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**FOR IMMEDIATE RELEASE**



Ferring Pharmaceuticals announces the U.S. Food and Drug Administration (FDA) approval to market ENDOMETRIN<sup>®</sup> (progesterone) Vaginal Insert, 100mg. ENDOMETRIN administered as a progesterone vaginal insert is indicated to support embryo implantation and early pregnancy by supplementation of corpus luteal function as part of an Assisted Reproductive Technology (ART) treatment for infertile women. The FDA approval of ENDOMETRIN was based on findings from the largest *in vitro* fertilization (IVF) trial in the world, conducted at 25 U.S. centers, across a wide range of patient types.

## **FDA APPROVES FERRING PHARMACEUTICALS' ENDOMETRIN<sup>®</sup> FOR LUTEAL PHASE SUPPORT IN ASSISTED REPRODUCTIVE TECHNOLOGY TREATMENT**

### **Targeted Efficacy Demonstrated in Largest IVF Trial Ever Conducted**

PARSIPPANY, NJ – June 21, 2007 – Ferring Pharmaceuticals, a leader in the infertility market, announced today that it has received approval from the U.S. Food and Drug Administration (FDA) to market ENDOMETRIN<sup>®</sup> (progesterone) Vaginal Insert, 100 mg. The approval was based on findings from the largest *in vitro* fertilization (IVF) trial in the world, conducted at 25 U.S. centers, across a wide range of patient types.

ENDOMETRIN administered as a progesterone vaginal insert is indicated to support embryo implantation and early pregnancy by supplementation of corpus luteal function as part of an Assisted Reproductive Technology (ART) treatment for infertile women. It is the first new alternative to current forms of progesterone supplementation in a decade. Progesterone is necessary to increase endometrial receptivity for implantation of an embryo and to support early pregnancy.

ENDOMETRIN 100 mg is an insert administered vaginally two or three times daily, with a disposable matched applicator, starting at oocyte retrieval and continuing for up to 10 weeks total duration. Vaginal absorption of the micronized progesterone insert results in high tissue levels at the endometrium as well as measurable serum levels.

Results of Ferring's IVF trial showed that ENDOMETRIN provides unprecedented luteal phase support, measured by continuing pregnancy and live birth rates, with highly efficient delivery of progesterone.

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“Adequate progesterone support is an extremely important step in the ART process for a successful pregnancy,” said Kenneth B. Kashkin, M.D., Senior Vice President, Global Clinical Research and Development and Chief Medical Officer at Ferring Pharmaceuticals. “Ferring’s landmark IVF clinical trial demonstrated the efficacy of ENDOMETRIN, based on excellent pregnancy and live birth rates. It combines highly efficient, targeted delivery of progesterone at the uterine level with easy, patient-friendly administration. A pharmacokinetic study of ENDOMETRIN compared to progesterone 8% gel showed that ENDOMETRIN (both twice daily and three times daily) achieves higher progesterone serum concentrations in the blood faster than the gel. As a result, the endometrium is exposed to sustainable progesterone levels faster, which better prepares it for implantation of the embryo. Our research also confirmed that gel build-up is another common patient concern.”

“Like all of our fertility products, our new progesterone supplement was designed to give patients an effective natural medication with easy administration,” said Wayne Anderson, President of Ferring Pharmaceuticals. “A recent survey of 350 patients conducted on the American Fertility Association (AFA) Web site showed that 86 percent of patients are dissatisfied with current progesterone formulations. They find that progesterone suppositories can be leaky and messy, progesterone-in-oil IM injections can cause pain and inconvenience, and gels often leave vaginal build-up. Oral and vaginal tablets are considered less efficacious than other forms. Now patients will have access to a convenient alternative with targeted efficacy.”

The addition of ENDOMETRIN will give Ferring the broadest portfolio of fertility treatments in the U.S. Currently, ENDOMETRIN is marketed by Ferring in Israel and Hong Kong.

### **Landmark IVF Trial**

The safety and efficacy of ENDOMETRIN compared with an active control were evaluated in a multicenter, randomized, open-label, assessor-blinded trial in 1,211 women, ages 18-42, undergoing IVF. Efficacy was measured by continuing pregnancy and live birth rates. An analysis was also conducted to evaluate once-daily compared with twice-daily dosing of gonadotropins during the stimulation phase.

MENOPUR<sup>®</sup> (menotropins for injection, USP) and BRAVELLE<sup>®</sup> (urofollitropin for injection, purified) were used for the stimulation phase of IVF, with a minimum of one vial of MENOPUR per day. The centers had the option of combining MENOPUR and BRAVELLE and administering them as one single daily injection, which was done for approximately two thirds of

the patients (777). On the day of oocyte retrieval, patients were randomized to ENDOMETRIN 100 mg twice daily, ENDOMETRIN 100 mg three times daily, or an active control ((progesterone vaginal gel (90 mg) QD)).\* In the study, 97 percent of patients randomized to participate in the trial received an embryo transfer.

The results showed that ENDOMETRIN was efficacious, with no significant differences in efficacy parameters between treatment arms. Continuing pregnancy rates were 44 percent with ENDOMETRIN TID and 40 percent with ENDOMETRIN BID. Live birth rates were also high: ENDOMETRIN BID 36.5 percent, ENDOMETRIN TID 39.7 percent. The groups showed equivalent tolerability, with no significant differences in the incidence of adverse events.

The efficacy of ENDOMETRIN was also evaluated in harder-to-treat patients – women over age 35 or with elevated basal follicle stimulating hormone (FSH) or body mass index (BMI). Excellent continuing pregnancy rates were observed across a broad range of patient types with the use of BRAVELLE, MENOPUR, NOVAREL<sup>®</sup> (chorionic gonadotropin for injection, USP) and ENDOMETRIN.

In a randomized, open-label, pharmacokinetic/pharmacodynamic and tolerability study of 58 women, ages 18 to 40, progesterone concentrations peaked within eight to 12 hours after insert administration. Compared to 50 mg progesterone IM, the vaginal inserts resulted in mean endometrial tissue progesterone concentrations that were 10 times greater: 7.1 ng/g protein (ENDOMETRIN 100 mg BID (n=9) versus 0.71 ng/g protein ((IM progesterone 50 mg QD (n=10)). ENDOMETRIN adequately transformed the endometrium from a proliferative state to a secretory state.

### **Patient Satisfaction**

According to Ferring's patient research, what patients liked most about ENDOMETRIN is that it is easy to administer, convenient, painless (does not require an injection), and for those who had previously used suppositories, less messy/leaky. In fact, nearly 80 percent would recommend it to a friend, which is appreciably higher than rates for other progesterone supplements, which ranged from zero for gel to 50-54 percent for the other forms.

### **About Luteal Support**

Successful implantation of the embryo depends on adequate preparation of the endometrium, the mucous membrane lining the uterus. The corpus luteum, formed after the oocyte is released, secretes progesterone to induce secretory transformation of the endometrium. Since natural progesterone production may be compromised by IVF, progesterone supplementation is believed to be necessary to provide the proper support for

implantation and the early stages of pregnancy. Studies have shown that luteal support with ART can result in increased pregnancy rates.

Currently available progesterone supplements come in oral, intramuscular (IM) injection, vaginal gel and suppository forms. ENDOMETRIN is the second FDA-approved product for progesterone supplementation in ART. In IVF, patients typically begin progesterone support on the day of egg retrieval and continue it until the 10<sup>th</sup> week of pregnancy. Progesterone supplementation is utilized by nearly all patients undergoing ART and about 60 percent of ovulation induction (OI) patients.

#### **About ENDOMETRIN**

ENDOMETRIN administered as a progesterone vaginal insert is indicated to support embryo implantation and early pregnancy by supplementation of corpus luteal function as part of an Assisted Reproductive Technology (ART) treatment for infertile women.

Only physicians thoroughly familiar with infertility treatment should prescribe ENDOMETRIN. In clinical trials (n=860), adverse reactions that occurred at a rate greater than or equal to 2 percent included: uterine spasm (3% to 4%) and vaginal bleeding (3%). Vaginal irritation, itching, burning or discomfort, urticaria, and peripheral edema were reported at an incidence of less than 2 percent. ENDOMETRIN is expected to have adverse reactions similar to other drugs containing progesterone (breast tenderness, bloating, mood swings, irritability, and drowsiness).

#### **About BRAVELLE and MENOPUR**

BRAVELLE (urofollitropin for injection, purified) and MENOPUR (menotropins for injection, USP), like all gonadotropins, are potent substances capable of causing mild to severe adverse reactions, including OHSS (incidence of 6.0% and 3.8%, respectively), with or without pulmonary or vascular complications, in women undergoing therapy for infertility. Like other products for ovarian stimulation, treatment with BRAVELLE and/or MENOPUR may result in multiple gestations. Only physicians thoroughly familiar with infertility treatment, including the risk of multiple births and adverse reactions, should prescribe these medications

#### **About Ferring Pharmaceuticals**

Ferring Pharmaceuticals, part of the Ferring Group, a privately owned, international pharmaceutical company, manufactures and markets the largest family of fertility treatments of any manufacturer in the U.S. The Company markets BRAVELLE, MENOPUR, REPRONEX<sup>®</sup> (menotropins for injection, USP), NOVAREL and ENDOMETRIN in the U.S. to infertility specialists and their patients. Ferring also offers the Q-CAP<sup>™</sup>, the first and only needle-

free reconstitution device, for use with its fertility treatments.

Ferring's line of orthopaedic and urology products includes EUFLEXXA™, hyaluronic acid for pain from osteoarthritis in the knee. Other products include ACTHREL® (corticotropin ovine trifluate for injection) for the differential diagnosis of Cushing's syndrome and DESMOPRESSIN ACETATE in injectable and rhinal tube forms for the treatment of diabetes insipidus and primary nocturnal enuresis.

The Ferring Group specializes in the research, development and commercialization of compounds in general and pediatric endocrinology, urology, gastroenterology, obstetrics/gynecology and infertility. For more information, call 888-337-7464 or visit [www.ferringusa.com](http://www.ferringusa.com) or [www.ferringfertility.com](http://www.ferringfertility.com).

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\*Crinone (progesterone vaginal gel) 8% is marketed by Columbia Laboratories.

*Please call Andrea Preston at 203-762-8833 for Full Prescribing Information.*