

Esure

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 *Esure* system is indicated for women who desire permanent birth control (female sterilization) by bilateral occlusion of the fallopian tubes.

CONTRAINDICATIONS:

The *Esure* 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 *Esure* 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 *Esure* 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 *Esure* procedure should be considered irreversible. There are no data on the safety or effectiveness of surgery to reverse the *Esure* 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 *Esure* micro-insert will conduct energy if directly or closely contacted by an active electrosurgical device. If this occurs, then there is a risk of patient injury. Therefore, electrosurgery 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 electrosurgical 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 *Esure* micro-inserts. Consequently, if using RF energy to perform endometrial ablation, direct contact with the *Esure* micro-inserts should be avoided. Global auto-ablative systems that employ RF energy should not be used in women with the *Esure* 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 *Esure* micro-insert placement. No specific studies have been conducted to evaluate *Esure* expulsion rates or contraception rates following *Esure*-THERMACHOICE procedures. No other thermal endometrial ablation technologies have been studied in conjunction with *Esure*.
- There are no data regarding cryoablation techniques or the use of laser for endometrial ablation of the uterus with the *Esure* micro-inserts in place.
- There are also no data regarding the use of endometrial ablation devices that operate at microwave frequencies with the *Esure* 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 *Esure* micro-inserts therefore should be avoided.
- Although not reported in the clinical trials of the *Esure* system, there is a theoretical increased risk of ectopic pregnancy in patients with the *Esure* micro-inserts, should they become pregnant.
- A very small percentage of women in the *Esure* 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 *Esure* 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 *Esure* 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 *Esure* micro-insert implantation could interrupt the ability of the *Esure* 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 *Esure* micro-inserts can involve risks associated with intrauterine procedures that, at this time, have not been identified.
- Performing endometrial ablation immediately following placement of *Esure* 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 *Esure* 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 *Esure* procedure in 2 separate clinical investigations to evaluate the safety and effectiveness of the *Esure* 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 *Esure* 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 *Esure* 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 *Esure* procedure. In addition, all of the patients who chose to undergo a second *Esure* procedure following a micro-insert expulsion achieved successful micro-insert placement and were subsequently able to rely on the *Esure* micro-inserts for contraception. The most frequent adverse events and side effects reported as a result of the hysteroscopic procedure to place the *Esure* micro-inserts were as follows: cramping (29.6%), pain (12.9%), nausea/vomiting (10.8%), dizziness/lightheadedness (8.8%), and bleeding/spotting (6.8%). Hypovolemia occurred in <1% of cases. During the first year of reliance on the *Esure* micro-inserts for contraception (approximately 15 months after micro-insert placement), the following episodes were reported as at least possibly related to the *Esure* 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 *Esure* System Instructions for Use.

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Drug Samples Create Ethical Divide

BY PATRICE WENDLING

Chicago Bureau

TUCSON, ARIZ. — Physicians are divided over whether it is ethical to use free sample medications in their primary care practices, Dr. Nancy Sohler, Ph.D., and Dr. Diane McKee reported at the annual meeting of the North American Primary Care Research Group.

Accepting samples was viewed either as being ethically questionable or as a useful way of helping provide health care to low-income patients, according to findings from a study of 24 family medicine and general internal medicine physicians, nurses, and administrators in practices affiliated with a large urban medical center serving low- and middle-income patients in New York.

Interactions with pharmaceutical representatives were viewed as a direct conflict of interest, an influence that could be controlled, or a source of useful information that helped keep the practice up to date on new medications.

Of the total, 10 respondents felt that they could control the influence of drug firm representatives by keeping them away from residents, by setting limits on what gifts or favors could be accepted, or by always being mindful that representatives are selling a product, Dr. Sohler said in an interview.

For the respondents who drew a hard ethical line, “It wasn’t that they thought giving out samples [to patients] was unethical, but that it wasn’t good practice,” she said. “They understood why others did it, but they worried about conflicts of interest with their interactions with the reps.”

Those who accepted samples said inadequacies in the health care system forced them to rely on gifts to care for their most needy patients.

All the respondents evaluated marketing practices from the perspective of protecting and serving their patients, said

Dr. Sohler, professor of community health and social medicine, City University of New York, New York. No one was concerned that physicians were ignoring clinical symptoms to prescribe the “right drugs,” he said.

The study included in-depth, qualitative interviews and was prompted by an administrative decision at the medical center to ban samples and pharmaceutical representatives from the community practices.

That decision left many providers uncertain about how to care for patients

without adequate health care coverage. Others suggested that the policy was changed because the administration did not want physicians taking the time to talk to sales representatives, didn’t trust that staff would avoid entering into agreements with pharmaceutical firms, and did want a single policy, because teaching sites had a “no-rep” policy and other sites didn’t need samples.

Dr. Sohler said further study would be needed to determine whether samples help poor patients more than they harm them, and whether representatives influence prescribing practices in mostly helpful or harmful ways.

“The empirical, quantitative evidence isn’t good on whether free medications help or harm our patients,” Dr. Sohler said. “We realize that all marketing has an influence, but we don’t know if it harms our patients.”

“People are drawing on their different values and perspectives to make a decision. We need hard evidence to make a policy, but in the meantime, we should keep these perspectives in mind as the data come in.”

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Consensus Is Elusive on Financial Disclosure

BY MICHELE G. SULLIVAN

Mid-Atlantic Bureau

Officials in charge of disclosing financial interests in research agree that disclosure is important, but are confused about how to do so effectively and appropriately, Kevin P. Weinfurt, Ph.D., and his colleagues reported.

Their survey of 42 such officials revealed widely varying opinions on when disclosure should be made, the financial limits that should trigger it, and how much information to share with prospective research subjects, said Dr. Weinfurt of the department of psychiatry at Duke University, Durham, N.C., and his co-investigators.

“Part of their struggle relates to a lack of clarity regarding the ultimate goals of disclosure,” the researchers wrote. “There is also a lack of systematic data regarding how potential research participants can and will use such information in their decision making” (J. Law Med. Ethics 2006; 34:581-91).

The study was based on detailed personal interviews with eight investigators, 23 review board chairs, and 14 conflict-of-interest committee chairs.

The survey was designed to elicit respondents’ understandings of how disclosure is done at their institutions and their thoughts on the importance of disclosure, including its risks and benefits to the institution and research subjects.

More than half of those interviewed agreed that disclosure should occur under

all circumstances; the rest said disclosure would depend on the degree of the financial relationship.

The most commonly expressed reason for disclosing a financial relationship was to facilitate better-informed decision making for potential subjects.

Other reasons included trust and transparency issues, reducing liability risk, and managing public perception of the institution.

About 80% of respondents said the disclosure should include the name of the funding source. But some said the name of the company or organization wasn’t as important as a description—whether it was a nonprofit organization, pharmaceutical company, or government body, for instance.

They also differed on whether the amount of financial interest should be disclosed. Conflict-of-interest committee chairs were most likely to want to share this information (93%), while investigators were least likely (63%).

Those who expressed concern about disclosing the amount felt that level of detail could become cumbersome or confusing in the informed consent statement, and that research subjects might overestimate the impact that particular amounts might actually have on research outcomes.

There was no consensus on what amount should trigger disclosure—the lower limit ranged from \$1 to \$50,000.

There was general agreement that the nature of the relationship should be dis-

closed, but no agreement about whether the disclosure should explain the possible impact of those relationships.

Again, concern about overcomplicating the consent statement seemed to be at the root of these issues.

Some respondents said the disclosure should include an explanation of how an unscrupulous investigator might alter the research results.

Most respondents dismissed the idea that disclosure could lower enrollment. There was little sympathy among the group for researchers who complained that full disclosure was an invasion of their financial privacy.

There was also concern about how to best highlight disclosure information without overemphasizing its importance or potential risk to a study’s integrity.

Some respondents said their consent form highlights the information in bold type, while others place it strategically in the document—at the very beginning, for example.

Many also emphasized that the informed consent process should include a discussion of conflict of interest, not just a read-through of the document.

“Our data suggest that it will be difficult to achieve agreement on the issue of substantial understanding of financial interests,” the researchers concluded. “Before we can resolve what counts as substantial understanding, there must be agreement about what risks are important for potential research participants to understand.”