

The Centre For Women's Reproductive Care

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WHEN YOUR DOCTOR PRESCRIBES CLOMID

You have been advised to take Clomid (Clomiphene citrate) also sold as Serophene. This is a mild fertility drug, similar in structure to the natural hormone oestrogen. It does not stimulate ovulation (egg release) directly but induces a series of events that promotes release of Follicle Stimulating Hormone (FSH) from the pituitary gland located at the base of the brain. FSH, together with its close relative, Luteinising Hormone (LH), stimulates the ovaries to prepare and then release one or more eggs from the ovary. The response can be monitored with blood tests and pelvic ultrasound scans.

When to Take Clomid

Clomid is usually started within day 3 – day 7 of a cycle and where day 1 is the first day after last period. It is therefore commonly referred to as a "kick start" for ovulation, which then occurs up to one or even two weeks after the last tablet, is taken. The usual dose is one tablet (50 mg) daily but individual requirements differ and it is usual to monitor at least one or two cycles carefully to ensure that the desired outcome is achieved. The cycle is monitored by an ultrasound scan at about day 12.

How Successful is Clomid?

Whether given to induce ovulation for women who are not producing a monthly egg or to enhance fertility in others requiring assisted conception the chance of pregnancy in any one month that Clomid is used is no more than 15-20%. Several cycles of treatment are therefore usually required. The exact reasons why some women who appear to ovulate but do not conceive with Clomid are unclear. For some there may be other factors which are impairing fertility, for example problems with sperm or the tubal transport of eggs and embryos. For others the eggs may not actually be released from the ovary despite many of the other signs of ovulation. It can also be shown that Clomid has some anti fertility effects, for example

by thickening mucus in the cervix and impairing sperm penetration. Recent studies suggest a pregnancy screen rate of 63% within a year.

Multiple Pregnancy

The usual rate of multiple pregnancy in this community is around 1:80 or 1.25% of all pregnancies. The chance of a multiple pregnancy with Clomid may be 5 or 6-fold higher than this. However, this means a twin rate of only 6-8%, while triplets and higher order multiples are rare.

Side Effects

It is not possible to guarantee that any drug is 100% free of side effects and 100% safe in both the short and long term. As for many things we undertake in life, it is a matter of weighing the possible benefits i.e. pregnancy and a baby, against the known and unknown risks. The following symptoms may occur while taking Clomid:

Hot flushes (about 10%), sore breasts, tiredness, feeling bloated or light headed, headaches, nausea, loss of appetite, muscle aches and pains, mood swings with anxiety and depression. Blurred or double vision (1-3%). Painful ovulation is not uncommon.

Clomid has been used for more than 40 years and there is a large body of information about its effects in both animals and man. There is no evidence that Clomid causes any long term hormonal effects in women, for example, those relating to weight, hair growth, acne, mood changes, mental illness or premature exhaustion of the ovaries.

Pregnancy Outcome after Clomid

About 15% (or one in six) pregnancies conceived naturally miscarry and the rate after ovulation induction may be slightly higher. Some of these occur in older women who have other medical

problems with a high risk of miscarriage. Pregnancy is also diagnosed earlier after assisted conception than natural conception and this alone may contribute to an apparently higher rate of miscarriage.

There is some evidence that, if Clomid is given after a conception has occurred, then it can cause miscarriage. It is for this reason it is recommended that Clomid should not be taken until pregnancy is first excluded by testing and/or a full and normal menstrual period has commenced.

Ectopic pregnancy is the implantation of a pregnancy outside the uterus and usually in the fallopian tubes. Whereas after spontaneous conception 1-2% of pregnancies are ectopic, this rate is slightly higher after ovulation induction.

There is no convincing evidence that the rate of birth deformities is higher than normal when Clomid has been used to assist the conception. One or two babies in every hundred born (1-2%) have a significant birth defect. You may discuss with the doctor the tests which are available to detect abnormalities of the baby during the early months of the pregnancy but keeping in mind that the only "treatment" that can be offered in most cases is termination of the pregnancy.

Ovarian Hyper stimulation and Cysts

A very rare but significant complication of Clomid relates to the stimulation of multiple follicles (cysts) in the ovaries which, in turn, causes the ovaries to enlarge to several times their normal size. This results in lower abdominal discomfort, a bloated feeling and sometimes distension of the abdomen or discomfort during intercourse. There is sometimes vomiting with a risk of dehydration.

Eggs within the ovary develop and are released from follicles that are fluid filled cysts. They reach a size of almost 1 inch (2 cm) in the few days before release of the egg(s) i.e. ovulation. For

some women this rapid growth of a follicle or follicles is painful. Sometimes these follicles continue to grow after ovulation and a larger cyst may form. Ovarian cysts caused by Clomid resolve spontaneously in most instances.

Fertility Drugs and Cancer

It has been argued that the use of Clomid may increase a woman's risk of ovarian cancer. This is based on two observations. Firstly, women who take the contraceptive pill and thereby suppress ovulation over a long period of time have a lower incidence of ovarian cancer. Secondly, ovarian cancer has been shown to occur more frequently in women who have used ovulation-inducing drugs. However, it is worth noting that about one woman in 100 will develop an ovarian cancer in a lifetime and women with fertility problems have a higher risk of ovarian cancer than others. It is uncertain how much this contributes to the apparently increased risk of ovarian cancer in women who have used Clomid. It is recommended that the use of Clomid should proceed only with medical evaluation and surveillance, 6 monthly.

There have also been claims that the high oestrogen levels that are generated in women during ovarian stimulation may trigger breast cancer since it is known that some breast cancers are stimulated to grow by oestrogen. Women who breast-feed for long periods of time have a lower risk of breast cancer and it is known that breast-feeding suppresses the ovarian production of oestrogen. However, it is not certain that oestrogen actually causes a breast cancer and, because breast cancer is very common (about one woman in every 12 will develop this cancer in a lifetime), it is not surprising that some women who received Clomid have subsequently developed breast cancer. It is of interest and possible relevance that a drug that is closely related to Clomid and called Tamoxifene is used to treat and possibly prevent breast cancer.