

Clomid® 50mg

Clomiphene



Hoechst Marion Roussel

COMPOSITION

Clomiphene (INN) citrate or Chloro-2 [(diethylamino-2 ethoxy)-4 phenyl]-1-diphenyl-1, 2 ethylene citrate.

- per tablet : 0.050 g.

PROPERTIES

Ovulation inducer : competitive inhibiting action on oestrogen retro-control at the level of the hypothalamus causing an increase in FSH responsible for follicle maturation. Follicular maturation is accompanied by an increase in oestradiol secretion encouraging the formation of an LH peak which stimulates ovulation and the formation of a secreting corpus luteum. Out of 5413 patients with ovulatory problems, treatment with Clomid led to ovulation in more than 70 %.

METABOLISM

The product is well absorbed following oral administration, excretion is mainly fecal, the product and its metabolites are slowly eliminated due to entero-hepatic recycling.

INDICATIONS

1. Treatment of sterility caused by normoprolactinaemic anovulation or dysovulation of functional origin :

- sterility due to anovulation
- sterility due to dysovulation :
 - an inadequate corpus luteum
 - a short luteal phase.
 - polycystic ovary syndrome after allowing the ovary to rest for 2 cycles.

2. Clomid test to be used once for diagnostic or therapeutic purposes in certain amenorrhoeas of hypothalamo-pituitary origin and in persistent amenorrhoea following oral contraception after having checked that plasma prolactin levels are normal.

CONTRA-INDICATIONS

- Serious or recent liver complaints
- Gynaecological haemorrhage of unknown aetiology
- Neoplastic diseases of the genital organs
- Organic ovarian cysts
- Visual problems during treatment or following previous treatment.
- PREGNANCY : a teratogenic effect in animals is suspected in humans.

WARNINGS

Ensure that the woman is not pregnant before administering Clomid. In case of doubt, carry out a sensitive and reliable pregnancy test (see the patient before each treatment).

Ensure that sterility is not due to :

- primary ovarian insufficiency
 - hypothalamo-pituitary insufficiency of organic origin : tumours or Morsier's hypogonadotrophism.
- Clomid may cause ovarian hypertrophy. Particular attention should be paid to a patient complaining of pelvic pain during treatment. When ovarian hypertrophy or the presence of several follicles has been confirmed by echography, additional courses of Clomid should not be given until the ovary has returned to its initial volume; the dosage and the duration of treatment should then be reduced. These symptoms regress spontaneously within several days or weeks. Rest and medical surveillance are required. Surgery should not be used except in cases of haemorrhage, torsion or rupture. In polycystic ovary syndrome, it is advisable to use the lowest effective dose and to precede the first treatment by resting the ovary for 2 months. The couple should be warned of an increased probability of a multiple pregnancy and its possible complications.

PRECAUTIONS

For use only after an accurate diagnosis has been made. Clomid should be used only under specialised medical supervision and strict biological control : hormone assays of oestradiol and progesterone on the 4th day of the temperature surge in the monthly thermal curve. If the surge does not occur carry out a simple oestradiol assay 12 days after withdrawing Clomid.

Before starting treatment, it is essential that its use is justified and that the following conditions are adhered to :

- before the first treatment cycle and before starting a new one, check by an examination and tests that the patient is not pregnant

- look for and if necessary treat appropriately other possible causes of infertility.

In cases of failure with Clomid, it is recommended that one cycle should be left untreated before another course since spontaneous ovulation can often occur during this intermediate period.

When Clomid is administered over a prolonged period, it may interfere with the syntheses of cholesterol (elevation desmosterol) : BSP retention may also rise above 5 %.

No haematopoietic or renal abnormalities have been reported.

DRUG INTERACTIONS

An association with HCG, as has been proposed, can only be justified after several failures to induce ovulation with Clomid alone and when clinical ovarian hypertrophy and the presence of several follicles by echography are absent. This combination considerably increases the risk of ovarian hyperstimulation and multiple births. It should only be used exceptionally.

SIDE EFFECTS

Ovarian hypertrophy (see Warnings).

Moderate risk of multiple births.

Insufficiency of cervical fluid due to the antioestrogen effect of Clomid may require associated local oestrogen therapy.

Visual problems : a sensation of visual blurring, a persistence of luminous images, spots and phosphenes (scintillating scotomata) have been observed in about 2 % of cases (frequently increasing with the dose). These signs usually disappear several days or weeks after discontinuing treatment. Some rare cases of posterior subcapsular cataract have been reported.

Hot flushes.

Digestives problems.

There have also been reports of : nausea and vomiting, fatigue/ depression, vertigo, giddiness and feelings of light headedness, headache, hypermenorrhoea, intermenstrual bleeding, nervousness, insomnia, urticaria and allergic dermatitis, pollakiuria.

DOSAGE AND ADMINISTRATION

1. Treatment of sterility

The initial dose is 50 mg daily (one tablet) for 5 days starting on the 5th day of a natural or induced cycle or, if there is no cycle, at any day chosen by the physician.

If ovulation occurs at this dosage, there is no advantage in increasing the dose for subsequent

cycles. If ovulation does not take place, a second treatment cycle of 100 mg daily for 5 days (2 tablets in a single daily dose) should be prescribed leaving one month between the first and second treatment in case spontaneous ovulation occurs during the intermediate cycle.

An increase in the dose beyond 100 mg/day for 5 days is not recommended.

If this dosage does not lead to ovulation after three treatments, this therapeutic trial should be considered as ended.

If, at the 50 or 100 mg dose, ovulation takes place but is not followed by pregnancy, treatment may be continued for a total of six cycles respecting the rule of leaving one month free between each treatment.

It is extremely important that coitus coincides with the period presumed fertility.

2. Clomid test (and indications) : the dose is 100 mg daily for 5 consecutive days during a single cycle.

This test may be repeated once with an interval of one month. Depending on 3 criteria (thermal surge, plasma oestradiol E₂ and menstruation), it can be used to determine 3 types of response :

- profound hypothalamo-pituitary insufficiency (all 3 criteria negative).
- moderate insufficiency with the possibility of a type III response following repetition of the test : elevation of E₂ levels (if there is a considerable increase) and menstruation without the thermal surge.
- optimal response at pituitary and ovarian levels : all 3 criteria positive.

PHARMACEUTICAL PRECAUTIONS

The tablets should be stored away from light and moisture and excessive heat.

OVERDOSAGE

No cases of acute toxicity have been reported. In cases of overdose, nausea, vomiting, hot flushes, visual problems, ovarian hypertrophy with abdominal and pelvic pain may be observed.

PACKINGS

Box of 5 scored tablets, each tablet containing fifty milligrams of clomiphene citrate.

Licence holder:

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