



## **Letrozole (Femara)**

Letrozole (Femara) is a medication that was first reported to be effective for ovulation induction in 2000. It is classified as an Aromatase Inhibitor (AI) and was developed to reduce the risk of recurrence of breast cancer. Even though its use is considered “off label” for fertility treatment, there is good evidence supporting its efficacy and safety for ovulation induction.

### **How does it work?**

Letrozole works by binding to aromatase, an enzyme needed to make Estrogen. By temporarily decreasing Estrogen levels at the beginning of a menstrual cycle, Letrozole signals the pituitary gland to release more Follicle Stimulating Hormone (FSH). FSH stimulates the development of ovarian follicles, the fluid filled structure in which eggs reside and mature. Letrozole may lead to one or more eggs being ovulated and regulate the menstrual cycle. Ovulation typically occurs 5-8 days after the last letrozole tablet. When a mature follicle is present, a surge of LH hormone is released by the pituitary which causes the egg to be released from the follicle. Ovulation will occur 24-48 hours after the surge.

### **What is the standard dose?**

The Letrozole dosage is 2.5mg for five consecutive days – typically cycle Day 3 to 7 (with cycle day 1 being the first day of full menstrual flow). It is taken orally at approximately the same time each day.

### **How do I know when I am going to get an LH surge?**

The easiest way to detect your LH surge is with an ovulation predictor kit (OPK). This is a urine test that is done daily beginning a couple of days before you expect to ovulate. If you are doing an IUI, an orientation session will be scheduled with one of the nurses to review your treatment cycle with you in detail.

### **Why is the use of Letrozole for ovulation induction “off label”?**

In November 2005, a small Canadian study was presented comparing 150 babies born as a result of treatment with letrozole. The study reported an increased incidence of locomotor malformations and cardiac anomalies in the babies born after taking letrozole. This led to a warning from the manufacturer and Health Canada stating that Letrozole should not be used due to the risk of fetal toxicity. This was a very small study that was never published and was very misleading due to statistical limitations. Since then, we have accumulated better data for many babies conceived with the help of letrozole. The research clearly shows no increased risk of birth defects due to letrozole. Our long term data is growing and is very reassuring. The use of letrozole for ovulation induction or unexplained infertility is fully supported by The Canadian Fertility and Andrology Society, the Society of Obstetricians and Gynecologist of Canada and the American Society for Reproductive Medicine. Please speak to your physician if you would like more in depth information on this.

**What are the side effects?** Side effects are relatively common but generally mild. They include: hot flashes, mood swings, breast tenderness, bloating, nausea, vomiting, pelvic discomfort, insomnia, constipation, light-headedness, and a change in menstrual flow.

**What are the risks?** 3-5% risk of congenital malformations (the same as a spontaneous pregnancy) No increased risk of miscarriage 4% chance of a twin pregnancy and less than 1% chance of triplets.