29-08-2022
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210mm

Samclom® Tablet
(Clomiphene Citrate)

QUALITATIVE AND QUANTITATIVE COMPOSITION
Samclom® 50mg Tablet
Each tablet contains:
Clomiphene Citrate BP..... 50mg

PHARMACEUTICAL FORM
Tablet

CLINICAL PARTICULARS
THERAPEUTIC INDICATIONS:
Samclom® is indicated for the treatment of ovulatory failure in women desiring pregnancy. **Samclom®** is indicated only for patients in whom ovulatory dysfunction is demonstrated. Other causes of infertility must be excluded or adequately treated before giving **Samclom®**.

POSOLOGY AND METHOD OF ADMINISTRATION:
Posology: ***Adults:*** The recommended dose for the first course is 50mg (1 tablet) daily for 5 days.
Therapy may be started at any time in the patient who has had no recent uterine bleeding. If progestin-induced bleeding is planned, or if spontaneous uterine bleeding occurs before therapy, the regimen of 50mg daily for 5 days should be started on or about the fifth day of the cycle.
When ovulation occurs at this dosage, there is no advantage to increasing the dose in subsequent cycles of treatment. If ovulation appears not to have occurred after the first course of therapy, a second course of 100mg daily (two 50mg tablets given as a single daily dose) for 5 days should be given. This course may be started as early as 30 days after the previous one.
Increase of the dosage or duration of therapy beyond 100mg/day for 5 days should not be undertaken.
The majority of patients who are going to respond will respond to the first course of therapy, and 3 courses should constitute an adequate therapeutic trial. If ovulatory menses have not yet occurred, the diagnosis should be re-evaluated. Treatment beyond this is not recommended in the patient who does not exhibit evidence of ovulation.
Long-term cyclic therapy. Not recommended. Efficacy and safety of clomiphene for more than 6 treatment cycles have not been demonstrated.

Special Populations:
Special care with lower dosage or duration of treatment is particularly recommended if unusual sensitivity to pituitary gonadotrophin is suspected, such as in patients with polycystic ovary syndrome.

Method of Administration:
Oral.

CONTRAINDICATIONS:
- Pregnancy.
- Contraindicated in patients with liver disease or a history of liver dysfunction.
- Contraindicated in patients with hormone-dependent tumors or in patients with abnormal uterine bleeding of undetermined origin.
- Ovarian cyst: Should not be given in the presence of an ovarian cyst, except polycystic ovary, since further enlargement of the cyst may occur. Patients should be evaluated for the presence of ovarian cyst prior to each course of treatment.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
Warnings: ***General:*** Good levels of endogenous estrogen (as estimated from vaginal smears, endometrial biopsy, assay of urinary estrogen, or endometrial bleeding in response to progesterone) provide a favorable prognosis for ovulatory response induced by clomiphene. A low level of estrogen, although clinically less favorable, does not preclude successful outcome of therapy. Therapy is ineffective in patients with primary pituitary or primary ovarian failure.
Clomiphene therapy cannot be expected to substitute for specific treatment of other causes of ovulatory failure, such as thyroid or adrenal disorders. For hyperprolactinemia there is other preferred specific treatment.
Clomiphene is not first line treatment for low weight related amenorrhea, with infertility, and has no value if a high FSH blood level is observed following an early menopause.
Ovarian Hyperstimulation Syndrome: Ovarian Hyperstimulation Syndrome (OHSS) is known to be reported in patients receiving clomiphene therapy for ovulation induction. The following symptoms are known to be reported in association with this syndrome: pericardial effusion, anasarca, hydrothorax, acute abdomen, renal failure, pulmonary oedema, ovarian haemorrhage, deep venous thrombosis, torsion of the ovary and acute respiratory distress. If conception results, rapid progression to the severe form of the syndrome may occur.
To minimize the hazard of the abnormal ovarian enlargement associated, the lowest dose should be used. The patient should be instructed to inform the physician of any abdominal or pelvic pain, weight gain, discomfort or distension after taking clomiphene.
Maximal enlargement of the ovary may not occur until several days after discontinuation of the course. Some patients with polycystic ovary syndrome who are unusually sensitive to gonadotropin may have an exaggerated response to usual doses of clomiphene.
The patient who complains of abdominal or pelvic pain, discomfort, or distension after taking clomiphene should be examined because of the possible presence of an ovarian cyst or other cause.
Due to fragility of enlarged ovaries in severe cases, abdominal and pelvic examination should be performed very cautiously. If abnormal enlargement occurs, clomiphene should not be given until the ovaries have returned to pre-treatment size.
Ovarian enlargement and cyst formation associated with clomiphene therapy usually regress spontaneously within a few days or weeks after discontinuing treatment. Most of these patients should be managed conservatively. The dosage and/or duration of the next course of treatment should be reduced.
Visual Symptoms: Patients should be advised that blurring or other visual symptoms such as spots or flashes (scintillating scotomata) may occasionally occur during or shortly after therapy with clomiphene. These visual disturbances are usually reversible; however, cases of prolonged visual disturbance are known to be reported including after clomiphene discontinuation. The visual disturbances may be irreversible especially with increased dosage or duration of therapy.
Hypersensitivity reactions: Hypersensitivity reactions including anaphylaxis and angioedema are known to be reported. In case of allergic reactions, treatment must be discontinued and appropriate symptomatic treatment initiated.
Precautions: Pre-existing or family history of hyperlipidemia and use of higher than recommended dose and/or longer duration of treatment with clomiphene are associated with risk of hypertriglyceridemia. Periodic monitoring of plasma triglycerides may be indicated in these patients.
Multiple Pregnancy: There is an increased chance of multiple pregnancy when conception occurs.
Ectopic Pregnancy: There is an increased chance of ectopic pregnancy (including tubal and ovarian sites) in women who conceive following clomiphene therapy. Multiple pregnancies, including simultaneous intrauterine and extrauterine pregnancies, have been reported.
Uterine Fibroids: Caution should be exercised in patients with uterine fibroids.
Pregnancy Wastage and Birth Anomalies: Among the birth anomalies spontaneously reported in the published literature as individual cases, the proportion of neural tube defects has been high among pregnancies associated with ovulation induced by clomiphene, but this has not been supported by data from population-based studies. The patient should be informed of the greater pregnancy risks associated with certain characteristics or conditions of any pregnant woman: e.g. age of female and male partner, history of spontaneous abortions, Rh genotype, abnormal menstrual history, infertility history (regardless of cause), organic heart disease, diabetes, exposure to infectious agents such as rubella, familial history of birth anomaly, and other risk factors that may be pertinent to the patient for whom clomiphene is being considered.
Ovarian Cancer: There have been rare reports of ovarian cancer with fertility drugs; infertility itself is a primary risk factor.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
None stated.

PREGNANCY AND LACTATION:
Pregnancy: Not indicated during pregnancy. To avoid inadvertent clomiphene administration during early pregnancy, appropriate tests should be utilized during each treatment cycle to determine whether ovulation occurs. The patient should have a pregnancy test before the next course of clomiphene therapy.
Lactation: It is not known whether clomiphene is excreted in human milk. Clomiphene may reduce lactation.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Patients should be warned that visual symptoms may render such activities as driving a car or operating machinery more hazardous than usual, particularly under conditions of variable lighting.

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UNDESIRABLE EFFECTS:
Symptoms/Signs/Conditions: During the investigational studies, the more commonly reported adverse effects are known to include: Ovarian enlargement (13.6%), vasomotor flushes (10.4%) abdominal-pelvic discomfort (distention, bloating) (5.5%), nausea and vomiting (2.2%), breast discomfort (2.1%), visual symptoms (1.5%), headache (1.3%), intermenstrual spotting or menorrhagia (1.3%).
Ovarian enlargement: At recommended dosage, abnormal ovarian enlargement is known to be infrequent although the usual cyclic variation in ovarian size may be exaggerated. Rare instances of massive ovarian enlargement are known to be recorded. Such an instance is known to be described in a patient with polycystic ovary syndrome whose clomiphene therapy consisted of 100mg daily for 14 days. Abnormal ovarian enlargement usually regresses spontaneously; most of the patients with this condition should be treated conservatively.
Immune system disorders: Not known: Hypersensitivity reactions including anaphylaxis and angioedema.
Eye/visual Symptoms: Symptoms described usually as "blurring" or spots or flashes (scintillating scotomata) are known to increase in incidence with increasing total dose. Symptoms often first appear or are accentuated with exposure to bright-light environment. Ophthalmologically definable scotomata, phosphenes and reduced visual acuity is known to be reported.
Cataracts and optic neuritis are rarely known to be reported. These visual disturbances are usually reversible. However, cases of prolonged visual disturbance have been reported, including after clomiphene have been discontinued. The visual disturbances may be irreversible, especially with increased dosage or duration of therapy.
Genitourinary: There are known reports of new cases of endometriosis and exacerbation of pre-existing endometriosis during clomiphene therapy.
Multiple pregnancies, including simultaneous intrauterine and extrauterine pregnancies, are known to be reported. Chance of ectopic pregnancy is known to be increased in women who conceive following clomiphene therapy.
Reduced endometrial thickness (frequency not known).
Tumours/neoplasms: Isolated reports are known to be received on the occurrence of endocrine-related or dependent neoplasms or their aggravation.
Central nervous system: Convulsions are known to be reported; patients with a history of seizures may be predisposed, transient paresthesia (frequency not known), dizziness (frequency not known). After prescription availability, there were isolated additional reports of these conditions and also reports of other conditions such as syncope/fainting, cerebrovascular accident, cerebral thrombosis, psychotic reactions including paranoid psychosis, neurologic impairment, disorientation and speech disturbance.
Psychiatric disorders: Anxiety (frequency not known), depression (frequency not known), mood disturbances (including mood altered, mood swings and irritability) (frequency not known), nervousness (frequency not known), insomnia (frequency not known).
Skin and subcutaneous tissue disorders: Dermatitis and rash were reported by investigational patients. Conditions such as rash and urticaria were the most common ones reported after prescription availability but also reported were conditions such as allergic reaction, ecchymosis and angioneurotic oedema. Hair thinning (alopecia) is known to be reported very rarely.
Liver function: Bromsulphalein (BSP) retention of greater than 5% is known to be reported in some patients. Retention was usually minimal unless associated with prolonged continuous clomiphene administration or with apparently unrelated liver disease. One patient taking 50mg of clomiphene daily developed jaundice on the 19th day of treatment; liver biopsy revealed bile stasis without evidence of hepatitis.
Metabolism disorders: Hypertriglyceridemia (frequency not known), in some cases with pancreatitis, is known to be observed in patients with pre-existing or a family history of hypertriglyceridemia and/or with dose and duration of treatment exceeding the label recommendations.
Cardiac disorders: Tachycardia (frequency not known), palpitations (frequency not known).
Hepatobiliary disorders: Increased Transaminases.
Gastrointestinal disorders: Pancreatitis (frequency not known).

OVERDOSE:
Toxic effects of acute overdosage of clomiphene have not been reported but the number of overdose cases recorded is small. In the event of overdose, appropriate supportive measures should be employed.

PHARMACOLOGICAL PROPERTIES
PHARMACODYNAMIC PROPERTIES:
Pharmacotherapeutic group: Ovulation stimulants, synthetic. **ATC code:** G03GB02.
Mechanism of action: The ovulatory response to cyclic clomiphene therapy is mediated through increased output of pituitary gonadotrophins, which in turn stimulates the maturation and endocrine activity of the ovarian follicle.
Pharmacodynamic effects: Clomiphene is a triarylethylene compound (related to chlorotrianisene and triparanol). It is a non-steroidal agent which stimulates ovulation in a high percentage of appropriately selected anovulatory women.

PHARMACOKINETIC PROPERTIES:
Based on innovator data orally administered ^{14}C labelled clomiphene citrate is known to be readily absorbed when administered to humans. Cumulative excretion of the ^{14}C label by way of urine and feces averaged about 50% of the oral dose after 5 days in 6 subjects, with mean urinary excretion of 7.8% and mean fecal excretion of 42.4%. A mean rate of excretion of 0.73% per day of the ^{14}C dose after 31 – 35 days and 0.45% per day of the ^{14}C dose after 42 – 45 days is known to be seen in fecal and urine samples collected from 6 subjects for 14 – 53 days after clomiphene citrate ^{14}C administration.
The remaining drug/metabolites may be slowly excreted from a sequestered enterohepatic recirculation pool.

SHELF LIFE
See expiry on the pack.

AVAILABILITY
Samclom® 50mg tablet in a pack of 10's

INSTRUCTIONS
Dosage: As advised by the physician.
To be sold on the prescription of a registered medical practitioner only.
Keep out of the reach of children.
Do not store over 30°C, and protect from heat, light and moisture
Improper storage may deteriorate the medicine.

سیمکلوم® ٹیبلٹ
(کلومیفین سائٹریٹ)

ہدایات:
خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،
گرمی، روشنی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
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