What is Endometrin?

IMPORTANT: For Vaginal Use Only.

Inform patients of the importance of reporting irregular vaginal bleeding to their doctor as soon as possible. It is important to complete the vagina insert program and inform your doctor if you do not get your period within five months after starting Endometrin.

How should I store Endometrin?

Endometrin may be stored at room temperature 70°F (21°C). Do not refrigerate.

Who should not use Endometrin?

Do not use Endometrin:

- If you are allergic to any of its ingredients
- If you are pregnant or think you may be pregnant
- If you are breast feeding
- If you have any bleeding without a known cause
- If you have liver disease
- If you have a prostatic or breast cancer
- If you have endometriosis
- If you have a history of heart disease
- If you have a history of stroke
- If you have diabetes
- If you have a history of blood clots
- If you have a history of asthma
- If you have a history of depression

What should I tell my doctor before starting Endometrin?

Tell your doctor about all the medicines you take including prescription and nonprescription medicines, vitamins, herbal supplements, and food additives. If you take any of these medicines, do not start Endometrin without first talking to your doctor.

What is Endometrin® used for?

Endometrin is used to correct or prevent conditions of abnormal endometrial growth and endometrial hyperplasia. It is also used for the prevention of endometrial hyperplasia and premenstrual syndrome (PMS) symptoms. Endometrin is also used as an assist in in vitro fertilization (IVF) and other fertility treatments. Endometrin is also used to assist with the implantation of embryos and to support the development of the uterus during pregnancy.

17.1. Clinical Studies Experience

In a prospective study involving 258 subjects treated with Endometrin three times daily, 145 subjects had livebirths (37% of study population). Among the 203 livebirths, 185 (91%) were term deliveries. 18 of the 203 livebirths (9%) were preterm deliveries. Five of the 18 preterm deliveries resulted in infants born less than 32 weeks of gestation. The seven subjects who reported fetal birth defects included a known case of Down syndrome, one case of congenital heart anomalies, one case of a cleft lip, and one case of an atrial septal defect. One fetus had an atrial septal defect.

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Table 2. Mean (±Standard Deviation) Serum Progesterone Pharmacokinetic Parameters  

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Single Dosing</th>
<th>Twice Dosing</th>
<th>Three Times Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/mL)</td>
<td>28.4 ± 10.4</td>
<td>30.8 ± 12.6</td>
<td>32.9 ± 14.1</td>
</tr>
<tr>
<td>Cmin (ng/mL)</td>
<td>8.9 ± 4.5</td>
<td>10.9 ± 6.7</td>
<td>17.3 ± 7.4</td>
</tr>
<tr>
<td>AUC0-24 (hr/mL)</td>
<td>17.3 ± 9.4</td>
<td>21.8 ± 10.9</td>
<td>24.1 ± 5.6</td>
</tr>
<tr>
<td>Tmax (hr)</td>
<td>6.9 ± 1.9</td>
<td>8.9 ± 2.9</td>
<td>10.9 ± 6.7</td>
</tr>
<tr>
<td>Mean (±Standard Deviation)</td>
<td></td>
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</tbody>
</table>

Table 3: Ongoing Pregnancy Rates* in Patients Receiving Endometrin for Luteal Supplementation and Early Pregnancy While in an Assisted Reproductive Technology Treatment Program  

<table>
<thead>
<tr>
<th>Subjects With FSH &lt;10 IU/L (N)</th>
<th>Ongoing Pregnancy: n (%): Endometrin 100 mg Twice Daily</th>
<th>Ongoing Pregnancy: n (%): Endometrin 100 mg Three Times Daily</th>
<th>Pregnancy Rate Percentage Difference Between Endometrin and Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>347</td>
<td>116 (33%)</td>
<td>111 (32%)</td>
<td>-3.6%</td>
</tr>
<tr>
<td>51</td>
<td>16 (31%)</td>
<td>20 (39%)</td>
<td>12.2%</td>
</tr>
<tr>
<td>160</td>
<td>45 (28%)</td>
<td>54 (33%)</td>
<td>-10.1%</td>
</tr>
</tbody>
</table>

16 CLINICAL STUDIES  

16.1 Luteal Supplementation During Assisted Reproductive Treatment Studies  

Endometrin was compared with a standard comparator in two randomized double-blind, placebo-controlled, parallel-arm studies of luteal phase supplementation.  

By definition, all patients included in these studies were infertile. The ongoing pregnancy rate was defined as the proportion of patients who conceived a viable pregnancy following embryo transfer. The study randomized to Endometrin 808 infertile women (74.9% White; 10.3% Hispanic, 5.4% Black, 5% Asian, and 4.6% Other) between 19 and 42 years of age (mean age 33) who had a body mass index (BMI) < 35 kg/m² and a serum follicle-stimulating hormone (FSH) level < 10 IU/L.

The ongoing pregnancy rates for subjects treated with both dosing regimens of Endometrin were non-inferior to the results from the comparator with respect to ongoing pregnancy rates. In women age 35 and older and in women with serum FSH levels between 10 and 15 IU/L, results from both dosing regimens were non-inferior to the results from the comparator with respect to ongoing pregnancy rate.  

In subjects under the age of 35 or with serum FSH levels less than 10 IU/L, results from both dosing regimens were non-inferior to the comparator with respect to ongoing pregnancy rates.  

The results of this study are shown in Table 3.

General information about Endometrin  

Endometrin is contraindicated in patients who are allergic to progesterone or any of its ingredients. Endometrin Vaginal Insert is contraindicated in patients with a history of uterine cancer or breast cancer.