NON-IVF TREATMENT

- Clomiphene
- IUI
- OI with FSH
Clomiphene Citrate (CC) and Letrozole treatment

Clomiphene was the original ‘fertility pill’ and is still widely used for women who don’t have regular menstrual cycles, and for women with a shorter duration of unexplained infertility. Letrozole is a new alternative to Clomiphene.

How clomiphene and letrozole work
As we’ve mentioned earlier in the section called ‘Hormones and medications’, the pituitary gland at the base of the brain produces a hormone called FSH which makes follicles grow in the ovary, and the follicles make a hormone called estradiol. When the pituitary gland senses increasing levels of estradiol, it reduces the amount of FSH it releases.

Clomiphene blocks the action of estradiol on the pituitary gland, so the pituitary gland pumps out more FSH than usual. Letrozole has a similar effect on FSH by reducing the amount of estradiol made in the ovary. It is the extra FSH that restores the menstrual cycle in women who aren’t ovulating or who have irregular cycles, and which can be beneficial for those with unexplained infertility. Producing one follicle is the aim for women having clomiphene or letrozole to restore a regular cycle, while 2-3 follicles is the aim when using clomiphene treatment for unexplained infertility.

Problems and solutions
There aren’t any tests to predict the right dose of clomiphene or letrozole for a particular woman, so common problems are:
• The initial dose isn’t high enough to be effective. This can be picked up by blood tests or an ultrasound scan. The solution is to increase the dose the next month.
• The initial dose causes too many follicles to grow, increasing the risk of multiple pregnancy such as twins or triplets. This can be picked up by blood tests or an ultrasound scan. The solution is to reduce the dose the next month.

Clomiphene partially blocks the action of estradiol in all types of tissue, including the cervix. This means it may reduce the quality of cervical mucus around the time of ovulation which may make it harder for sperm to swim through the mucus on their way to the egg. It is hard to measure this, although some women are good at detecting their mucus around ovulation. Letrozole does not affect cervical mucus.

Risks and side effects
• Multiple pregnancy Blood tests and ultrasound scans give a good idea about how many follicles are growing in the ovary in a particular month of treatment but they are not perfect. In addition, for many women the aim is to grow 2-3 follicles. As a consequence,
about 10% of pregnancies from clomiphene treatment are twins, and about 1% are triplets. Quadruplets or more are possible but very rare. The chance of twins is lower with letrozole – below 5%.

Twins are associated with 2-3 times more risk for both the mother and children for a wide range of adverse outcomes, from maternal death to cerebral palsy. See our Fertility Facts on the risk of twins. www.fertilityfacts.co.nz

• Ectopic pregnancy When an embryo implants in the Fallopian tube, the cervix or the abdomen it is called an ectopic pregnancy. Ectopic pregnancies can be dangerous because the placenta can burrow into a blood vessel and cause major internal bleeding. Clomiphene or letrozole don’t increase the risk of ectopic pregnancy, but all women having fertility treatment need to be aware of the possibility of ectopic pregnancy. We can usually detect an ectopic pregnancy by the level of hCG in the pregnancy test and an early ultrasound scan, but not always. Symptoms include severe, localised abdominal pain.

Other side effects
About 10% of women using clomiphene experience hot flushes because of the way clomiphene blocks the action of estradiol. Other side effects can include nausea and breast tenderness. Mood swings are common but seldom severe; but if so please talk to us. Headaches and blurred vision are rare side effects. Tell us if you experience any of these while on treatment. These side effects occur less often with letrozole.

Pain is your body’s way of saying that something may be wrong. We need to know about any symptoms that might be concerning you.

Clomiphene has been used for over 40 years without any evidence of an increased risk of birth defects. It is unclear whether clomiphene could increase the risk of ovarian cancer or breast cancer – as a precaution most experts recommend that clomiphene should not be used for more than twelve months. Letrozole was originally designed to help treat breast cancer and it is not yet registered to treat infertility in New Zealand. Because of this, we will ask you to sign a consent form.

Clomiphene and letrozole options
There are two approaches to clomiphene or letrozole treatment.

• Monitored cycles where follicle growth is monitored by ultrasound scans and often blood tests around the middle of your cycle. Your nurse will give you the results and advice about what to do next each day you have a test.

• Reviewed cycles where the doctor gives you a prescription and a form for blood tests, usually for days 12 and 21 of your cycle. The results of these tests are not used to monitor your cycle at the time, but they help your doctor plan the next cycle if you don’t become pregnant.

Reviewed cycles are simpler and cheaper but they provide less protection against multiple pregnancy. Many doctors prefer to start with a monitored cycle even if the overall choice is to have reviewed cycles.

With both options, your doctor will review your results before you start your next cycle. You will usually have a follow up appointment with your doctor every 3-4 cycles if you do not become pregnant.

Success with clomiphene and letrozole
Over 80% of women who otherwise have irregular cycles will ovulate using clomiphene or letrozole.

Like any fertility treatment, the chance of becoming pregnant per month depends on the woman’s age, falling off after 35 years. About 20–40% of women aged 37 and younger will have a child over a course of 3-4 cycles of clomiphene or letrozole.
Step by step through clomiphene or letrozole

The 'day 1' call

Your day 1 call to the clinic is how you start your clomiphene or letrozole cycle. Day 1 is the first day of your cycle that you wake up with your period. If your period starts in the afternoon then the next day is day 1. If you do not have periods, your doctor will arrange for you to take Provera or Norethisterone tablets to induce a period.

Please call the clinic before 10:30am on your day 1 – if the person you call is busy just leave a voice message. We will act on your message the same day Monday to Saturday for all clinics, and also on Sunday for our Auckland, Hamilton and Wellington clinics. This also applies to public holidays apart from Christmas and New Year statutory holidays.

The nurse who takes your call will give you instructions on when to start clomiphene or letrozole, and when your first blood test and scan will be if you are having a monitored cycle. If you haven’t already got a prescription for clomiphene or letrozole, she will arrange that too.

Paying for private treatment

The clinic will tell you the cost of treatment before you start. We will invoice you for each cycle soon after your day 1 call. Feel free to call our accounts staff if you have any questions.

Blood tests and scans

There are a variety of places you can have blood tests taken – they include most cities and several places in the larger cities such as Auckland and Wellington. The blood tests for monitored clomiphene differ from other blood tests you may have had because we have special arrangements to ensure we get the results in time for making decisions each day.

You will need to have these blood tests done by 9 am while on treatment.

Ultrasound scans are usually done between 8 am and 9 am at the Auckland, Hamilton, Wellington and Christchurch clinics, but times later in the morning can be arranged. Each clinic has its own way of recording when you arrive so that the doctor doing the scanning knows who is waiting – the nursing or reception staff will let you know how it works.

Decisions

Every day you that have a blood test or scan in a monitored cycle we will get back to you with an instruction about what to do next. Our doctors, nurses and embryologists look at the results around lunchtime to make a decision. We usually TXT instructions or call when there is something more significant.

We will have nearly always made the decision by 2 pm so you can expect a TXT or a call between 2pm and 5pm on weekdays unless you have arranged something different with your nurse. The nurses do not go home until they have cleared the day’s telephone calls about treatment decisions. If we TXT, please TXT back to confirm that you have read our message.

• We strongly suggest you write down each instruction as soon as we TXT or call you. Fertility treatment can be complex enough without having to carry stuff in your head.
• There are some blank pages at the back of this magazine that can be used as a treatment diary.
• We have found that when people call the clinic instead of us calling them, many calls get diverted to voice mail because staff are already speaking to other patients. We then need to listen to voice messages instead of answering new calls.
• Please phone the clinic if you have not heard from us by 4:30 pm.

No response to clomiphene or letrozole
A relatively low dose is usually chosen in the first cycle of treatment to reduce the chance of too many follicles maturing. For some women this dose will be too low to stimulate any follicles to develop, and they will need to use a higher dose in the next cycle of treatment. Occasionally it may take two or even three cycles to decide on the right dose for an individual woman.

There will also be women who do not respond to clomiphene or letrozole at all and who will need other types of hormone treatment to induce ovulation.

Stopping treatment because there are too many follicles
Although the dose of clomiphene or letrozole is designed to stimulate only 1–2 follicles to mature, sometimes more develop. A particular woman can also respond differently to the same dose in different treatment cycles.

If you develop too many follicles the chance of triplets or quadruplets may be too high, so we will advise you to use a condom as barrier contraception, or not to have sex. A lower dose will be tried in the next treatment cycle.

Having sex
It is important to have intercourse close to ovulation. If you are having monitored clomiphene or letrozole, the blood tests and scans will give us some idea about when you will ovulate, but this is not exact. The size of the follicle at ovulation can differ between women, and between different cycles in the same woman. We recommend you have sex once your largest follicle is expected to be 18 mm in diameter, and then every day or couple of days for the next 3 to 4 days. Having regular sex over the days when ovulation may occur is more important than trying to predict the actual day of ovulation. There is no advantage to ‘saving up’ – sperm quality can fall with increasing duration of abstinence.

If you are using the reviewed cycle option, then you should have sex every couple of days from about day 11 of the cycle onwards.

The quality of cervical mucus is greatest on the day before, or the few days before, ovulation, and then falls once the LH surge starts. The sperm of most men can survive for two or more days in good quality cervical mucus, so it is important to have sex leading up to ovulation rather than afterwards.

We discourage the use of LH urine tests to try to detect ovulation. Clomiphene and letrozole raise the level of LH as well as FSH and may cause the urine test to show a ‘false-positive’ result. Also, the quality of the cervical mucus may have decreased by the time the LH level is high enough to give a positive result in the test.

Triggering ovulation
Women having clomiphene or letrozole usually have a natural surge of the hormone LH that triggers ovulation. In some women this does not happen reliably. Ovulation can be triggered with an injection of hormone hCG. We will tell you whether you need an hCG trigger, and how and when to give it.

Waiting for the pregnancy test
Most people say that waiting to see whether you are pregnant is the most stressful part of treatment. Please feel free to make an appointment to speak with a counsellor if you would like some extra support during this time.