

## Letrozole Patient Information sheet

Letrozole is an oral drug which can be an effective fertility treatment for women with ovulation problems, particularly for women with PCOS and potentially those with unexplained infertility.

This medication is in a class of drug called aromatase inhibitors. Letrozole has mainly been used to treat hormone receptor positive breast cancer.

### How does Letrozole induce Ovulation?

When the enzyme aromatase is inhibited by the letrozole medication, estrogen levels are suppressed in young women. This results in the brain and pituitary gland increasing the output of FSH (follicle stimulating hormone). In women that have polycystic ovary syndrome or anovulation, the increase in FSH hormone can result in development of a mature follicle in the ovary and in turn ovulation.

Letrozole has sometimes been used as an alternative to clomiphene when

- Women do not respond to Clomid at all.
- Unpleasant side effects with Clomid
- Poor cervical mucous and endometrial lining with Clomid

A recent international collaboration published in Clinical Endocrinology in 2018 (backed by NHMRC) recommended that Letrozole <sup>1</sup>

“Letrozole should be considered first line pharmacological treatment for ovulation induction in women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation, pregnancy and live birth rate”

### Pharmacy

Letrozole is marketed under the name Femara. One tablet is of 2.5 mg each. Letrozole is stored at room temperature. The most common dose is 2.5mg. Sometimes it is given in higher doses of 5 mg or 7.5 mg per day depending upon the response

### How and when to take Letrozole?

**First**, remember day 1 of the cycle is the first day of full menstrual flow. Letrozole is taken for 5 days early in the menstrual cycle - from day 3 to 7 of the cycle. Orally at approximately the same time every day.

### Are there any risks?

Letrozole has not been the drug of choice in the past because of concerns from a 2005 report from some Canadian fertility doctors suggesting a possible higher incidence of birth defects in pregnancies from using letrozole. This study was from a small group of pregnancies and the study has been severely criticized for having an improper design

Letrozole, has a relatively short half-life (~ 45 hours). It is cleared quickly from the body. It is therefore extremely unlikely that a drug that is given from days 3 – 7 of the cycle (at least a week before ovulation) can cause birth defects. It is believed that the drug has cleared from the system before the egg is fertilized. <sup>ii</sup>

At the 2013 meeting of the American Society for Reproductive Medicine (ASRM), the results of the PPCOS II study were presented. In this study, 750 PCOS women were randomized to receive either letrozole or Clomid for up to 5 treatment cycles. The findings convincingly showed that as compared with clomiphene, letrozole was associated with higher live-birth and ovulation rates among infertile women with the polycystic ovary syndrome. <sup>iii</sup>

## What are the side effects?

Letrozole works based on its ability reduce estrogen levels. The data on side effects comes from women who have been using letrozole for an extended period of time in order to treat breast cancer. The treatment duration for letrozole is only five days. Side effects are similar to those seen with clomiphene citrate:

- Hot flashes
- Headaches
- Breast tenderness
- Fatigue
- Dizziness
- Bloating
- Night Sweats
- Blurred vision
- Upset stomach
- Difficulty sleeping
- Spotting or unusual menstrual bleeding

## Getting the timing right

If your cycles are 28 days, you will ovulate on day 14, but if your cycles are shorter, 25 days, by subtracting 14 days, you will ovulate on day 11. It is recommended that you have intercourse three or four days prior to, on your ovulation day and just after in order to maximize your likelihood of becoming pregnant There are many ovulation calendars available online which automatically calculate your most fertile

days based on your provided dates. try [www.babycenter.com.au/tools/ovu/](http://www.babycenter.com.au/tools/ovu/) or [www.mydr.com.au/ tools/ovulation](http://www.mydr.com.au/tools/ovulation) Calculation

## How often is enough?

Not having intercourse for five days' increases sperm count but may affect the motility (active movement of the sperm). Having intercourse, more than once a day is probably too much. To be on the safe side, when you are close to ovulating, have intercourse at least every other day, if not every day is probably best.

## Day 21 Progesterone testing

Please remember to get your blood test done on the 21<sup>st</sup> day of your cycle and phone in to check your results if we have not already contacted you as you may not conceive during the first cycle. Indeed, some patients require a few months of Letrozole treatment and sometimes dosage adjustments are required. We will advise the dose for your upcoming cycle based on the progesterone levels of your previous cycle.

## When should I test for pregnancy?

Most menstrual cycles are approximately 28 days long and ovulation occurs 14 days prior to the onset of menstrual flow. If you are pregnant the menstrual flow will not come unless you are on progesterone tablets for luteal phase support. Test for pregnancy using a home pregnancy test.

If your menstrual period does not come 35 days after your last period and the pregnancy test remains negative consider Primolut withdrawal as advised. Please also contact us if you do become pregnant!

Please remember you may not conceive during the first cycle. Indeed, some patients require a few months of Letrozole treatment and many times dosage adjustments are required.

## Increase your intake of folic acid

Increasing your intake of folic acid (known as folate in its natural form) before conceiving and for the first three months of pregnancy can reduce the risk of having a baby with neural tube defects, such as spina bifida. Folic acid is readily available in tablet form from pharmacies (at least 0.4–0.5 mg of folic acid each day)

## Warning!

\*\* Letrozole is a drug that is approved for the treatment of breast cancer after surgery. It is currently used (“off label”) for ovulation induction. This information sheet does not replace any urgent queries you may have. Please do not hesitate to contact us in case of an emergency

## References

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<sup>i</sup> Teede HJ, Misso ML, Costello MF, et al.; On behalf of the International PCOS Network. Recommendations from the international evidence- based guideline for the assessment and management of polycystic ovary syndrome. *Clin Endocrinol (Oxf)*. 2018;00:1–18.

<sup>ii</sup> <https://www.nih.gov/news-events/news-releases/new-treatment-increases-pregnancy-rate-women-infertility-disorder>

<sup>iii</sup> Legro RS<sup>1</sup> Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2014 Jul 10;371(2):119-29