YSP CLOMIPHENE TABLET 50mg

Clomiphene Citrate is a synthetic, non-steroidal triphenylethylene estrogen derivative. It is the drug most widely used for treatment of anovulation. Clomiphene has become a valuable drug for treating anovulatory infertility since its discovery in 1961.

Ingredient(s):
Each tablet contains:
Clomiphene Citrate 50mg

Pharmacodynamics:
1. Clomiphene is chemically related to chlorotrianisene. It stimulates the secretion of pituitary gonadotrophic hormones probably by blocking the effect of estrogens at receptor sites in the hypothalamus and pituitary.

2. Clomiphene is the drug of choice for anovulatory or oligo-ovulatory women who have endogenous estrogen activity and an intact hypothalamic-pituitary-ovarian axis. Most anovulatory patients respond promptly to low dosages of Clomiphene Citrate. Approximately 75% of patients ovulate following treatment with the 50mg/day or 100mg/day regimen. Moreover, side effects are mild.

Pharmacokinetics:
Clomiphene is readily absorbed orally in human, and is excreted principally in the feces. Due to enterohepatic recirculation the biological half-life is reported to be 5 days.

Route of Administration:
To be taken orally.

Indication(s):
Induction of ovulation in patients with persistent ovulatory dysfunction who desire pregnancy. It should only be used after careful evaluation has established ovulatory dysfunction as the cause of infertility.

Dosage and Administration:
The usual dose by mouth is 50mg daily for 5 days, starting on or about the 5th day of the menstrual cycle or at any time if there is amenorrhea. If ovulation does not occur, a course of 100mg daily for 5 days may be started. This course may begin as early as 30 days after the previous one. Do not increase dosage or duration of therapy beyond 100mg/day for 5 days. The majority of patients who respond to do so during the first course of therapy, and 3 courses constitute an adequate therapeutic trial. If ovulatory menses do not occur, the diagnosis should be re-evaluated. To be dispensed on doctor's prescription.

Contraindication(s):
Clomiphene is contraindicated in patients with liver disease or a history of liver dysfunction, endometrial carcinoma or ovarian cysts, polycystic ovary, and during pregnancy.

Symptoms and Treatment for Overdosage, and Antidote(s):
There is no specific antidote for its overdose, therefore, management of the patients should consist of symptomatic and supportive therapy.

Precaution(s) / Warning(s):
This product is ineffective in patients with primary pituitary or primary ovarian failure. This product cannot be expected to substitute for specific treatment of other causes of ovulatory failure, such as thyroid or adrenal disorders. For hyperprolactinaemia, there is other preferred specific treatment. This product is not first line treatment for low weight related amenorrhoea, with infertility, and has no value if a high FSH blood level is observed following an early menopause.

Ovarian Hyperstimulation Syndrome: Ovarian Hyperstimulation Syndrome has been reported in patients receiving this product therapy for ovulation induction. The following symptoms have been reported in association with this therapy: pericardial effusion, anasarca, hydrothorax, renal failure, pulmonary oedema, ovarian haemorrhage, deep venous thrombosis, torsion of ovary and acute respiratory distress. If conception results, rapid progression to the severe form of the syndrome may occur. The lowest dose consistent with expectation of good results should be used. The patient who complains of abdominal or pelvic pain, weight gain, discomfort, or distension after taking this product should be examined very cautiously because of the possible presence of ovarian cyst or other cause and fragile enlarged ovaries. Treatment should not be given until the ovaries have returned to pretreatment size. Ovarian enlargement and cyst formation associated with therapy usually regress spontaneously within a few days or weeks after discontinuing treatment. The dosage and/or duration of the next course of treatment should be reduced.

Pre-existing or family history of hyperlipidemia and use of higher than recommended dose and/or longer duration of treatment 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 in relationship to clomiphene citrate therapy. The potential complications and hazards of multiple pregnancy should be discussed with the patient.

Ectopic pregnancy: There is an increased chance of ectopic pregnancy (including tubal and ovarian sites) in women who received this therapy. Multiple pregnancy, including simultaneous intrauterine and extrauterine pregnancies, have been reported.

Uterine Fibroids: Caution should be exercised when using this product in patients with uterine fibroids due to potential for further enlargement of the fibroids.

Pregnancy wastage and birth anomalies: The patient should be informed of the greater pregnancy risks associated with certain characteristics or conditions of any pregnant women: 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 citrate is being considered. Based upon the evaluation of the patient, genetic counselling may be indicated.

Ovarian cancer: There have been rare reports of ovarian cancer with fertility drugs; infertility itself is a primary risk factor. Epidemiological data suggest that prolonged use of this product may increase this risk. The recommended duration of treatment should not be exceeded.

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. These visual disturbances are usually reversible; however cases of prolonged visual disturbance have been reported including after discontinuation. The visual disturbances may be irreversible especially with increased dosage or duration of the therapy. The significance of these visual symptoms is not understood. If the patients has any visual symptoms, treatment should be discontinued and ophthalmologic evaluation performed.

Effects on the 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.

Side Effect(s) / Adverse Reaction(s):
Adverse effects appeared to be dose-related, occurring more frequently at the higher dose and with the longer courses of treatment used.

The more commonly reported adverse effects included ovarian enlargement, vasomotor flushes, abdominal-pelvic discomfort (distention, bloating), nausea and vomiting, breast discomfort, visual symptoms, headache and intermenstrual spotting or menorrhagia.

Ovarian enlargement: At recommended dosage, abnormal ovarian enlargement is infrequent although the usual cyclic variation in ovarian size may be exaggerated. Similarly, cyclic ovarian pain (mittelschmerz) may be accentuated. With higher or prolonged dosage, more frequent ovarian enlargement and cyst formation may occur, and the luteal phase of the cycle may be prolonged. Rare instances of massive ovarian enlargement are recorded. Abnormal ovarian enlargement usually regresses spontaneously; most of the patients with this condition should be treated conservatively.

Eye/Visual symptoms: Symptoms described usually as “blurring” or spots or flashes (scintillating scotomata) increased in incidence with increasing total dose. Ophthalmologically definable scotomata, phosphenes and reduced visual acuity have been reported. There are rare reports of cataracts and optic neuritis. The visual disturbance are usually reversible. The visual disturbances may be irreversible, especially with increased dosage or duration of therapy.

Genitourinary: There are reports of new cases of endometriosis and exacerbation of preexisting endometriosis during therapy. Multiple pregnancies, including simultaneous intrauterine and extrauterine pregnancies, have been reported. There is an increased chance of ectopic pregnancy in women who conceive therapy. Reduced endometrial thickness (frequency not known).

Tumour/ neoplasms: Isolated reports have been received on the occurrence of endocrine-related or dependent neoplasms or their aggravation. Ovarian cancer (*see Precautions/Warnings*).

Central Nervous System: Convulsions have been reported; patients with a history of seizures may be predisposed. The symptoms include conditions of dizziness, lightheadedness/ vertigo, nervous tension/insomnia, and fatigue/depression were reported. 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.

Dermatoses: Dermatitis and rash were reported. Conditions such as rash and urticaria were the most common ones reported after prescription availability but also reported were conditions such as allergic reaction, erythema multiforme, ecchymosis and angioneurotic oedema. Hair thinning (alopecia) has been reported very rarely.

Liver function: Bromsulphalein (BSP) retention of greater than 5% was reported. Retention was usually minimal unless associated with prolonged continuous administration or with apparently unrelated liver disease.

Metabolism disorders: Hypertriglyceridemia (frequency not known), in some cases with pancreatitis, has been 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, palpitation (frequency not known).

Hepatobiliary disorders: Increased transaminases.

Gastrointestinal disorders: Pancreatitis (frequency not known).

Pregnancy & Lactation:
Statement on usage during Pregnancy and lactation
Pregnancy
Clomiphene use is contraindicated during pregnancy. Prior to administration of each cycle of clomiphene treatment, pregnancy should be ruled out.

Lactation
It is not known whether it is excreted into human milk. Clomiphene may reduce lactation in some nursing women. Caution should be exercised when administering clomiphene to a nursing woman.

Shelf-Life:
3 years from the date of manufacture.

Storage Condition(s):
Keep in a tight container. Store at temperature below 30°C. Protect from light and moisture.

Product Description & Packing(s):
A slightly yellow color round tablet, one side impressed with a mark “ ”.

Blister packing of 10’s x 10.

YSP CLOMIPHENE TABLET 50mg

Bahan Aktif:
Setiap tablet mengandungi:
Clomiphene Citrate 50mg

Indikasi:
Untuk merangsang proses ovulasi. Hanya digunakan apabila punca ketidak-suburan disebabkan oleh masalah ovulasi.

Dos:
Pemberian oral: 50mg sehari selama 5 hari, bermula pada hari kelima kitaran haid atau pada sebarang hari sekiranya berlaku amenorea. Jika ovulasi masih tidak berlaku, dos 100mg sehari selama 5 hari harus diberi. Dos pusingan kedua boleh dimulakan 30 hari selepas dos pusingan pertama. Jangan tingkatkan dos atau jangka masa terapi melebihi 100mg/hari selama 5 hari. Kebanyakan pesakit bergerakbalas semasa dos pusingan pertama. Tiga pusingan dos adalah memadai untuk tujuan percubaan terapeutik. Jika haid ovulatori tidak berlaku, diagnosis harus dinilai semula. Didispens mengikut preskripsi doktor.

Y. S. P ®

Manufacturer and Product Registration Holder:
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