapor is carefully controlled to treat the lining of your uterus. The water vapor treatment takes 2 minutes, with the total procedure, from device insertion to removal, taking 4 minutes.



Mara Water Vapor Ablation System



Mara Water Vapor Probe Tip in the Uterus

7. WHO CANNOT HAVE ENDOMETRIAL ABLATION WITH THE MARA WATER VAPOR TREATMENT?

Mara should not be performed in patients who have, or had, the following conditions:

- 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 endometrial hyperplasia as confirmed by histology
- Some previous surgeries that can thin the uterine wall. Your physician will need to decide if endometrial ablation is appropriate for you
- A patient currently on medications that could thin the uterine muscle, such as long-term steroid use (except for inhaler or nasal therapy for asthma)
- A patient with a uterine length < 6cm
- A patient with a history of a prior completed endometrial ablation procedure

  REPEAT ABLATION MAY RESULT IN SERIOUS PATIENT INJURY
- A patient with active genital or urinary tract infection at the time of treatment
- A patient with a systemic bacterial infection
- A patient with an intrauterine device (IUD) currently in place
- A patient with active pelvic inflammatory disease or known or suspected hydrosalpinx based on history or ultrasound at screening
- A patient with an undiagnosed cause of abnormal vaginal bleeding

8. WHAT ARE THE RISKS OF THE MARA WATER VAPOR TREATMENT?

With any procedure, there are risks related to the treatment and to the anesthesia used during the treatment. Your doctor will talk to you about the risks of the Mara treatment and will give you details about your individual situation. It is important for you to know the risks of the Mara treatment.

Following extensive research, laboratory testing, and a feasibility clinical study, the Mara Water Vapor Ablation System was tested in the Mara Pivotal Clinical Study, with a total of 221 patients. The first 66 patients were treated and followed for 3-6 months for their safety results. This is called the "Safety Study." The next 155 of these patients were treated and followed for one year to assess the safety and effectiveness of the Mara Water Vapor Ablation System. This study is called the "Pivotal Study." Patients in the pivotal study were followed for an additional two to three years to collect additional longer term outcomes. This portion of the study is called the "Post Approval Study."

Please see **Section 13** for an explanation of how the Pivotal/Post Approval studies were done.

Any surgical procedure has risk, and some risks were seen during this testing of the Mara Water Vapor Ablation System. These risks are listed in the following tables and cover the entire three years following the Mara treatment. It is also important to know how often these risks may happen. In these tables, this information is shown using the actual number of cases and as a percent (%). You can discuss these risks with your doctor for more information.

Risks of the Mara Water Vapor Treatment

The risks listed in the tables on the right and on page 10 are for the two groups tested:

1. The 66 three-month or six-month follow-up "Safety" patients examined for safety after the treatment.
2. The 155 one-year follow-up "Pivotal" patients examined for both safety and effectiveness of the treatment. Two additional tables are provided with the two- and three-year follow-up outcomes.

There is also information about the number of women who had hysterectomies throughout the entire study. Please see **Section 13** about the Clinical Studies for more information about how the two study groups were evaluated.

Table 1. Safety Patients Number and Percentage of Patients with One or More Related[a] Adverse Events by Time of Occurrence through 3-6 months

N=66						
Adverse Event	**Day of Ablation**	**Day 1 After Ablation**	**>Day 1 to ≤2 Weeks**	**>2 Weeks to 3 Months**	**>3 Months to 6 Months[b]**	**Total**
Uterine Cramping	32 (48.5%)	1 (1.5%)			1 (2.8%)	34 (51.5%)
Vaginal Infection			3 (4.5%)	1 (1.5%)		4 (6.1%)
Nausea	2 (3.0%)					2 (3.0%)
Vomiting	2 (3.0%)					2 (3.0%)
Cough	1 (1.5%)					1 (1.5%)
Transient Redness on Buttock	1 (1.5%)					1 (1.5%)
Spotting	1 (1.5%)					1 (1.5%)
Endometritis			1 (1.5%)			1 (1.5%)
Abdominal Pain				1 (1.5%)		1 (1.5%)
Uterine Tenderness				1 (1.5%)		1 (1.5%)

[a] Possible, probable or definitely related to device or procedure
[b] 36 patients were followed at 6 months

Table 2. Pivotal Patients Number and Percentage of Patients with One or More Related[a] Adverse Events by Time of Occurrence through 12 months

N=155					
Adverse Event	**Day of Ablation**	**Day 1 After Ablation**	**>Day 1 to ≤2 Weeks**	**>2 Weeks to 1 Year**	**Total**
Uterine Cramping	53 (34.2%)	3 (1.9%)	2 (1.3%)	6 (3.9%)	62[b] (40.0%)
Nausea	10 (6.5%)				10 (6.5%)
Vomiting	5 (3.2%)				5 (3.2%)
Vaginal Infection		1 (0.6%)	3 (1.9%)	1 (0.6%)	4[b] (2.6%)
Abdominal Pain	4 (2.6%)				4 (2.6%)
Abdominal Distension	1 (0.6%)	1 (0.6%)	1 (0.6%)		3 (1.9%)
Endometritis			2 (1.3%)		2 (1.3%)
Fainting	1 (0.6%)				1 (0.6%)
Back Pain	1 (0.6%)				1 (0.6%)
Difficulty With Bowel Movement or Urination		1 (0.6%)			1 (0.6%)
Fever		1 (0.6%)			1 (0.6%)
Urinary Tract Infection (UTI)		1 (0.6%)			1 (0.6%)
Vaginal Bleeding			1 (0.6%)		1 (0.6%)
External Vaginal Itching			1 (0.6%)		1 (0.6%)
Lightheadedness			1 (0.6%)		1 (0.6%)
Spotting			1 (0.6%)		1 (0.6%)
Intermittent Vaginal Spotting				1 (0.6%)	1 (0.6%)
Prolonged Spotting				1 (0.6%)	1 (0.6%)
Hematometra				1 (0.6%)	1 (0.6%)
Low Back Pain				1 (0.6%)	1 (0.6%)
Irregular Uterine Bleeding				1 (0.6%)	1 (0.6%)

[a] Possible, probable or definitely related to device or procedure
[b] Patients with more than one occurrence of same event are only counted once

Table 3. Number and Percentage of Patients with One or More Gynecologic Adverse Events >12-24 Months

Adverse Event	N=143
Menorrhagia	5 (3.5%)
Endometriosis	2 (1.4%)
Hematometra	1 (0.7%)
Dysfunctional Uterine Bleeding	1 (0.7%)
Pelvic Pain	1 (0.7%)
Uterine Cramping	1 (0.7%)
Cyclic Uterine Cramping	1 (0.7%)
Intermittent Uterine Cramping	1 (0.7%)
Irregular Cycle	1 (0.7%)
Menstrual-Related/Cyclic Headaches	1 (0.7%)
Headache	1 (0.7%)
Anemia	1 (0.7%)
Cervical Polyp	1 (0.7%)
Ovulation Pain	1 (0.7%)
Vaginal Dryness	1 (0.7%)
Night Sweats	1 (0.7%)
Recurrent Yeast Infections	1 (0.7%)
Ruptured Ovarian Cyst	1 (0.7%)
Vulvar Condyloma	1 (0.7%)

Table 4. Number and Percentage of Patients with One or More Gynecologic Adverse Events >24-36 Months

Adverse Event	N=136
Menorrhagia	4 (2.9%)
Uterine Cramping	3 (2.2%)
Dysfunctional Uterine Bleeding	2 (1.1%)
Cyclic Uterine Cramping	1 (0.7%)
Intermittent Uterine Cramping	1 (0.7%)
Dysmenorrhea	1 (0.7%)
Adenomyosis (pain)	1 (0.7%)
Abnormal Uterine Bleeding	1 (0.7%)
Clots with Menses	1 (0.7%)
Irregular Cycle	1 (0.7%)
Ovarian Pain and Cramping Prior to Cycle	1 (0.7%)
Right Ovarian Pain	1 (0.7%)
Ovulation Pain	1 (0.7%)
Right Lower Quadrant Pain	1 (0.7%)
Pelvic Pain	1 (0.7%)
Menstrual-Related/Cyclic Headaches	1 (0.7%)
Headache	1 (0.7%)
Endometriosis	1 (0.7%)
Recurrent Yeast Infections	1 (0.7%)
Intramural Leiomyoma	1 (0.7%)
Vulvar Condyloma	1 (0.7%)
Menopausal Symptoms	1 (0.7%)
Night Sweats	1 (0.7%)
Climacteral Complaints	1 (0.7%)

Over the three-year duration of the trial, there were 10 (6.5%, 10/155) women who had a hysterectomy. Six of the hysterectomies were for ongoing heavy menstrual bleeding and four were for pain. After the hysterectomies were done, it was discovered by a pathologist (a scientist who studies the causes and effects of diseases) that six of the ten women had an underlying disease of the inner lining of the uterus called adenomyosis. Adenomyosis is a known cause for continued heavy menstrual bleeding and pain, even after having an endometrial ablation.

Additional Risk-Related Information

Endometrial ablation with the Mara Water Vapor Ablation System is a surgical procedure. As with all surgeries, serious injury or death can occur. The following have been reported with the use of other endometrial ablation techniques and are also possible risks with Mara:

1. Injury (e.g., tear) of the uterus
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 heated instruments with the skin outside of the uterus can cause a burn
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 Mara Water Vapor Ablation System does not protect women from future pregnancy. Patients will still need to use contraception until menopause or undergo a permanent sterilization procedure.**
13. Life-threatening infection. Patients 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
14. Other risks and complications leading to serious injury or death. **Undergoing an endometrial ablation procedure may make it more difficult to diagnose endometrial cancer in the future.**

9. BENEFITS OF ENDOMETRIAL ABLATION WITH THE MARA WATER VAPOR TREATMENT

Mara has been shown in clinical trials to effectively reduce heavy menstrual bleeding.

One year[1] after the treatment in the Pivotal study, the following results were seen:

- 79% (122/155) of patients had their heavy menstrual bleeding reduced to a normal level or less
- 19% (30/155) of patients had no menstrual bleeding

Three years[2] after treatment the following results were seen:

- 48.8% (61/125) of patients reported light bleeding, 22.4% (28/125) reported moderate bleeding, 3.2% (4/125) reported heavy bleeding and 2.4% (3/125) reported very heavy bleeding
- 23.2% (29/125) of patients reported no menstrual bleeding

Procedure Time and Location

The procedure time from insertion to removal of the Mara Water Vapor Probe tip is about 4 minutes, including 2 minutes of water vapor treatment.

The treatment can be done in an office or clinic, and you do not need general anesthesia. In the Pivotal study, 73% of the procedures in the United States were conducted in a physician's office.

Quality of Life

Using a questionnaire that asks about how heavy periods can affect a woman's life (the MIQ), patients reported an improvement in quality of life following the Mara treatment. An improvement in quality of life is noted when the MIQ score decreases.

One year after the treatment in the Pivotal study, patients reported the following:

- In 141 patients, the average MIQ score decreased from 14.7 before the treatment, to 6.6, one year after the treatment

Three years after treatment patients reported the following:

- In 125 patients, the average MIQ score decreased from 14.7 before the treatment, to 6.3, three years after the treatment

[1] Menstrual bleeding outcomes, collected with a patient diary, including no menstrual bleeding represent the most recent menses within ± 8 weeks of the one-year follow-up.

[2] Menstrual bleeding outcomes, collected with a telephone questionnaire, including no menstrual bleeding represent the most recent menses within ± 8 weeks of the three-year follow-up.

Patient Satisfaction

Patients reported high satisfaction with the Mara treatment.

One year after the treatment in the Pivotal study, patients reported the following:

- 91% (128/141) of patients were either satisfied or very satisfied
- 93% (130/140) of patients said they would recommend the treatment to a friend

Three years after the treatment, patients reported the following:

- 91% (114/125) of patients were either satisfied or very satisfied
- 94% (118/125) of patients said they would recommend the treatment to a friend

Return to Work

Patients reported a quick return to work following the Mara Treatment. Patients in the Pivotal study reported the following:

- 89% (121/136) of patients returned to work within 3 days or less
- 79% (107/136) of patients returned to work within 2 days or less

Menstrual Cramping

Patients with menstrual cramping before the treatment reported a decrease in menstrual cramping. One year after the Mara treatment in the Pivotal study, patients reported the following:

- 72% (81/112) of patients with menstrual cramping before undergoing the treatment said their cramping decreased after the Mara treatment

Sex Life

Patients whose periods affected their sex life reported an improvement in their sex life. One year after the treatment in the Pivotal study, patients reported the following:

- 85% (77/91) of patients whose periods affected their sex life had an improvement in their sex life after treatment

Treatment in Patients with Fibroid Tumors or Prior C-Section

- Mara can be performed in patients with fibroid tumors
- Mara can be performed if you have had a prior 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 MARA WATER VAPOR TREATMENT PERFORMED?

Prior to coming into the treatment room, you may be asked to take specific medications at the direction of your physician. Before treatment, you will be taken to the procedure room. The nurse will take your blood pressure, temperature, and other important information. Nurses may place a monitor on your finger or tape a number of wires on your chest to keep track of how well your heart and lungs are working, as well as ask whether you have taken the prescribed medications as directed.

Your endometrial lining should be thin prior to the Mara treatment. Your physician may choose to perform the treatment 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 treatment.

At the time of the treatment, the doctor will insert a speculum (a medical tool that opens your vagina) so that your doctor can see inside and gain access to your cervix. The doctor may make your cervix numb with an injection around your cervix to help reduce discomfort during the treatment. You will also be given some medication to help you with any pain and make you relax. An oxygen mask may also be placed on your face to help you breathe. Your doctor's assistant will prepare you for the treatment by cleaning your vagina with a special solution that kills germs.

The doctor will turn on the Mara Console, and then gently insert the soft tip of the Mara Water Vapor Probe into your uterus. The Console will inflate balloons that are designed to protect your cervix and vagina from the water vapor. Safety tests will be conducted to verify that there are no leaks within the uterine cavity, and confirm cervical sealing and proper device placement. Upon successful completion of the safety tests, water vapor is carefully delivered to treat the lining of your uterus for 2 minutes. At the end of the treatment, the balloons will deflate, and the doctor will remove the device from your uterus.

The time from insertion to removal of the Mara Water Vapor Probe tip is 4 minutes, including 2 minutes of water vapor treatment.

No part of the Mara Water Vapor Probe remains in the uterus after the treatment.

After treatment, you will be watched for about 1 hour to make sure you are okay. You may experience some mild to moderate low abdominal cramping and pain. The recovery room nurse may give you some medication for this. You will then be released to go home. It is important that someone is with you to take you home. You cannot drive immediately after the treatment if you were given medication to sedate you during the treatment.

Most patients experience some uterine cramping for a few days, which usually is treated with over the counter (non-prescription) pain medication that your doctor will recommend. Patients also reported vaginal discharge following the treatment. During the first few days, the discharge is likely to be bloody in color, but it will gradually turn clear. The total time of vaginal discharge is expected to last for two to four weeks, so you will need to wear some sanitary protection during this time.

Your doctor's office will likely call you to check on you after your treatment. However, **if after the treatment you are experiencing increasing pain, increased bleeding, change to a greenish color vaginal discharge, or have 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 to 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 excessive uterine bleeding due to benign causes, in the absence of structural abnormalities within your uterus such as fibroids, benign tumors or polyps. 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, using combination estrogen-progestin or progestin-only medicines are conveniently available as oral contraceptive pills, patches, or injection, and are frequently used first, before trying surgical treatments. There are also several types of progestin-containing intrauterine devices that are inserted by a professional into the uterine cavity for contraception and control of bleeding. Hormone therapies require long-term use to maintain the effect and may have unpleasant side effects. There is no permanent effect on a woman's fertility, however.

Dilatation and Curettage (D&C)

D&C was previously used more frequently to treat heavy menstrual bleeding while providing useful information through examination 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 menses, and the procedure may need to be repeated. A D&C is now best used to obtain uterine lining samples for examination when necessary. If used frequently, a woman's fertility may be impacted by the formation of scarring in the uterus.

Endometrial Ablation

Endometrial ablation uses heat, cold, 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 indicated for women who do not wish to preserve fertility. The Mara Water Vapor Ablation System provides endometrial ablation using sterile natural water vapor (steam)

Hysterectomy

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

The table 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

	Endometrial Ablation	Progestin IUD[a]
Treatment 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.
Treatment 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	• Reduces bleeding problems in most women • Provides contraception for 5 years • Does not affect future childbearing potential
Treatment Disadvantages	• Procedure only for women who have completed childbearing • Requires anesthesia Side effects include: • Pain/cramping • Vaginal discharge • Infection • Bleeding or spotting	• Must be removed and replaced every 5 years • 70% of women experience bleeding/spotting between menstrual periods • 30% of women experience hormonal side effects that may include depression, acne, headache, nausea, weight gain, and hair loss • In 3-5% of women, the uterus will push the IUD out of the uterine cavity (expulsion) Other side effects include: • Uterine wall perforations following insertion • Abdominal pain • Infection • Difficulty inserting the device that requires cervical dilation

[a] Mirena Prescribing Information, NDA 21225 Mirena; FDA Approved 21 Dec 2016

Hormonal Therapy	D&C	Hysterectomy
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.
• Reduces bleeding in about half of 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
• Results may vary depending on hormone used • Not suitable for smokers Side effects may include: • Nausea • Headache • Weight gain	• No longer considered a long-term solution for treatment of excessive bleeding • Requires anesthesia • Reduction in bleeding is temporary Side effects include: • Uterine wall perforation • Abdominal pain • Infection	• Major surgical procedure, requires general anesthesia • 2-8 week recovery time • Irreversible and permanent loss of fertility Possible complications include: • Bleeding (which, if excessive, can require transfusion) • Wound infection • Injury to bladder or other organ • Hospitalization (1-3 days)

12. HOW DO I KNOW IF THE MARA WATER VAPOR TREATMENT 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 excessive 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 excessive 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 with the Mara Water Vapor Treatment.

Tell your doctor if you have Essure® inserts. Endometrial ablation should not be performed prior to the 3-month confirmation test that shows that your fallopian tubes are blocked.

13. HOW WERE THE MARA CLINICAL STUDIES DONE?

The Mara Water Vapor Ablation System was tested in multicenter clinical studies. Doctors who did these clinical studies were gynecologists who regularly treat women with heavy bleeding. The women treated with Mara were from 30 to 50 years old, had excessive menstrual bleeding, and did not want to have more children. All of the women were examined to see if there was a cause of their excessive menstrual bleeding and to make sure they were otherwise healthy and had no infection.

The Mara Pivotal clinical study was done by 14 doctors at different hospitals and clinics. There were two study groups: 1) the “Safety” group, and 2) the “Pivotal” group.

Sixty-six (66) women in the Safety group had the Mara Treatment, and were followed for three to six months to make sure there were no unexpected risks of the treatment.

There were an additional 155 women included in the Pivotal group. These women were evaluated for any adverse events, and also kept a record of their bleeding using a special diary. They filled out the diary to document the amounts of their daily menstrual bleeding during their period before the Mara treatment, and then recorded the same information in a diary 12 months after treatment. Each diary was collected and the amount of bleeding each patient had before and then after the treatment was determined. In order to be in the clinical study, the patient’s bleeding level had to be more than a certain amount. The Mara treatment was considered successful if a patient had a bleeding level that was normal or below normal at 12 months following the treatment.

Patients were also contacted by telephone at 24- and 36-months after their endometrial ablation to ask questions about their menstrual bleeding, quality of life and satisfaction with the endometrial ablation procedure.

14. WHAT WERE THE RESULTS OF THE CLINICAL STUDY?

At one year after the Mara treatment, 79% of patients had bleeding that was reduced to a normal level or less, with 19% of those patients treated who completely stopped their monthly periods.[3] The majority of patients with menstrual cramping (72%) indicated that their monthly cramping decreased after the Mara Treatment. The overall patient satisfaction with the treatment was 91%. Eighty-five percent (85%) of patients whose periods affected their sex life said they had an improvement in their sex life and 93% of patients said they would recommend the treatment to a friend.

The Mara Treatment has been performed in the presence of Essure® Permanent Birth Control devices in 8 women. There were no serious device or treatment related adverse events in these patients.

At three-years after treatment, 48.8% (61/125) of patients reported light bleeding, 22.4% (28/125) reported moderate bleeding, 3.2% (4/125) reported heavy bleeding and 2.4% (3/125) reported very heavy bleeding. 23.2% (29/125) of patients reported no menstrual bleeding.[4] The overall patient satisfaction with the treatment was 91% and 94% said they would recommend the treatment to a friend.

15. POST-ABLATION CAVITY EVALUATION (PACE) STUDY

A follow-up study, PACE (Post-Ablation Cavity Evaluation), was conducted by eight of the Pivotal study Investigators/sites and enrolled 72 patients who completed the three-year follow-up in the Pivotal study. Data from two subjects were excluded from analysis due to one patient that did not meet the study inclusion criteria and visualization of the uterine cavity could not be evaluated per protocol in one patient.

The goal of the PACE study was to examine access to and visualization of the uterine cavity more than three years after having an endometrial ablation with the Mara Water Vapor Ablation System. Access may be important for any needed future evaluations or therapies.

In 90% (63/70) of women, cavity access was achieved allowing a diagnostic visual exam to see inside of the uterine cavity. In 86% (47/63) of cavities accessed, there were no adhesions (47/63) or minimal adhesions (7/63) (bands of scar tissue across the inside of the uterine cavity).

[3] Menstrual bleeding outcomes collected with a patient diary, including no menstrual bleeding represent the most recent menses within ± 8 weeks of the one-year follow-up.

[4] Menstrual bleeding outcomes, collected with a telephone questionnaire, including no menstrual bleeding represent the most recent menses within ± 8 weeks of the three-year follow-up.

16. PLACES TO FIND OUT MORE ABOUT YOUR CONDITION

To find out more about your condition and the Mara Water Vapor Treatment, please see the Mara Treatment website at **www.maratreatment.com**.

Other sources of information are the following:

1. ACOG.org American College of Obstetricians and Gynecologists — provides many useful publications on Women's Health
2. American Association of Gynecologic Laparoscopists — excellent source of information
3. CooperSurgical, Inc. Vapor System Summary of Safety and Effectiveness Data (SSED), www.accessdata.fda.gov/cdrh_docs/pdf16/P160047B.pdf

17. REFERENCES

Mara® Water Vapor Ablation System Instructions for Use.

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AW0257 · Rev. B · 11/2022