Prolifen®
(Clomiphene citrate)

COMPOSITION
Each capsule contains Clomiphene citrate B. P. 50 mg.
PHARMACO-THERAPEUTICAL CLASSIFICATION
Ovulation stimulating drug.

INDICATIONS
PROLIFEN® is indicated for the treatment of anovulatory states or short luteal phases in patients desiring pregnancy. The drug is also indicated in the classical forms such as functional uterine haemorrhages, secondary amenorrhea or servere oligomenorrhea the Stein - Leventhal syndrome. The administration of PROLIFEN® is only indicated in cases where ovary function has been demonstrated. An oestrogen secretion that is normal or slightly below the norm (detected with vaginal smears endometrium biopsy, urinary oestrogen levels or haemorrhage in response to progesterone) are favourable elements for PROLIFEN® treatment; reduced oestrogen levels do not, however, exclude successful treatment. Treatment with PROLIFEN® generally has little effect in patients with hypophyseal deficiency or primary amenorrhea precluding the possibility of stimulating normal functioning. PROLIFEN® cannot obviously be considered as a replacement for specific treatment of alterations in other organs that may cause anovularity (thyroid, adrenal glands, etc)

CONTRAINDICATIONS
PREGNANCY - Since Clomiphene causes abortions and foetal malformations in rats or rabbits, PROLIFEN® should not be administered during pregnancy; to avoid this it is necessary to examine ovulation exactly, measuring the basal temperature during all the treatment cycles. LIVER DISORDERS - Since PROLIFEN® is metabolised in the liver, it must not be administered to patients with liver alterations. Dubious cases require clinical and laboratory tests to examine hepatic functions. MENOMETRORRHAGIA - PROLIFEN® is contraindicated in patients with menometrorrhagia. VISUAL DISTURBANCES - PROLIFEN® is contraindicated in patients with past or present visual disorders. Dubious cases should be referred for an ophthalmic examination. Patients should be warned of the possible onset of visual disorders and blurring of vision during treatment with PROLIFEN®. These disorders can interfere with some operations that require particularly acute vision, especially under variable light conditions (driving a car, operating machinery, etc.). If they appear, treatment with PROLIFEN® should be suspended.

PRECAUTIONS
An accurate examination of the pelvis should be made before treatment and repeated before each successive treatment cycle. PROLIFEN® should not be administered in the presence of ovarian cysts due to the danger of a further increase in the size of the ovaries. Special attention must be given to patients in the later stage of reproductive life due to the major incidence of anovulatory disorders and the increased tendency for the onset of endometrial carcinoma. Similar attention should be given to patients with abnormal haemorrhages before treatment: in particular it is necessary to ensure that there are no occult neoplastic lesions. In both categories of patients it is necessary to perform a biopsy of the endometrium. PROLIFEN® therapy must always be preceded by a clinical examination of hepatic functions. To reduce to a minimum the risk of abnormal ovarian swelling, it is important to use the minimum dose of PROLIFEN® that gives a positive result. Some patients with a polycystic ovarian syndrome may have an exaggerated response to normal PROLIFEN® doses. In this case the doses and cycle duration should be reduced. Finally, it should be remembered that the maximum swelling of the ovary, whether this is physiological or abnormal, only occurs several days after suspension of the recommended PROLIFEN® doses.

SPECIAL PRECAUTIONS
PROLIFEN® is a very potent drug that must only be administered under direct and constant medical control. Do not exceed the dose or the treatment duration prescribed by the physician.

DOSAGE AND ADMINISTRATION
An initial test cycle with 50 mg (1 capsule) a day for 5 days of PROLIFEN® between meals. In the case of patients with menses present or in whom the menses must be induced by administration of progesterones, treatment should be started approximately on the 5th day of the cycle onwards. In patients who have not had recent uterine haemorrhages the treatment can be started at any time. If ovulation occurs with this dose there is no need to increase the dose in the following treatment cycles. If after the first test cycle ovulation does not occur, it is possible to start a second treatment cycle, 30 days after the first one, lasting for 5 days with 100 mg (2x50 mg capsules) a day in two doses between meals. Dosage must never be higher than 100 mg/day and treatment has not to be continued for more than 5 days. If necessary, a third treatment cycle may be given in the same manner. Most of the carefully selected patients will have ovulation during the first cycle. Amenorrhea lasting for a few years might make the endometrium less sensitive, and two or three cycles might be necessary before and effective menses occurs. Three treatment cycles may be a sufficient therapeutic test: ovulation is rarely obtained after 3 cycles of unsuccessful treatment. If ovulatory menses are not obtained after three treatment cycles it is advisable to re-examine the diagnosis. Once ovulation has occurred, to achieve a regular ovulatory cycle it is important to start each treatment cycle on the 5th day of the menstrual cycle. The number of treatment cycles must be determined by the physician. If pregnancy does not occur after 6 treatment cycles, it is unlikely that another cycle will be successful and further treatment is not recommended. Patients who wish to become pregnant should be informed of the great importance of selecting the appropriate time for coitus. As it still has not been demonstrated that prolonged cyclic treatment does not have side effects, PROLIFEN® must not be administered as a monthly maintenance treatment in patients who fail to ovulate when treatment is suspended. In patients with amenorrhea or oligomenorrhea, treatment with PROLIFEN®, if effective, restores regular menses with ovulation. A simple and relatively safe method to establish whether ovulation has taken place even in patients under treatment for anovulatory haemorrhage, is to measure the temperature increase that occurs during the luteal phase (basal temperature). It can be considered that ovulation has occurred if the patient has found an increase in the basal temperature which is maintained for 10-12 days and followed by menses. The presence of menses not preceded by the normal increase in basal temperature or a prolonged increase in temperature not followed by menses, must be considered as a negative response. To avoid the administration of PROLIFEN® during the first period of pregnancy, if the basal temperature is biphasic and is not followed by menses., it is necessary to examine the patient carefully to determine the presence of an ovarian cyst and carry out a pregnancy test. The next treatment cycle must not be started until an exact diagnosis has been made. The basal temperature test may be completed with a cervical smear, vaginal cytology and biopsy of the endometrium.

SIDE EFFECTS
At the recommended doses (short treatments) the side effects are not severe and do not interfere with treatment. The incidence of side effects is however directly proportional to the doses and the duration of treatment. The most common side effects include: Vasomotor symptoms. Consisting of hot flushes, at times accompanied by sweating. These events, probably linked to neurovegetative modifications, may be partially determined by hypophyseal secretions and partially by the anticestrogen effects of the drug. These disorders are encountered quite frequently, but they do not generally cause discomfort and disappear as soon as treatment is suspended.
Abdominal symptoms. These are caused by abdominal tension, sense of swelling, pain and tender gonads. These occur quite frequently and may also be intense. Gonad pain is often related to ovulation ("mittelschmerz" in German: the phenomenon is the fundamental sign of the premenstrual syndrome); or with ovarian swelling. The patients suffering from pelvic pain must be examined carefully to detect any enlargement of the ovaries.
Enlargement of the ovaries and ovarian cysts This complication, certainly undesirable, is reported by almost all authors: however at the recommended doses and abnormal ovarian enlargement occurs in a limited number of cases and does not generally cause any discomfort to the patient. It can be detected by and abnormally high increase in temperature or with the normal gynaecological examinations and in general disappear with the suspension of treatment. There are only two cases mentioned in literature which required surgery. If enlargement of the ovaries occurs, it is necessary to suspend treatment until the ovaries return to normal dimensions, and a reduced dose and/or duration must be used for the successive treatments. The treatment of every cystic enlargement should always be conservative, unless surgery is indicated.
Visual disturbances. These disturbances, consisting of clouding, spots or flashing, that appear with or are accentuated by exposure to intense light. They are probably linked to the a mydriatic effect of the drug and disappear when treatment is suspended. Only one case of severe reduction in visual acuity has been described, that was reversed when treatment was suspended. Treatment must be suspended at the onset of visual disturbances and an ophthalmologic examination should be performed.
Other disturbances. Other disturbances less frequently reported and generally occurring for prolonged cycles include: nausea, vomiting, nervousness, tiredness, vertigo or sensation of light-headedness, insomnia, headache, painful breasts, abundant menses, urticaria or allergic dermatitis, increase in weight, polyuria or pollakiuria, slight loss of hair that is reversible. A large number of patients treated with Clomiphene reveal sulfobromophthalein sodium retention caused by intrahepatic cholestasis generally without symptoms. There has been just one case reported of jaundice.
Effects on pregnancy and multiple pregnancies. Amongst the 2269 full-term pregnancies previously reported in mothers treated with clomiphene, the birth of 58 babies with congenital malformations has been reported. The malformations reported were: congenital heart defects (8), Down's syndrome (5), club foot (4), congenital defects of the intestines (4), hypospadias (3), microcephaly (2), hare-lip and cleft palate (2), congenital dislocation of the hip (2), haemangioma (2), retained testis (2), polydactylia (2). Siamese twins with teratomatous malformations (patent arterial duct, amaurosis (blindness), arteriovenous fistula, inguinal hernia, umbilical hernia, syndactyli, apectus excavatum, myopathy, dermoid cysts of the scalp, omophalocele, occult spina bifida, ichthyosis; persistance of lingal frenula), multiple somatic malformations (7). Eight neonates out of the entire group of 58 were born from 7 of the 158 mothers who underwent a cycle of clomphene citrate during the first 6 weeks after conception. Moreover, the following conditions were reported for which there was no demonstration of the cause and effect: 4 cases of capsular cataract (in experimental studies), one case of detachment of the posterior vitreous body, one case of retinal arteriospasm, one case of thrombosis of the temporal retinal arteries, 8 cases of cystic moles. It has been proved that clomiphene markedly increases the incidence of multiple pregnancies. Therefore the patient and her husband must be warned of this possibility and of the potential risks associated with multiple conceptions.
Please, notify your doctor or chemist of any adverse effects not described in this leaflet.

PACKAGE
Box of 10 capsules.
TO BE SOLD ON THE PRESCRIPTION OF REGISTERED MEDICAL PRACTITIONER ONLY.
KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN.
STORE BELOW 25°C IN A DRY PLACE. PROTECT FROM LIGHT.
DO NOT USE THE DRUG AFTER THE EXPIRY DATE INDICATED ON THE PACKAGE.
THIS DATE REFERS TO THE PRODUCT CORRECTLY STORED IN ITS UNOPENED PACKAGE.

Chiesi

Manufactured by:
HIGHNOON LABORATORIES LTD.
17.5 K.M. Multan Road, Lahore - Pakistan.
Under Licence of:
CHIESI FARMACEUTICI S.p.A., PARMA - ITALY.

پرولی فن: (کلومی فن سائٹریٹ) ۵۰ ملی گرام

اجزائے ترکیبی اور وضاحت:

ایک پرولی فن کیپسول میں ۵۰ ملی گرام کلومی فن سائٹریٹ ہوتا ہے۔

علامات:

جب بانجھ پن بیضہ دانی کے فعل میں خلل یا ناکامی کی وجہ سے ہو،
حیض میں کمی کے مریض، کثیر حصالتی بیضہ دانی، حیض کی بندش کے مریض۔

ممانعت برائے علاج:

حمل، جگر کے افعال میں کمی، حیض کے دوران یا بعد میں خلاف معمول خون کا نکلنا۔

ترکیب استعمال:

پہلے کورس میں حیض شروع ہونے کے پانچویں دن سے ایک پرولی فن
کیپسول روزانہ ۵ دن تک دیا جاتا ہے۔ اگر دوا کے استعمال سے بیضہ دانی سے انڈا نکلے
مگر حمل واقع نہ ہو تو پرولی فن کیپسول کے ۶ کورسز دیئے جاسکتے ہیں۔
اگر پہلے کورس سے انڈا نہ نکلے تو پرولی فن کیپسول کی مقدار دوگنی کر کے صرف ۲ کورس بحالت
انڈا نہ نکلنے کی صورت میں دیئے جاسکتے ہیں۔ اگر دوگنی خوراک سے انڈے نکلنا شروع ہو
جائیں مگر حمل واقع نہ ہو تو زیادہ سے زیادہ ۶ کورس دیئے جاسکتے ہیں۔
بندش حیض کی صورت میں پرولی فن کیپسول کسی دن بھی شروع کر کے ۵ دن تک دیا جاتا ہے۔

منفی و مضر اثرات:

مضر اثرات خوراک کی مناسبت سے ہوتے ہیں۔ اس لئے مجوزہ خوراکوں
سے زیادہ خوراک لینے سے ظاہر ہوتے ہیں اور شاذ و نادر ہی مجوزہ خوراکوں میں
ظاہر ہوتے ہیں۔ ہاٹ فلشز عموماً شدید نہیں ہوتے اور دوا بند کرنے سے ختم ہو
جاتے ہیں۔ پیٹ میں کھچاؤ محسوس ہونا۔ ورم کا احساس ہونا۔ اور درد محسوس ہونا۔
نظر کا دھندلا جانا۔

پیکنگ:

۱۰ کیپسول ایک ڈبیہ میں دستیاب ہیں۔

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت کی جائے۔
تمام ادویات بچوں کی پہنچ سے دور رکھیں۔
دوا کو 25°C سے کم درجہ حرارت پر نمی اور روشنی سے محفوظ رکھیں۔

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