CLOMIPHENE CITRATE

FERTILE-M
50mg Tablet

Formulation: Each tablet contains Clomiphene (as Citrate)......50mg

Indications: Anovulatory infertility, amenorrhea or oligomenorrhea w/anovulatory cycles, oligosperma.

Adverse Effects
The incidence and severity of adverse effects of clomifene citrate tend to be related to the dose used. The most commonly reported adverse effects are reversible ovarian enlargement and cyst formation, vasomotor flushes resembling menopausal symptoms, and abdominal or pelvic discomfort or pain, sometimes with nausea or vomiting. Ovarian hyperstimulation syndrome has occurred. Breast tenderness, abnormal uterine bleeding, weight gain, headache, and endometriosis have also been reported. Transient visual disturbances such as after-images and blurring of vision may occur, and there have been rare reports of cataracts and optic neuritis. Skin reactions such as allergic rashes and urticaria have occasionally been reported and reversible hair loss has been reported rarely. CNS disturbances have included convulsions, dizziness, lightheadedness, nervous tension, fatigue, vertigo, insomnia, and depression. Abnormalities in liver function tests and jaundice have sometimes been reported.

There is an increased risk of multiple births with clomifene therapy, but rarely more than twins. There is also an increased risk of ectopic pregnancy. Although there have been reports of congenital disorders such as neural tube defects or Down’s syndrome in infants born to women treated with clomifene the role of the drug in the causation of these defects has not been established and the incidence is reported to be similar to that for the general population.

Precautions
Clomifene is contra-indicated in patients with liver disease and the potential for toxicity should be considered in patients with a history of liver dysfunction. It should not be used in pregnancy, or in patients with undiagnosed abnormal uterine bleeding; some sources suggest it should also be avoided in patients with hormone-dependent tumours, and in those with pre-existing mental depression or thrombophlebitis because of the risk of exacerbation. The cause of infertility should be investigated. The patient should be warned of the possibility of multiple births.

Patients taking clomifene, particularly those with polycystic ovaries, should receive the lowest doses possible to minimise ovarian enlargement or cyst formation. The patient should be instructed to report any abdominal or pelvic pain as this may indicate the presence or enlargement of ovarian cysts. They should also be evaluated for the presence of ovarian cysts before each cycle of treatment. If abnormal enlargement occurs, clomifene should not be given until the ovaries have returned to pre-treatment size, and subsequent doses should be reduced. Clomifene should be used with caution in patients with uterine fibroids, due to the potential for enlargement of the fibroids.

Treatment should be stopped if visual disturbances develop and the patient warned that this might affect their ability to drive or operate machinery. Long-term cyclic therapy is not recommended, because of the uncertainty regarding increased risk of ovarian cancer: a maximum of 6 cycles of treatment has generally been advised but see also under Carcinogenicity.

Pharmacokinetics
Clomifene citrate is absorbed from the gastrointestinal tract. It is metabolised in the liver and slowly excreted via the bile. Unchanged drug and metabolites are excreted in the faeces. The biological half-life is reported to be 5 days although traces are found in the faeces for up to 6 weeks. Enterohepatic recirculation takes place. The E-isomer is reported to be less well absorbed and more rapidly eliminated than the Z-isomer.

Uses and Administration
Clomifene is a nonsteroidal compound that has both oestrogenic and anti-oestrogenic properties, the latter residing principally in the E-isomer. Its action in stimulating ovulation is believed to be related to its anti-oestrogenic properties. It stimulates the secretion of pituitary gonadotrophic hormones, probably by blocking the negative feedback effect of oestrogens at receptor sites in the hypothalamus and pituitary.

Clomifene is the most widely used drug in the treatment of anovulatory infertility. Therapy with clomifene will not be successful unless the woman, though anovulatory, is capable of ovulation and her partner is fertile. It is ineffective in primary pituitary or primary ovarian failure. The usual dose by mouth is 50 mg of clomifene citrate daily for 5 days, starting on or about the 5th day of the menstrual cycle or at any time if there is amenorrhoea. If ovulation does not occur, a course of 100 mg daily for 5 days may be given starting as early as 30 days after the previous one. Women should be examined for pregnancy and ovarian enlargement or cysts between treatment cycles. In general, 3 courses of therapy are adequate to assess whether ovulation is obtainable. If ovulation has not occurred, the diagnosis should be re-evaluated. Once ovulation is established, each treatment cycle of clomifene should be started on or about the 5th day of the menstrual cycle. If pregnancy has not occurred after a total of about 6 treatment cycles, some consider further clomifene therapy is not recommended (but see also under Carcinogenicity).

Clomifene has also been used with gonadotrophins and in in-vitro fertilisation programmes.

Clomifene has also been used in the treatment of male infertility due to oligospermia to stimulate gonadotrophin release and enhance spermatogenesis, but there is limited convincing evidence of benefit.

STORAGE: Store at temperatures not exceeding 30°C. Keep away from the reach of children.

AVAILABILITY: In aluminum foil pack of 10’s; box of 20’s

CAUTION: FOODS, DRUGS, DEVICES and COSMETICS ACT prohibit dispensing without prescription.

Manufactured by: Seagull Pharmaceuticals Pvt. Ltd.
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