

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 uterine resection, hysterectomy, and other procedures in which electrocautery is used. 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 electrocautery device. If this occurs, then there is a risk of patient injury. Therefore, electrocautery 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 electrocautery 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 auto-ablative 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/lightheadedness (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.

Conceptus Incorporated
331 East Evelyn Avenue, Mountain View, CA 94041 USA

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Diabetics Need Lower Blood Pressure Targets Than Guidelines Recommend

BY MITCHEL L. ZOLER

Philadelphia Bureau

VIENNA — Evidence is catching up with the blood pressure targets for patients with diabetes.

In 2003, the most recent update of the U.S. hypertension treatment guidelines, JNC 7, set the goal pressure for patients with diabetes at 130/80 mm Hg. But no major trial results have ever proved that a target this low helps patients. Results from the Action in Diabetes and Vascular Disease: Preterax and Diamicon-MR Controlled Evaluation (ADVANCE) trial took a step toward supplying the proof in a study of more than 11,000 patients with diabetes.

Treatment with an antihypertensive regimen that combined the ACE inhibitor perindopril and the diuretic indapamide produced an average systolic blood pressure of 135 mm Hg. The treatment also produced a 14% relative drop in all-cause deaths and an 18% relative fall in cardiovascular deaths, both of which were significant, compared with patients not on the tested regimen, Dr. Stephen MacMahon reported at the annual meeting of the European Society for Cardiology. The average systolic pressure among patients in the control arm was 140 mm Hg.

The findings are important because they provide evidence that patients benefit when systolic pressure is reduced to 135 mm Hg instead of 140 mm Hg, commented Dr. Sidney C. Smith Jr., director of the Center for Cardiovascular Science and Medicine at the University of North Carolina at Chapel Hill.

“The current target is 130/80 mm Hg, but we don’t have good evidence supporting the systolic target. That’s why this trial is important. This is further, confirmatory evidence that reducing blood pressure is important. But we need more data because we’re still not at the target level,” said Dr. Smith, who is also vice chairman of the task force that produces treatment guidelines for the American College of Cardiology and the American Heart Association.

He cited the importance of another, large ongoing study that will compare achieved systolic blood pressures of 120 and 140 mm Hg in patients with diabetes.

The new findings “strengthen the argument” in favor of a blood pressure target of 130 mm Hg for patients with diabetes, agreed Dr. Raymond J. Gibbons, professor of medicine at the Mayo Clinic in Rochester, Minn. He voiced hope that a stronger evidence base will better motivate diabetic patients and their physicians to follow the JNC 7 blood pressure guidelines.

The ADVANCE trial was run at 215 centers in 20 countries, and was sponsored in part by Servier, which markets a formulation of perindopril and indapamide (Preterax). A formulation that combines both of these drugs has not been approved by the Food and Drug Administration. The trial included another randomization that is testing the value of glycemic control with the drug gliclazide (Diamicon), but that analysis is not completed.

The study enrolled patients with type 2 diabetes who were at least 55 years old and had at least one other cardiovascular disease risk factor. Eligible risk factors included a history of major cardiovascular disease, microalbuminuria, smoking, hypercholesterolemia, and age of 65 or older. During a run-in period, all patients were treated with a daily, fixed-dose, combination tablet of 2 mg perindopril and 0.65 mg indapamide. Other treatments could continue at the discretion of each patient’s physician.

Patients who were maintained on an ACE inhibitor before entering the study were switched to either a 2- or 4-mg daily dosage of perindopril. All patients who tolerated the study drug during the run-in could participate in the main study, which randomized patients to continue on active treatment or switch to placebo. After 3 months, daily dosages were doubled to 4 mg perindopril plus 1.25 mg indapamide.

During an average follow-up of 4.3 years, the mean systolic blood pressure was 135/75 mm Hg in the active arm and 140/77 mm in the control group. Patients

in both groups were taking an average of one to two antihypertensive drugs in addition to the study medications.

The study’s primary end point was a composite that included cardiovascular death, nonfatal myocardial infarction or stroke, and several types of microvascular events such as macroalbuminuria or need for renal replacement therapy.

These events occurred in 15.5% of the 5,569 patients who received the combination drug, and in 16.8% of the 5,571 patients in the placebo group, a 9% relative risk reduction that just barely achieved statistical significance, reported Dr. MacMahon, professor of cardiovascular medicine and epidemiology at Australia’s University of Sydney. Another benefit of treatment was a 21% relative drop in the rate of new renal disease. The results were reported in an article in *The Lancet* that was released online concurrent with the report at the meeting (doi:10.1016/S0140-6736[07]61303-8).

The active treatment in ADVANCE was well tolerated. By the end of the study, adherence was 73% to the study regimen and 74% to placebo.

An editorial that accompanied the article questioned whether the results were specific for treatment with the perindopril and indapamide combination used in the study, and suggested that any regimen that reduced blood pressure to the same level would probably have the same benefit. Dr. MacMahon made it clear that he agrees with using any safe and effective regimen that brings down a patient’s blood pressure.

“The results suggest a broader role for blood pressure lowering. Lowering the blood pressure of everyone with diabetes is a critical component of preventing complications,” he said. “The critical issue is to get as many people as possible on treatment.”

The new findings “will strengthen the current guidelines, and will also push [the guidelines] forward,” commented Dr. Guiseppe Mancia, head of internal medicine at San Gerardo Hospital, Milan, and a co-investigator in the study. ■

Metabolic Syndrome Tied to Mortality After CABG

Patients with metabolic syndrome are nearly three times as likely to die following coronary artery bypass graft surgery as are patients without the syndrome, according to a large study.

Patients with both metabolic syndrome and diabetes had a 2.7-fold increase in the risk of mortality, and patients with metabolic syndrome but without diabetes had a 2.4-fold increase in risk. In the multivariate analysis, there proved to be no significant increase in the risk of mortality in patients who had diabetes but not metabolic syndrome, wrote Dr. Najmeddine Echahidi of the Centre de Recherche de l’Hôpital Laval, Quebec, and colleagues (*J. Am. Coll. Cardiol.* 2007;50:843-51).

The retrospective analysis involved 5,304 consecutive patients who underwent an

isolated coronary artery bypass graft (CABG) between 2000 and 2004 at a single institution. An analysis of prospectively collected laboratory and physical data revealed that 46% met criteria for metabolic syndrome as set out by the National Cholesterol Education Program Adult Treatment Panel III.

The study’s primary end point was death from any cause, either within 30 days of surgery or after any interval if the patient was not discharged from the hospital. Results were adjusted for gender, peripheral vascular disease, chronic obstructive pulmonary disease, preoperative renal failure, preoperative myocardial infarction, and preoperative stroke.

The overall unadjusted mortality was 1.6%, but was significantly higher (2.4%)

among patients with metabolic syndrome, and significantly lower (0.9%) among patients without metabolic syndrome.

In addition to metabolic syndrome, several other factors increased the risk of mortality following CABG. These included age older than 75 years (relative risk 3.4), body mass index (kg/m²) less than 18.5 (RR 10.3), renal failure (RR 3.4), myocardial infarction within 7 days before surgery (RR 4.0), urgent surgery (RR 2.5), and emergent surgery (RR 6.4).

Considering the prevalence of metabolic syndrome, the investigators suggested that patients be assessed for metabolic syndrome before surgery, and that metabolic syndrome be incorporated into operative risk algorithms.

—Robert Finn