

## **Clomiphene Citrate Therapy (Clomid)**

Clomiphene citrate (CC) is an oral fertility drug that is used in the treatment of patients who do not ovulate or who ovulate infrequently. Serophene and Clomid are the two brands of clomiphene citrate manufactured in the USA. There is no difference between these two fertility drugs, although sometimes one or the other can be less expensive. Clomiphene citrate is used in other situations besides ovulatory disorders. In patients for whom there is no known cause for their infertility, clomiphene citrate — in conjunction with intrauterine inseminations (IUI) — has been found to improve the ability to conceive.

Clomiphene citrate plus intrauterine insemination is used when sperm concentration and/or motility is low, or when antisperm antibodies are a factor in infertility. Patients with endometriosis who have not conceived following medical or surgical treatment are candidates for clomiphene citrate. Finally, patients who have abnormal ovulation, that is a “luteal phase defect,” can also be successfully treated with clomiphene citrate therapy.

## **Clomiphene Citrate Protocol**

Clomiphene citrate is administered as a 50 mg tablet. The dosage ranges from one to four tablets per day on days 4 through 8 of the menstrual cycle, (alternatively, clomiphene citrate may be administered on days 4 through 7, or 5 through 9). Clomiphene citrate stimulates the body to produce increased amounts of the hormone FSH. FSH in turn stimulates the eggs to grow and mature. Typically, two to four eggs will mature when clomiphene citrate is administered. Ovulation will occur in one of two ways: one, a naturally occurring surge of the hormone LH (as detected by the change in color of an ovulation kit); and two, by administration of a fertility drug referred to as human chorionic gonadotropin (hCG). This medication goes by the trade names Ovidrel®, Profasi®, Novarel®, and Pregnyl®, and is administered when we determine that the eggs are mature and ready to ovulate. This is determined by monitoring blood levels of estradiol and the size of the egg sacs by ultrasound. It is well known that ovulation will occur approximately 36 to 40 hours after the injection, and therefore inseminations are timed accordingly. This hormone is produced by the placenta in pregnancy and is extracted from the urine of pregnant women. It is similar in chemical structure and function of LH, therefore, in the same manner, it can cause the dominant follicle(s) to release the egg from the ovary. After the last dose of ovulation induction medication, and when the follicles are mature, an injection of hCG is necessary to trigger ovulation. Ovulation is the release of the mature egg from within the follicle to the fallopian tubes, which is the normal site of fertilization. hCG will provide the final maturation process of the eggs. Thirty-six to forty hours after the hCG is administered, ovulation should occur. This is determined by monitoring blood levels of progesterone and an ultrasound to confirm ovulation. Trade names for hCG are Ovidrel®, Profasi®, Novarel®, and Pregnyl®.

A typical treatment cycle involves taking two tablets of clomiphene citrate on days 3 through 7 of the menstrual cycle. On day 12, a blood test to measure estradiol and ultrasound measurement of the egg sacs is performed. As stated above, the intrauterine insemination will then take place 36 to 40 hours after hCG is administered. After hCG, the patient will notice a rise in her basal body temperature chart and possibly abdominal bloating and discomfort. This is due to enlargement of the ovaries caused by both clomiphene citrate and hCG administration. One week after hCG, progesterone levels are obtained to check for ovulation and adequate progesterone levels to “support” a pregnancy. At this time, a decision is made to administer progesterone if the levels are too low. A pregnancy test will be scheduled approximately two weeks after hCG to determine the success of the cycle.

## **Clomiphene Citrate Side Effects**

Clomiphene citrate acts by actually “deceiving” the body into believing that the estrogen level has been decreased. The side effects caused by clomiphene citrate are mostly the result of these “anti-estrogen” effects. These include hot flashes, vaginal dryness, mood swings, headaches, and visual disturbances. All of these symptoms may be experienced, and they will stop once you have completed the course of fertility drugs. Should you develop any symptoms, please inform us and stop taking clomiphene citrate.

A common concern in using clomiphene citrate is the possibility of multiple pregnancies. In approximately 10 percent of pregnancies, there will be more than one fetus. Another concern is the possible development of large ovarian cysts after hCG is administered. These cysts will typically cause abdominal discomfort and bloating. In rare instances the ovaries will become very enlarged, requiring hospitalization for administration of intravenous fluids and observation. This is a rare event that occurs in less than 1 percent of patients undergoing clomiphene citrate therapy. Typically, these cysts will disappear within two to three weeks, and surgery is rarely if ever required for their removal. When cysts do develop, it is suggested that physical activity be restricted, including withholding coital activity. Finally, it should be noted that clomiphene citrate has not been found to cause an increase in birth defects as compared to patients who conceive naturally.

## **Summary of the Clomiphene Citrate Treatment Cycle**

### **Day 2-4 of menses**

Come in for an ultrasound and baseline blood work. Appointments are necessary; please call on cycle day 1 or 2 to schedule your appointment. Blood tests and ultrasounds are performed from 7:30-10:00 a.m. weekdays and 7:30-9:00 a.m. on Saturdays and holidays.

Clomiphene citrate is usually started on days 3 through 7 or 4 through 8.

### **Day 11 or 12**

Blood E2 level and ultrasounds are performed. These are done to check the E2 levels and size of the follicles containing the egg and are used to check to see if the eggs are ready for ovulation (release) from the follicle. If so, we will call you of impending ovulation. If you are having an IUI, this will normally be done the day after hCG, usually in the late morning and repeated the following day. If having intercourse and not IUIs, begin the evening of hCG and continue daily or every other day until at least the second day after hCG.

### **3 to 4 Days after hCG Administration**

An ultrasound and blood progesterone level is determined to confirm ovulation. Progesterone support, usually vaginal suppositories, may be prescribed.

### **Approximately 14 days after hCG or ovulation**

We will schedule a pregnancy test. If the test is positive, continue your progesterone. If it is not positive, stop your progesterone support and return with the start of your cycle to begin another clomid cycle.

If your period does not start within 5 days after stopping your progesterone support return for another pregnancy test and consult.

### **Clomiphene Citrate Success Rate**

The success rate with clomiphene citrate therapy depends on the individual patient's clinical problems. For patients who do not ovulate or ovulate infrequently, close to 60- 80 percent will be able to ovulate using clomiphene citrate. The pregnancy rate per fertility drug cycle is approximately 15 percent, and 60 percent of patients will become pregnant within six cycles. These success rates will differ, however, when there are additional factors affecting a couple's fertility. These factors may include endometriosis, cervical factor, luteal phase defect, male factor, and unexplained infertility.