

## Ovulation-induction

This leaflet explains ovulation induction. Ovulation induction means encouraging your ovaries to release eggs. It is a treatment for women who want to become pregnant, but who have absent or very irregular ovulation.

### **The menstrual cycle**

On average, a menstrual cycle will last 28 days. The menstrual cycle runs from the first day of menstruation until the first day of the following menstruation. During the ripening of an egg cell certain hormones cause the endometrium to grow so that a fertilised egg cell can nestle in it. If fertilisation does not take place the built-up endometrium is discarded: the menstruation.

Women seldom have a cycle of exactly 28 days; an additional 7 days or a shorter cycle of 21 days is still regarded as normal. The most important thing is that there is ovulation in each cycle. If ovulation occurs less than 9 times a year, ovulation induction is regarded as a useful treatment.

### **Who qualifies for ovulation induction?**

#### *Women who have PCOS*

PCOS stands for polycystic ovary syndrome. This means literally that there are several (poly) cysts in the ovary. With PCOS the hormone balance is disrupted; often there is too much of the LH hormone and/or testosterone. This causes ovulation to be either very irregular or absent.

*Women with a normal hormone balance, but who have absent or irregular cycles.* These women have normal levels of all the hormones affecting the menstrual cycle, yet there is no or very irregular ovulation.

#### *Women with low LH and FSH values*

Part of the brain, the hypothalamus, produces the LHRH hormone. This hormone ends up in another part of the brain: the pituitary gland. This gland produces LH and FSH hormones. If the hypothalamus or transport to the pituitary gland does not function properly, this could result in a disturbance of the menstrual cycle and ovulation not taking place at all.

*Obesity* can be a cause, but also an additional symptom in women with irregular, very long or even absent cycles. Obesity may increase the risk of complications in ovulation induction. Furthermore, treatment is often more difficult and obese women have an increased risk of complications during pregnancy and birth. You may therefore receive the advice to first lose weight before treatment will commence. Often, the cycle will normalise if sufficient weight loss has been achieved.

### **Treatment**

Treatment depends on the exact cause of absent ovulation. In most cases ovulation can be induced by tablets (Letrozole), are injections of gonadotropins or by a computer-controlled pump (LHRH pump). These last two types of ovulation induction are

not performed at Amstelland Hospital. If this is necessary, you will be referred to Amsterdam UMC, Location VUmc. Before you start this medication, you must have a menstruation.

- If you have a spontaneous menstruation; the first day of clear red blood loss is cycle day 1.
- If you do not have a spontaneous menstruation; You will carry out a urine pregnancy test yourself. If the test is negative you will start taking progesterone tablets (Duphaston®). You will take 1 tablet one time a day during 10 days. A few days after the last tablet, you will have vaginal blood loss. The first day of clear red blood loss is cycle day 1. If you still do not have any blood loss 7 days after the last tablet, you will carry out a new pregnancy test yourself and phone the Gynaecology Outpatients Clinic, 020 - 755 7019.

#### **What is the likelihood of pregnancy?**

Ovulation occurs in approximately two-thirds of women receiving Letrozole. After six months of treatment with Letrozole, approximately 30% of women successfully conceive.

#### **What are the risks and complications?**

Treatment with Letrozole entails a small risk, roughly 3-4%, of developing a multiple pregnancy. In studies conducted into the incidence of congenital defects following the use of Letrozole, there was no increased risk found for the use of the drug with an increased risk of a child being born with a congenital defect. Letrozole may cause side effects. The most common of which include hot flashes, dizziness, gastrointestinal complaints and headaches.

#### **What should you do prior to the ovulation induction?**

You will take 0.4/0.5 mg folic acid every day to reduce the risk of a spina bifida baby. You will begin no later than the first day of your menstruation. If you do not spontaneously menstruate, you need to take a pregnancy test and, if it is negative, you should take progesterone tablets (Duphaston). You will also try to maintain a healthy weight or lose a few pounds, if possible. This will increase the effectiveness of Letrozol.

#### **Letrozole**

Letrozole is an aromatase inhibitor that is used to treat breast cancer in women. It is commonly used worldwide in the treatment of women with PCOS (Polycystic Ovarian Syndrome); however, the drug is not registered for this in the Netherlands. Here, this is referred to as an 'off-label' usage of the medication. Letrozole ensures that testosterone (a male hormone) from the ovaries is not converted into oestradiol. In addition, Letrozole leads to more FSH (follicle stimulating hormone) being released from the pituitary gland, which stimulates the growth of the follicles (egg vesicles). The precise mechanism of action of ovulation is not yet known.

You must take Letrozole for five days. You will start taking the medication on the 3d day of your cycle and continue taking it up to and including the 7th day respectively. The first day of the menstruation is what we call day 1.

The effect of Letrozole on ovulation is checked during the first cycle by the level of the progesterone hormone in the blood around cycle day 22.

If you have an ovulation whilst taking Letrozole you will usually be provided with the medication for a period of a few months. The only thing you have to do is to take Letrozole from day 3 up to and including day 7 of each menstruation. If

your cycle with Letrozole remains between 4 and 5 weeks, it will usually be accompanied by an ovulation. If the cycle is longer than 5 weeks, it may be that you are pregnant or that the Letrozole no longer works for you.

In both cases you must contact the Gynaecology Outpatients Clinic on telephone number 020 - 755 7019.

If you are pregnant, an appointment for a first pregnancy scan at 7-8 weeks pregnancy (= 5-6 weeks after ovulation) will be made. This is a vaginal scan. Advice for day to day life is provided in the leaflet "Pregnant!" (RIVM).

If you are still not pregnant after 6 months, you must contact the outpatients clinic to discuss follow-up treatment.

If you did not have an ovulation on the start dosage of Letrozole after one cycle, your physician will give you a higher dose for the next cycle. During this cycle, you will again check the progesterone around cycle day 20-22. You may be referred to Amsterdam UMC, Location VUmc for a different treatment.

If you are not pregnant after six menstrual cycles following treatment with Letrozole, a hysterosalpingogram (HSG) will be carried out. This is a test to check the passage of the ovaries.

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**Notes on this leaflet**

If any information in this leaflet is unclear or incomplete, please notify us. You can share your remarks with us via [voorlichting@zha.nl](mailto:voorlichting@zha.nl).