**PATIENT INSTRUCTIONS FOR LETROZOLE OVULATION INDUCTION**

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**What is Letrozole (LTZ)?** It’s an aromatase inhibitor, causing decreased estrogen production in many types of human tissue (ovaries, brain, fat, muscle, liver, breast), which in turn causes the pituitary gland in the brain to work harder at stimulating ovarian follicle development and ovulation. **Conceiving on Letrozole increases the chance of twins---3-4 % of pregnancies conceived on LTZ are twins.** Letrozole is an alternative to clomiphene citrate for ovulation induction. It might be a little better than clomiphene in some ways: fewer side effects in general, less adverse effects on the uterine lining, lower chance of twins, and it may be more effective than clomiphene in obese women.

**Letrozole is not “FDA Approved” for ovulation induction**. You need to know that, unlike clomiphene citrate, letrozole is not approved by the U.S. Food and Drug Administration (FDA) for ovulation induction. Presently the only FDA-approved indication for letrozole is to help treat certain breast cancers. Studies have shown that accidental consumption of letrozole while pregnant increases the risk of serious birth defects (4.7% risk, compared to 1.8% risk in the general population.) Thus, it is absolutely essential that you be certain you’re not pregnant before starting letrozole. **Please make sure you have a negative home urine pregnancy test before starting letrozole.** Since letrozole is rapidly cleared from the body after administration, using it for ovulation induction should not result in any fetal exposure to the drug.

**How to use LTZ effectively.** Effective use of LTZ requires *paying attention to the timing of your menstrual cycle, making sure you take the pills at the right time in your cycle, having plenty of sex around the time of ovulation, testing to prove that ovulation occurred, and being prepared to do home urine pregnancy testing*.

* **Pay attention to the timing of your menstrual cycle** I need you to have a period before starting LTZ, either naturally or induced by a week of progesterone pills. By definition, **“Cycle Day #1” is the first day of your period**. In general, sex is more fun if it’s not “scheduled.” However, if you are going to the trouble and expense of taking ovulation-inducing drugs, it’s very important to always know where you are in your cycle. You don’t want to waste cycles, time, and money by doing it wrong.
* **Make sure you take the pills at the right time in your cycle** Take one LTZ pill daily for 5 days, Cycle Days 3-7. The starting dose is 2.5 mg daily. If you don’t ovulate, we’ll increase the dose next cycle.
* **Have plenty of sex around the time of ovulation** If LTZ results in ovulation, it’ll probably be sometime between Cycle Days 11 and 17. Have sex daily from Cycle Days 11 to 19 (yay!) You don’t get pregnant by having sex at the moment of ovulation---sex within several days of ovulation could result in pregnancy.
* **Test to prove that ovulation occurred** To make sure the medicine worked, I need two types of tests (one you do yourself at home, the other at your lab).
	1. **Urinary LH testing once a day starting Cycle Day #10**, for up to 10 days. When your urine is positive for the LH surge, stop testing and have lots of sex in the next 2 days. You’ll probably ovulate within 14-48 hours of the positive urine test. If you don’t have an LH surge after 10 days of testing, stop testing---you’ll need a higher dose of LTZ next cycle. I ‘d get a good-sized box of the cheapest urine LH tests you can find. I just looked in some stores and found lots of brand-names, with prices ranging from $1.00 to $2.43 per test.
	2. **Progesterone level (a blood test in your lab) 6-8 days after the positive urine LH test**, to definitively prove that ovulation occurred. If you ovulated, you should have a nice high progesterone level. We’ll call you with your results.
* **Be prepared to do home urine pregnancy testing** Get lots of these. I want you to do them every cycle before starting LTZ, anytime you’re suspicious of pregnancy for any reason, and any ovulatory cycle when you don’t start bleeding by Cycle Day #35. I’d get the least expensive ones you can find in a store or online---they’re all very accurate if you follow the instructions. Some of them you pee on, and some of them you pee into a cup and dip the test strip into the urine. They all use the same technology. I just checked in some stores and online, and found prices ranging from 50 cents to $4 per test.

**Once there is evidence of ovulation (LH surge followed by a high progesterone level) I’ll keep you on that same dose in subsequent cycles** (if you didn’t get pregnant), and I don’t need you to keep doing urine LH testing and progesterone levels every cycle! (If you’d like you can continue urine LH testing to help with timing of sex).

**If you don’t detect an LH surge after ten days of testing, stop testing---you probably didn’t ovulate, you probably didn’t conceive, and you will need a higher dose of LTZ next cycle**. Don’t get frustrated! If your bleeding doesn’t start spontaneously by Cycle Day 40, make sure a home urine pregnancy test is negative, and take another week of progesterone pills to initiate a period before starting the higher dose. I will **increase your LTZ dose to 5 mg/day the next cycle, and I’ll need you to continue urine LH testing.** I’ll prescribe up to 7.5 mg/day. If you don’t ovulate on 7.5 mg/day, I’d try something different (referral to an Infertility Specialist, or possibly trying another medicine like clomiphene citrate or metformin).

 **I do not encourage Basal Body Temperature (BBT) charting, or routine ultrasounds to check ovarian follicle development**. Charting BBT is tedious, stressful, and does not help plan timing of intercourse. BBT charting also gives a high rate of confusing or misleading results. I do not routinely do ultrasounds to check for follicle development during LTZ treatment. Ultrasound exams are tedious, stressful, costly, and has not been shown to improve pregnancy rates.

**What are some possible side-effects, of risks of LTZ?**

* Short-term use of LTZ for ovulation induction usually results in either no side-effects or relatively mild side-effects, including hot flashes, headache, breast tenderness, fatigue, or dizziness.

**SUMMARY OF DR. FARRINGER’S LETROZOLE INSTRUCTIONS:**

1. **Have a period, either naturally or progesterone-induced. The first day of bleeding is called “Cycle Day #1.”**
2. **Take LTZ daily for 5 days, Cycle Days 3-7 (starting dose 2.5 mg/day).**
3. **Have sex daily, Cycle Days 11-19.**
4. **Do urine LH testing daily, starting Cycle Day 10. When you have your LH surge, stop testing (and have sex a lot). If you don’t detect an LH surge after 10 days of testing, stop testing and notify us. You’ll need a higher dose next cycle.**
5. **Go to your lab 6-8 days after your urine LH surge for a blood progesterone level, to definitively prove that you ovulated. We’ll call you with the results.**
6. **One of three things will happen each cycle:**
* **YOU COULD OVULATE AND CONCEIVE: If you ovulate and don’t start bleeding by Cycle Day 35, do a urine pregnancy test. You’re probably pregnant. If your pregnancy test is positive, congratulations! Call for an ultrasound appointment.**
* **YOU COULD OVULATE, BUT NOT CONCEIVE: If you do ovulate but don’t conceive, you’ll probably start bleeding around Cycle Day 28-32. Don’t get frustrated---healthy human couples sometimes take a while. Make sure you have a negative urine pregnancy test, repeat the same LTZ dose Cycle Days 3-7 next cycle and have plenty of sex. Urine LH testing is now optional, but I don’t need another progesterone level since we’ve already found a dose that makes you ovulate.**
* **YOU MAY NOT OVULATE: If you don’t ovulate, don’t get frustrated! We’ll increase the LTZ dose to 5 mg/day, and eventually 7.5 mg/day if necessary. If you don’t start bleeding by Cycle Day 40, make sure your urine pregnancy test is negative then take progesterone pills to induce a period, and resume the LTZ at the higher dose. I do need urine LH testing again, with a blood progesterone level 6-8 days after your LH surge, since we haven’t yet found the dose that makes you ovulate.**