Specialists In Reproductive Medicine & Surgery, P.A.

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Aromatase Inhibitors
General Patient Information

Definition:
An Aromatase Inhibitor (Letrozole®, Femara® and others) is a medication that inhibits the conversion of androgens (male hormones) to estrogens (female hormones). This class of medications is usually given to postmenopausal women to decrease the risk of recurrent breast cancer.

Anatomy/Physiology:
The pituitary gland and hypothalamus, glands located at the base of the brain, interact with each other and the body's hormone levels to release both Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH). These two hormones, in turn, stimulate the ovaries to produce follicles which contain eggs which are eventually released through the process of ovulation.

During the egg production process, the ovary produces androgens, which are converted to estrogens though the Aromatase enzyme. These estrogens, in turn, feed back to the pituitary gland and ultimately reduce amount of LH & FSH released. It is thought that the Aromatase Inhibitors temporarily decrease the concentration of estrogen wherein the pituitary gland produces more LH & FSH. With greater levels of LH & FSH released, more follicles and eggs are often produced.

In some men whose pituitary release of LH & FSH is reduced, called hypogonadotropic hypogonadism, treatment has results in an increase in LH & FSH release thereby increasing testosterone levels and improving semen parameters.

Indications:
The following issues may best benefit from the Aromatase Inhibitor treatment:
- Ovulatory dysfunction (Polycystic Ovarian Syndrome: PCOS)
- Clomiphene Citrate resistant patients (failed to ovulate on clomiphene citrate)
- Women who develop a thin lining with Clomiphene Citrate or other adverse effects
- Women with a decreased ovarian reserve
- Endometriosis not responsive to medical or surgical management (usually taken daily)
- Unexplained infertility in combination with Intra-Uterine Insemination (IUI)
- Hypogonadotropic hypogonadal men with low testosterone levels combined with abnormal sperm production.

This drug should not to be given alone as a non-specific fertility enhancer to subfertile women.

Contraindications:
Unless otherwise directed, women with any of the following should not use an Aromatase Inhibitor:
- Known sensitivity (allergy) to the Aromatase Inhibitor
- Ongoing pregnancy (class D medication; not to be used with pregnancy)

- Ovarian Failure
- Preexisting ovarian cysts deemed significant by your physician

Administration:

For ovulation induction, the Aromatase Inhibitor is taken by mouth following the onset of your menstrual cycle. The initial dose is usually two 2.5 milligram tablets (5 mg. total) per day, days three through seven of your menstrual cycle. Day one should be considered your first day of flow. Some preliminary protocols also suggest the medication may be given at a higher dose but for a briefer period of time. Since this medication is contraindicated during an ongoing pregnancy, a pregnancy test (blood or urine) may be requested before administration.

For men, the medication may be prescribed once per week or as often as once per day.

Complications:

Please note that Letrozole is usually given to women with a history of breast cancer. The women who take the drug to prevent the recurrence of breast cancer take it for an extended period of time wherein adverse drug effects become more likely. In the subfertile patient, the Aromatase Inhibitor will only be taken for a limited period. Preliminary studies in this population of women have shown almost no side effects for the brief course of treatment.

The following are some of the adverse drug effects seen with long-term treatment in the woman with breast cancer:

❖ Bone pain (20%)	❖ Coughing (11%)	❖ Headache (8%)
❖ Hot Flashes (18%)	❖ Lethargy (11%)	❖ Diarrhea (7%)
❖ Back Pain (17%)	❖ Constipation (9%)	❖ Emesis (7%)
❖ Nausea (15%)	❖ Chest Pain (8%)	❖ Decreased weight (6%)
❖ Joint Aches (14%)	❖ Extremity Pain (8%)	❖ Insomnia (6%)
❖ Breathing problems (14%)		

Multiple gestations may occur in 8-10% of all pregnancies, although this is uncertain. Of the cases of **multiple pregnancy**, 90% or greater will be twins and less than 10% will be triplets or more. A multiple gestation places the mother at a greater risk of developing hypertension, premature labor, toxemia, in addition to undergoing a surgical delivery and other pregnancy complications. For the babies, there is an increased risk of premature delivery. Premature babies are at higher risk for numerous serious illnesses, which can result in permanent disability and, in some cases, death during the neonatal period.

While the Aromatase Inhibitor is still being tested, there is no increased incidence of genetically abnormal infants or congenital abnormalities in infants conceived with this medication as long as the medication is taken before actual conception. It seems to clear long before implantation when taken correctly. If taken during pregnancy, the Aromatase Inhibitor may increase spontaneous losses. Malformations in animals have also included kidney, extremity and bone problems when the medication is taken during pregnancy although other studies in humans have found no increase in malformations.

For those older women taking the drug in a continuous fashion for an extended period, there may be a slight increase (2.5% above background) in the risk of spine fractures. Additional medications may be provided to minimize these risks. Bone density studies are often recommended each year.

No drug-drug interactions have been described with this medication so it may be taken with other medications you are currently taking. This medication should also be taken with food.

General Results:

Success rates with the Aromatase Inhibitors are still being collected. Preliminary evidence indicates that at least one-half of those women who don't ovulate on clomiphene citrate will ovulate on the Aromatase Inhibitor. It is likely that the overall pregnancy rates will be similar or perhaps slightly better than with Clomiphene Citrate. For ovulation induction, he Aromatase Inhibitor treatment is usually administered for no more than four to six months.

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