

Fertility Program

PATIENT'S FACT SHEET: **LETROZOLE USE FOR OVULATION INDUCTION**

Letrozole (brand name: Femara®) is one of the more recent additions to the drugs being used for fertility treatment. It is an oral medication which can be very useful to help induce ovulation in women who are not reliably ovulating on their own. Until recently, the main oral medication used for this purpose has been clomiphene (brand names: Clomid® or Serophene®). In several situations, however, letrozole seems to be a better choice, especially in women with polycystic ovarian syndrome (PCOS).

During a menstrual period, estrogen levels become very low, and this triggers the pituitary gland to produce an increased amount of FSH which in turn stimulates the ovary to make egg follicles grow. Letrozole is taken for 5 days early in the menstrual cycle (usually cycle days 3-7). Letrozole works by temporarily suppressing estrogen production, which results in the pituitary sending out larger than usual amounts of FSH. It also has an action to make the ripening eggs more sensitive to FSH. The half-life of the medication is about 45 hours, which means it is gone from the body very quickly.

As of this writing, several studies on the use of letrozole for ovulation induction have been published with very positive results, but new data is always coming out. Some authorities feel that as time goes by, letrozole may become the first line oral drug for ovulation induction.

POTENTIAL SIDE EFFECTS AND RISKS

Letrozole was originally developed for treatment of postmenopausal women with breast cancer, and, as of this writing, this remains the only use for which it is approved by the FDA. When used for this purpose, it works based on its ability to reduce estrogen levels, which can decrease the chance of recurrence of breast cancer, and it is given for long periods of time (years). Much of the data on side effects come from women who have been using it for extended periods of time to treat breast cancer.

When used for ovulation induction, it is given only for 5 days at a time; side effects are transient, and resolve shortly after use. The most common are hot flashes, headaches, and breast tenderness. There are no known long-term side effects when it is used for the short periods of time needed to induce ovulation. When clomiphene is used for ovulation induction, there is an increased chance of multiple pregnancy. Letrozole appears to be much less likely to cause this, if at all.

LETROZOLE IS NOT FOR USE DURING PREGNANCY

Letrozole should not be taken by women who are already pregnant. Because it inhibits estrogen production, it can have a negative effect on embryonic and fetal development. Studies of pregnancy in rats and mice have shown that letrozole during pregnancy increases the risk of fetal death and malformations. There are no controlled studies in humans, but it should be assumed that a similar effect is possible. In a preliminary report of 13 women who took it during pregnancy, two of the women had children with birth defects. Because of this, and because of the fact that the FDA-approved use of this drug is to treat postmenopausal women who have breast cancer, the manufacturer specifically states that the drug should not be used in women of childbearing age.

LETROZOLE SAFE TO USE BEFORE PREGNANCY

There are no confirmed reports of letrozole being associated with increased incidence of birth defects when given PRIOR to pregnancy, and there is at least one large multicenter study showing NO increase in birth defects when used for ovulation induction.

It is important to make the distinction that when used as a fertility medication, it is given before the establishment of pregnancy, and is out of the body long before a pregnancy occurs. The baseline rate for birth defects in humans is 2-3%, and there is some data showing that babies born to women with fertility issues in general may have a slightly higher birth defect rate. There is NO evidence that letrozole, when given PRIOR to establishment of pregnancy, increases the risk beyond this baseline rate.

Letrozole has been approved by the FDA only as a drug to treat breast cancer, and the company that manufactures it has not sought FDA approval as a fertility drug. It should be noted that other drugs are commonly used without FDA approval in modern medical practice. When a company produces a drug which already has FDA approval for one reason, it is usually not worth the huge financial investment involved in acquiring the data for the FDA to approve other indications.

Many American fertility experts are publishing studies about letrozole usage for ovulation induction, and are recommending its use, especially in women where clomiphene has not worked and in women with PCOS. At the October 2007 national annual meeting of the American Society for Reproductive Medicine, there were a presentations recommending the use of this drug. Studies are currently being done to seek FDA approval for use of a different drug in the same category for ovulation induction.

We try to keep abreast of the latest developments in treatment of infertility so that we can provide our patients with the most up-to-date care possible, and this information sheet will be updated as new data emerges.