

Clomiphene Citrate ^[1]

By: Zhu, Tian Keywords: Fertility ^[2] Reproductive assistance ^[3]

Clomiphene citrate, more commonly known by its brand names [Clomid](#) ^[4] and Serophene, is a medication prescribed to women to stimulate [ovulation](#) ^[5] in order to treat [infertility](#) ^[6]. It stimulates [ovulation](#) ^[5] in women who do not ovulate or ovulate irregularly. This drug was created by [Frank Palopoli](#) ^[7] in 1956 while he worked for Merrell Company. It first successfully induced [ovulation](#) ^[5] in women in 1961 and was approved by the [Food and Drug Administration](#) ^[8] (FDA) in 1967. This medication can be used to help women conceive naturally, to time [ovulation](#) ^[5] for intrauterine insemination, or to stimulate the maturation of eggs to be extracted and used in procedures such as [in vitro fertilization](#) ^[9] (IVF), gamete intrafallopian transfer (GIFT), and [zygote intrafallopian transfer](#) ^[11] (ZIFT).

Women with higher than normal levels of male [hormones](#) ^[12], known as [hyperandrogenism](#) ^[13], are good candidates for clomiphene therapy as are women with normal [estrogen](#) ^[14] levels but who do not ovulate, a condition called [anovulation](#) ^[15]. Certain conditions such as low [estrogen](#) ^[14] levels may limit the benefit of clomiphene therapy, especially when not used in conjunction with other assisted reproductive technologies (ART). Women with lower than normal [estrogen](#) ^[14] levels may still conceive by undergoing higher dosages of clomiphene therapy, but they will more likely benefit from [menotropin therapy](#) ^[16], another type of [hormone](#) ^[17] treatment. Also, women seeking clomiphene therapy must not have a history of liver disease (the liver metabolizes clomiphene resulting in further damage to the liver), no abnormal uterine bleeding, and no ovarian cysts (clomiphene may enlarge the cysts).

Physicians usually administer clomiphene between the third and fifth day of [menstruation](#) ^[18] (the first day being the day that [menstruation](#) ^[18] begins) and start with 50 mg per day for a five-day regimen (days five through nine of the menstrual cycle). Ovulation should occur five to ten days after the last dose of clomiphene is administered. If the 50 mg dose is not enough to stimulate [ovulation](#) ^[5], the physician will increase the dosage by 50 mg each trial until the minimum effective dosage that induces [ovulation](#) ^[5] is reached. Once that minimum effective dosage is determined, physicians typically recommend the patient undergo four to six treatment cycles at that level until the patient successfully becomes pregnant. The maximum dosage of clomiphene should not exceed 200-250 mg. These dosages have been found effective based on multiple clinical trials. Various methods that determine the exact timing of [ovulation](#) ^[5] are blood tests for [luteinizing hormone](#) ^[19] (LH) levels, urinary tests for LH levels, and ultrasounds to observe the condition of the pelvis. During [ovulation](#) ^[5], the physician instructs patients to have intercourse every other day for one week beginning on the fifth day following the last dose.

If the patient is unable to ovulate at the maximum daily dosage of 200-250 mg, the physician may combine clomiphene with other medications such as [human chorionic gonadotropin](#) ^[20] (hCG) or [dexamethasone](#) ^[21]. The addition of hCG to clomiphene therapy may benefit women who respond to clomiphene therapy with rising LH, [follicle stimulating hormone](#) ^[22] (FSH), and [estrogen](#) ^[14] levels but still fail to ovulate. Dexamethasone as an adjunct to clomiphene

therapy benefits women with dehydroepiandrosterone sulfate (DHEAS) levels above the normal threshold. DHEAS is a precursor molecule to male and female [sex hormones](#) [23] that can increase [androgens](#) [24] (male [hormones](#) [12]) in the body and result in [infertility](#) [6] problems.

Clomiphene citrate causes [ovulation](#) [5] by stimulating the [pituitary gland](#) [25] to secrete more FSH and LH while stimulating the ovaries to secrete [estrogen](#) [14]. After a five-day treatment with clomiphene, LH and FSH levels initially decline but [estradiol](#) [26] continues to increase resulting in a preovulatory peak and LH and FSH levels increasing once again.

Certain risk factors are associated with clomiphene therapy. One possible risk is [luteal phase defect](#) [27]. The luteal phase is the period beginning immediately after the end of [ovulation](#) [5] and continuing to the first day of [menstruation](#) [18]. During this period, a woman's body normally prepares the [endometrium](#) [28] (lining of the uterine wall) for a [fertilized egg](#) [29] to implant. However, if there is a defect during this phase the [endometrium](#) [28] is not prepared for [implantation](#) [30]. Another risk is that clomiphene will affect the cervical mucus, preventing [sperm](#) [31] from entering the [uterus](#) [32] and fertilizing the [egg](#) [33].

Most women who undergo fertility treatments first try [hormones](#) [12] such as clomiphene before undergoing more expensive procedures such as IVF, which can exceed \$10,000. However, clomiphene therapy does not treat male [infertility](#) [6] or female cervical mucus defects, in which case techniques such as IVF are recommended. Unlike most other assisted reproductive technologies, fertility medications such as [clomiphene citrate](#) [34] are considered an acceptable fertility treatment by the Catholic Church making them the preferred option for some patients.

Sources

1. Barbieri, Robert L., and Isaac Schiff. *Reproductive Endocrine Therapeutics*. New York: Alan R. Liss, 1988.
2. Mayo Clinic. "Hormone Therapy: Is it right for you?" Mayo Foundation for Medical Education and Research. <http://www.mayoclinic.com/health/hormonetherapy/WO00046> [35] (Accessed November 26, 2008).

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