

Essure

Patients should be counseled that this product does not protect against HIV infection (AIDS) or other sexually transmitted diseases.

IMPORTANT NOTE—This information is a BRIEF SUMMARY of the complete prescribing information (Instructions for Use) provided with the product and therefore should not be used as the basis for prescribing the product. This summary was prepared by deleting from the complete instructions for use certain text, tables, and references. The physician should be thoroughly familiar with the complete instructions for use before using or prescribing this product.

INDICATIONS FOR USE: The Essure system is indicated for women who desire permanent birth control (female sterilization) by bilateral occlusion of the fallopian tubes.

CONTRAINDICATIONS:

The Essure system should not be used in any patient who:

- Is uncertain about her desire to end fertility
 - Can have only 1 micro-insert placed (including patients with apparent contralateral proximal tubal occlusion and patients with a suspected unicornuate uterus)
 - Has previously undergone a tubal ligation
- Or any patient with any of the following conditions:
- Pregnancy or suspected pregnancy
 - Delivery or termination of a pregnancy less than 6 weeks before Essure micro-insert placement
 - Active or recent upper or lower pelvic infection
 - Known allergy to contrast media or known hypersensitivity to nickel confirmed by skin test

WARNINGS:

- The patient must use alternative contraception (cannot rely on the Essure micro-inserts for contraception) until a hysterosalpingogram (HSG), which is performed 3 months post-micro-insert placement, demonstrates satisfactory micro-insert location and tubal occlusion. During this time frame, the patient may be at an increased risk of ectopic pregnancy
- The Essure procedure should be considered irreversible. There are no data on the safety or effectiveness of surgery to reverse the Essure procedure. Any attempt at surgical reversal will likely require utero-tubal reimplantation. Pregnancy following such a procedure carries with it the risk of uterine rupture and serious maternal and fetal morbidity and mortality
- The Essure micro-insert will conduct energy if directly or closely contacted by an active electro-surgical device. If this occurs, then there is a risk of patient injury. Therefore, electro-surgery should be avoided in procedures undertaken on the uterine cornua and proximal fallopian tubes without either hysteroscopic visualization of the micro-inserts, or visualization of the proximal portion of the fallopian tube via open surgical procedures or laparoscopy. During Laparoscopic Assisted Vaginal Hysterectomy (LAVH) and other procedures in which electro-surgical instruments could contact the serosa of the fallopian tube, instruments should not be placed more proximal than the ampullary portion of the tube
- Bench studies suggest that endometrial ablation using radio frequency (RF) energy will cause significant damage to surrounding tissue if an active RF instrument comes into direct contact with the Essure micro-inserts. Consequently, if using RF energy to perform endometrial ablation, direct contact with the Essure micro-inserts should be avoided. Global ablatable systems that employ RF energy should not be used in women with the Essure micro-inserts in place
- Bench and clinical studies demonstrated that thermal endometrial ablation of the uterus can be safely and effectively performed with the Gynecare THERMACHOICE™ Uterine Balloon System immediately following Essure micro-insert placement. No specific studies have been conducted to evaluate Essure expulsion rates or contraception rates following Essure-THERMACHOICE procedures. No other thermal endometrial ablation technologies have been studied in conjunction with Essure
- There are no data regarding cryoablation techniques or the use of laser for endometrial ablation of the uterus with the Essure micro-inserts in place
- There are also no data regarding the use of endometrial ablation devices that operate at microwave frequencies with the Essure micro-inserts in place. The use of microwave energy near metallic implants has been shown to pose significant risk of serious injury to patients. Use of microwave endometrial ablation devices near the Essure micro-inserts therefore should be avoided
- Although not reported in the clinical trials of the Essure system, there is a theoretical increased risk of ectopic pregnancy in patients with the Essure micro-inserts, should they become pregnant
- A very small percentage of women in the Essure clinical trials reported recurrent or persistent pelvic pain, and only 1 woman requested device removal due to pain. However, if device removal is required for any reason, it will likely require surgery, including an abdominal incision and general anesthesia, and possible hysterectomy
- Patients may decide, in future years, to undergo in vitro fertilization (IVF) to become pregnant. The effects of the Essure micro-inserts on the success of IVF are unknown. If pregnancy is achieved, the risks of the micro-insert to the patient, to the fetus, and to the continuation of a pregnancy are also unknown

PRECAUTIONS:

- Women should be counseled that:
 - No contraceptive is 100% effective. Ectopic and intrauterine pregnancy can occur in contraceptive failure, even years after the procedure
 - Data on the Essure micro-inserts beyond 5 years are not yet available and may be different from current data
 - Women who undergo sterilization at a relatively young age are at greater risk of regretting their decision to undergo sterilization
- Any intrauterine procedure performed without hysteroscopic visualization following Essure micro-insert implantation could interrupt the ability of the Essure micro-inserts to prevent pregnancy. Following such procedures, device retention and location should be verified by hysteroscopy, x-ray, or ultrasound. In addition, the presence of the Essure micro-inserts can involve risks associated with intrauterine procedures that, at this time, have not been identified
- Performing endometrial ablation immediately following placement of Essure micro-inserts may increase the risk of post-ablation tubal sterilization syndrome, a rare condition that has been reported in women with a history of tubal sterilization who undergo endometrial ablation
- Testing to ensure safety and compatibility with magnetic resonance imaging (MRI) has been conducted using a 1.5 tesla magnet. The Essure micro-inserts were found to be MR safe at this field strength. Test results at 1.5 tesla indicate zero magnetic force and RF heating of 0.6°C in a phantom when a whole body specific absorption rate (SAR) of 1.3 W/kg was applied. The presence of the micro-inserts produces an MR artifact, which will obscure imaging of local tissue. The artifact is expected to be larger at higher field strength

ADVERSE EVENTS:

A total of 745 women underwent the Essure procedure in 2 separate clinical investigations to evaluate the safety and effectiveness of the Essure system (227 in the Phase II study and 518 women in the Pivotal trial). Some women underwent more than 1 procedure if successful bilateral placement was not achieved in the initial procedure. Placement of at least 1 Essure micro-insert was achieved in 682 women (206 in the Phase II study and 476 in the Pivotal trial). Adverse events, which prevented reliance on the Essure device for contraception, were reported as follows: failure to place 2 micro-inserts in first procedure (14%), initial tubal patency (3.5%), expulsion (2.2%), perforation (1.8%), or other unsatisfactory device location (0.6%). All of the patients who experienced tubal patency at the 3-month HSG were found to have bilateral occlusion at a repeat HSG performed at approximately 6 months after the Essure procedure. In addition, all of the patients who chose to undergo a second Essure procedure following a micro-insert expulsion achieved successful micro-insert placement and were subsequently able to rely on the Essure micro-inserts for contraception. The most frequent adverse events and side effects reported as a result of the hysteroscopic procedure to place the Essure micro-inserts were as follows: cramping (29.6%), pain (12.9%), nausea/vomiting (10.8%), dizziness/light-headedness (8.8%), and bleeding/spotting (6.8%). Hypervolemia occurred in <1% of cases. During the first year of reliance on the Essure micro-inserts for contraception (approximately 15 months after micro-insert placement), the following episodes were reported as at least possibly related to the Essure micro-inserts: back pain (9.0%), abdominal pain (3.8%), dyspareunia (3.6%). All other events occurred in less than 3% of women.

PATIENT INFORMATION:

Please see Patient Information Booklet.

PHYSICIAN INFORMATION:

For complete prescribing information physicians should refer to the Essure System Instructions for Use.

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HT for Women With Very Low Estradiol

BY ALISON PALKHIVALA

Contributing Writer

MONTREAL — Postmenopausal women with extremely low levels of bioavailable estradiol may benefit most from the bone-building effects of ultralow-dose hormone therapy, according to a study presented here at the annual meeting of the International Bone and Mineral Society.

It remains unclear, however, whether these women are also more vulnerable to the negative effects of hormone therapy. Although estrogen therapy has been shown to suppress bone turnover in postmenopausal women, the Women's Health Study also revealed in 2002 that it may increase cardiovascular risk. Experts are therefore exploring the possibility that a dose of estrogen exists, at least for some women, that is high enough to improve bone parameters but too low to affect cardiovascular risk.

Dr. Alison Huang, of the University of California, San Francisco, and colleagues

explored whether an ultralow dose of estradiol—only 0.014 mg/day delivered transdermally—could be of benefit to postmenopausal women with very low or even undetectable estradiol levels. This group of patients was considered to have a high likelihood of benefiting because, as a group, they have a lower bone mineral density (BMD), increased bone turnover, and are at an increased risk for hip and vertebral fractures.

For the trial, 417 postmenopausal women were randomized to a 0.014-mg/day transdermal estradiol patch or to placebo for 24 months. Bioavailable estradiol levels in these women were calculated as the ratio of total estradiol to sex hormone-binding globulin.

The investigators measured the women's levels of serum osteocalcin and bone-specific alkaline phosphatase (BSAP), both markers of bone turnover, at 12 months. They also measured total hip and lumbar spine BMD at 24 months in women who adhered at least 80% to the study protocol.

Women in the lowest quintile of bioavailable estradiol had significantly greater reductions in osteocalcin and BSAP than women in the highest quintile of bioavailable estrogen in response to therapy. In women in the lowest quintile, there was also a trend toward greater improvement in total hip BMD, compared with women in the highest quintile. There was no evident impact of treatment on spine BMD.

On the basis of these results, the authors concluded that "measurement of bioavailable estradiol levels identifies women for whom the ultralow-dose 0.014-mg/day transdermal estrogen therapy may have significant reductions in bone turnover."

During a press conference, however, Dr. Huang warned that it is still not clear whether the very women who appear to have most to gain from estradiol therapy—those with very low baseline bioavailable estradiol levels—may also have most to lose. That is, these women may be most vulnerable to the effects of hormone therapy on cardiovascular health. ■

Flaxseed May Reduce Hot-Flash Frequency

BY FRAN LOWRY

Orlando Bureau

Preliminary data from a phase II pilot study suggest that flaxseed may be a useful alternative to estrogen in the management of hot flashes, according to Dr. Sandhya Pruthi of the Mayo Clinic, Rochester, Minn., and associates.

A 6-week regimen of crushed flaxseed, given at 40 g daily, decreased the number of hot flashes from a mean of 7.3 per day to 3.6 per day in women who did not wish to receive estrogen therapy, Dr. Pruthi and associates reported in the *Journal of the Society for Integrative Oncology*.

Estrogen therapy has been the effective hot-flash treatment most commonly used, but fears that it may cause breast cancer have made many postmenopausal women reluctant to take it for their menopausal symptoms. Their concerns have prompted a search for nonhormonal alternatives.

The authors tested the tolerability and effect of flaxseed therapy in 28 women who had at least 14 bothersome hot flashes per week for more than 1 month before study entry. Participants were instructed to sprinkle 2 tablespoons of crushed flaxseed on cereal, in juice, in yogurt, or on fruit twice daily for 6 weeks. Each tablespoon provided 10 g of flaxseed, and the women were instructed to drink at least 150 mL of liquid for each 10 g of flaxseed they consumed (*J. Soc. Integr. Oncol.* 2007;5:106-12).

In the last week of flaxseed therapy, the hot-flash score—a measure of hot-flash frequency and severity—decreased by a mean of 57%, with a median decrease of 62%. The mean decrease in the number of hot flashes per day (from 7.3 to 3.6) was significant. Participants also reported a statistically significant improvement in quality of life, with less anger, anxiety, and fatigue at the end of the trial than at the beginning.

Abdominal distention or bloating was experienced by half of the women at some time during the study, and six women failed to complete the full 6 weeks of flaxseed therapy because of abdominal toxicities, weight gain, or taste intolerance, the authors reported. "These issues need to be evaluated further in a placebo-controlled manner. It is possible that initiating flaxseed therapy at a lower dose—and titrating the dose upward—may decrease abdominal toxicities," Dr. Pruthi and associates wrote.

Flaxseed contains weak estrogenic properties that "seem to account for the most likely mechanism of its effectiveness in reducing hot-flash activity," according to the investigators. ■

Endometriosis, Parity Not Linked in Ca Risk

BY KATE JOHNSON

Montreal Bureau

LYON, FRANCE — The increased risk of cancer seen in patients with endometriosis is unrelated to parity, according to a large study—the first to examine this association.

"We found that contrary to what one might expect, endometriosis and nulliparity did not combine to give a higher cancer risk," said Dr. Anna-Sofia Mellin, who presented the results at the annual meeting of the European Society for Human Reproduction and Embryology. "We could not show a difference in risk between parous and nonparous women."

Her study identified 63,630 women, using the National Swedish Inpatient Register, who were discharged from hospital with a diagnosis of endometriosis between 1969 and 2002. From this cohort, 3,822 cancer cases were subsequently identified, using the National Swedish Cancer Register.

The study found no overall increased risk of cancer associated with endometriosis (standardized incidence ratio [SIR] 1.01); however, significantly elevated risks were found for specific cancers such as endocrine tumors (SIR 1.38), ovarian cancer (SIR 1.37), kidney cancer (SIR 1.36), thyroid cancer (SIR 1.33), brain tumors (SIR 1.27), melanoma (SIR 1.23), and breast cancer (SIR 1.08), said Dr. Mellin of the Karolinska Institute in Stockholm.

Endometriosis was associated with a reduced risk of cervical cancer (SIR 0.71).

When parity was considered, no significant differences were noted between parous and nonparous women, although a nonsignificant decrease in ovarian cancer was noted with parity (from SIR 1.48 in nonparous women to SIR 1.3 in parous women).

Most of the increased cancer risk was seen in women with ovarian endometriosis, with only a small but significant increase seen in those with peritoneal endometriosis and no increased risk associated with adenomyosis, she said.

Although the findings are cause for concern, Dr. Mellin said it is too early to recommend that all endometriosis patients receive cancer screening.

"We don't even have any screening for ovarian cancer, so we don't know how to follow these patients. We know that even if you get an ultrasound every year you still get ovarian cancer and it still may have grown too far," she said in an interview. ■