

Ovulation Induction using Clomiphene Citrate

This information sheet outlines the steps involved in a cycle of ovulation induction using clomiphene citrate.

What is clomiphene citrate?

Clomiphene citrate is one of the most widely used drugs in fertility treatment. It is taken in tablet form and used to induce ovulation in women who do not ovulate regularly or not at all (such as those with polycystic ovarian syndrome).

How does it work?

Clomiphene citrate acts on the hypothalamus in the brain; its action causes an increase in the amount of Follicle Stimulating Hormone (FSH) and Luteinising Hormone (LH) that is released by the pituitary gland. These two hormones are the reproductive hormones which are involved in the control of the menstrual cycle; they stimulate the ovaries causing one or more follicles to develop and promote an egg to be released mid-cycle.

Are there any side effects with clomiphene?

The most commonly reported side effects with clomiphene citrate are:

>10%	Ovarian enlargement causing abdominal discomfort or bloating (14%) Hot flushes (10%)
1-10%	Breast tenderness (2%) Nausea and vomiting (2%) Headache (1%) Visual disturbances (2%)
<1%	Insomnia Nervousness

If you do experience some side effects they are usually mild and symptoms rapidly improve soon after stopping therapy. It is important to inform the fertility clinic if you have any symptoms you are concerned about.

The centre for Adverse Reactions Monitoring (CARM) recently received a report of ischaemic stroke in a patient taking clomifene. The patient was not reported to be taking any other medicines at the time of the stroke. Patients should be advised to stop taking clomifene and seek emergency treatment if they experience numbness, weakness or paralysis on one side of the body, slurred speech, sudden blurred vision, confusion or unsteadiness – these could be signs of stroke¹.

Is there a risk of multiple pregnancies with clomiphene?

Multiple pregnancies can occur using any fertility drug. With clomiphene, the risk of twins is approximately 7-9% and of triplets ~0.3%. This compares with an incidence of spontaneous multiple births of 1 in every 80 births. Multiple pregnancies may be harmful for both the mother and the foetuses therefore to minimise this risk, it is especially important that you have the blood tests when advised during your clomiphene cycle.

There is no evidence that clomiphene increases the risk of spontaneous miscarriage or causes any congenital abnormalities in offspring. Similarly, short term use of clomiphene is not believed to be associated with any increased risk of cancer or other health problems in women taking this drug.

Starting your clomiphene cycle:

Please note your first cycle will require enhanced monitoring (see below).

If you do not get periods very frequently you may be asked to do some initial blood tests and/or take a course of Provera to bring on a withdrawal bleed. Blood test forms will be mailed to you or given to you at your consultation.

1. Phone the nurses on day 1 of your period i.e. the first day of a full bleed. The dose of clomiphene you are to take will be confirmed and you will be given dates of the blood tests you are required to do.
2. Commence clomiphene tablets at the prescribed dose on day 2 of your cycle and take them once daily for 5 days.
3. On day 12 of your cycle, you need to have a blood test to check your estradiol level. **Please have this blood test before 9:00am.** This blood test assesses your response to clomiphene and is one way of monitoring if you are on the correct dose. **Please phone the nurses in the afternoon for your result.**

Note: If your estradiol level is very elevated, you may need an ultrasound scan to check the number of follicles that are developing on your ovaries. If a large number of follicles are developing, there is a greater risk of multiple pregnancies. In this situation you may be asked to abstain from sexual intercourse or use condoms to avoid the risk of a multiple pregnancy. A nurse will inform you if a scan is required.

4. Mid-cycle (day 14) is usually the day of ovulation and best time to have intercourse. This may vary by a few days from cycle to cycle therefore it is advised to have regular intercourse around this time.
5. On day 21 of your cycle, you will need to do a blood test to check your progesterone level. This is to confirm that ovulation has occurred. You may phone the nurse the next day for your result.
6. If your period is late please call the clinic so we can arrange a pregnancy blood test for you. If you do get a period, please call the clinic if you wish to start another clomiphene cycle.
7. Once your cycle is completed the results are reviewed by the doctor.

Clomiphene cycle with enhanced monitoring:

With enhanced monitoring, clomiphene tablet is still taken on days 2-6 of your cycle but more frequent blood tests and scans are performed to get a better understanding of when or if ovulation is occurring. The clinic will inform you if they feel you need this level of monitoring (based on your history or previous response to clomiphene).

The situations which require a cycle with enhanced monitoring are:

1. Your first cycle of clomiphene in our clinic
2. Women who have very irregular cycles or varied responses
3. Women who have a high estrogen level in any clomiphene cycle

Additional notes:

- Usually for your first cycle the clomiphene dose will be 50mg/day. Women differ however in their response and so the dose may be increased (or occasionally decreased) in 25-50mg increments on subsequent cycles depending upon the results of the monitoring. The doctor will review your results at the end of your cycle.

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- All blood tests are carried out at Lab Tests. We prefer you to do blood tests first thing in the morning using the blood form you will be given, as this allows us to receive the result that afternoon.
- 80% of women ovulate in response to clomiphene and 40% will conceive. 15-20% of women are “resistant” to clomiphene i.e. they fail to ovulate in response to increasing doses of clomiphene. For these reasons, it is important that you have regular reviews every 3-4 months with your doctor to determine if you should continue with clomiphene therapy or if any additional investigations are required.

Costs:

- Ovulation induction with clomiphene is not a publicly funded treatment. Charges cover the cost of blood tests, scans and interpretation of results, as follows:
 - \$125 for a clomiphene cycle
 - \$200 for a clomiphene cycle with enhanced monitoring
- Clomiphene is a prescription cost only.
- You will be invoiced for your treatment when you phone in on your Day 1.

Note: The nursing phones lines are often busy; please leave a detailed message and someone will get back to you as soon as possible (this may not be until the end of the day). If you leave a message after 4pm your call will not be returned until the following morning. If you have had a blood test and are awaiting further instructions you will receive a call the same afternoon.

Please do not hesitate to contact the nurses if you have any questions or concerns, on 09 630 9810 extension 3.

Reference:

1. Medsafe. New Zealand Medicines and Medical Devices Safety Authority. Ministry of Health. 2 Sept 2015