

Clomiphene

Clomiphene is a drug used in the treatment of ovulatory dysfunction. Indications include polycystic ovarian syndrome (PCOS) and infertility. As a selective estrogen receptor modulator (SERM), clomiphene acts as an estrogen antagonist in the hypothalamus. This causes increased release of gonadotropin releasing hormone (GnRH) and gonadotropins (FSH, LH). Increased gonadotropin levels cause stimulation of ovulation. Side effects of clomiphene include multiple gestation, visual disturbances, and hot flashes.



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Indications

Infertility

[Infertile-female-plant](#)

Clomiphene is commonly used to treat the oligoovulation or anovulation that is seen in patients with polycystic ovarian syndrome (PCOS). PCOS is a common cause of infertility.

Polycystic Ovarian Syndrome (PCOS)

[Peacock with PCOS](#)

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder characterized by hyperandrogenism, oligoovulation/anovulation and/or the presence of polycystic ovaries. In PCOS there is a disruption in the Luteinizing Hormone (LH) / Follicle Stimulating Hormone (FSH) balance resulting in impaired follicle maturation and anovulation/oligoovulation. Clomiphene is indicated in women with PCOS seeking treatment for infertility.

Mechanism of Action

Selective Estrogen Receptor Modulator (SERM)

[Selective-easter egg-receptor-mode-dial telephone](#)

Clomiphene is a selective estrogen receptor modulator (SERM). Clomiphene binds to estrogen receptors (ERs) and exerts its major effects on the hypothalamus, pituitary gland, ovary, and uterus. It antagonizes ERs thereby inhibiting the negative feedback that estrogen normally induces. This results in increased GnRH, FSH, and LH levels.

Hypothalamus

[Hippo-Thor](#)

Normally, circulating endogenous estradiol has a negative feedback on the hypothalamus leading to a decreased secretion of gonadotropins. Clomiphene works by inhibiting estrogen receptors in the hypothalamus.

Estrogen Antagonist

[Ant-toga with Easter-egg](#)

Clomiphene acts as an estrogen antagonist in the hypothalamus. This causes increased release of GnRH, FSH, and LH.

Increased GnRH, LH and FSH Secretion

Up-arrow Gonad-gopher-harmonica, Luge, and Fish

Impairment of estrogen negative feedback signal results in increased pulsatile GnRH secretion from the hypothalamus and subsequent pituitary gonadotropin (FSH, LH) release. This causes the growth of the ovarian follicle, followed by follicular rupture and subsequent oocyte extrusion which allows the egg to be fertilized.

Induction of Ovulation

Egg released

The ovarian actions of clomiphene are secondary to the effects of elevated FSH and LH on ovarian follicular development: promoting the growth of the ovarian follicle, luteinization of the follicle and the rupture of the follicle wall and release of a fertilizable ovum.

Side Effects

Multiple Gestations

Multiple Children

Multiple gestations or multiple pregnancies are side effects of clomiphene. This drug also increases the probability of multifetal pregnancy.

Visual Disturbances

Wavy Eyes

Visual symptoms, such as blurring, double vision, and/or scotomata, develop in 1 to 2 % of women and are usually reversible. The mechanism of visual disturbances is not well understood, it has been thought to represent retinal toxicity but some studies show that clomiphene appears to affect the visual cortex rather than the retina. Physicians should actively ask for visual changes in a patient receiving clomiphene.

Hot Flashes

Burning Flash

Hot flashes are common, occurring in 10 -20% of women. They may result from the hyperestrogenic environment induced by clomiphene. Other symptoms related to the hyperestrogenic environment include abdominal distention and pain , nausea and vomiting, and breast discomfort.