For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Chorionic Gonadotrophin Injection B.P.

HuCoG

5000 I.U.

Powder for Injection

For Subcutaneous / Intramuscular Injection only

COMPOSITION :

Each vial contains:

Chorionic Gonadotrophin B.P……..5000 I.U.

Excipients :

Mannitol B.P., Sucrose B.P., Sodium Ascorbate B.P., Anhydrous Di-sodium Hydrogen Phosphate B.P. and Phosphoric Acid B.P.

Each vial of **HuCoG** contains: Chorionic Gonadotrophin and each vial is accompanied by an ampoule of Sodium Chloride Injection B.P. 1ml.

One I.U. of Chorionic Gonadotrophin is defined as the activity contained in 1.279 mg of the 2nd International Standard Preparation.

PRODUCT DESCRIPTION :

Drug powder – A white or almost white amorphous powder or cake. Solvent for reconstitution - A clear colorless solution.

Reconstituted solution – A clear colorless liquid.

PROPERTIES :

Chorionic Gonadotrophin **(HCG)** is a hormonal substance obtained from urine of pregnant women. Its action is predominantly luteinizing.

PHARMACODYNAMICS :

(HCG) is a preparation of Human Chorionic Gonadotrophin obtained from the urine of pregnant women. It stimulates the steroidogenesis in the gonads by virtue of a biological effect similar to that of LH (Luteinizing hormone, which is the same as interstitial cell stimulating hormone). In the male it promotes the production of testosterone and in the female the production of estrogens and particularly of progesterone after ovulation. In certain cases, this preparation is used in combination with Human Menopausal Gonadotrophin **(HMG)**.

PHARMACOKINETICS :

(HCG) is administered by intramuscular injection. The maximum serum level of **(HCG)** is reached after 4 to 12 hours (dose-dependent) and decreases afterwards with a half-life of 29 to 36 hours. Due to the slow elimination, **(HCG)** may cumulate in serum after several (e.g. daily) intramuscular injections. **(HCG)** is metabolized renally whereby about 10 - 20% can be found in its original form in urine, while the main amount is probably excreted as the beta-core fragment.

INDICATIONS :

In the female: Ovulation induction in subfertility due to anovulation or impaired follicle- ripening. Preparation of follicles for puncture in controlled ovarian hyperstimulation programs (for medically assisted reproductive techniques). Luteal phase support. In the male: Hypogonadotropic hypogonadism (also cases of idiopathic dysspermias have shown a positive response to gonadotropins). Delayed puberty associated with insufficient gonadotropic pituitary function. Cryptorchidism, not due to anatomical obstruction.

DOSAGE AND ADMINISTRATION :
HuCoG is given by subcutaneous / intramuscular injection only. The injection should be reconstituted with Sodium Chloride Injection B.P. provided, immediately prior to use.

RECOMMENDED DOSE :
Dosage in the female: Ovulation induction in subfertility due to anovulation or impaired follicle-ripening Usually, one injection of 5000 I.U. **HuCoG** to complete treatment with an FSH-containing preparation. Preparation of follicles for puncture in controlled ovarian hyperstimulation programs Usually, one injection of 5000 I.U. **HuCoG** to complete treatment with an FSH-containing preparation. Luteal phase support Two to three repeat injections of 1000 to 3000 I.U. may be given within 9 days following ovulation or embryo transfer (for example on day 3, 6 and 9 after ovulation induction)

The ovulation cycle should be monitored with oestriol levels and ultrasonography.

Dosage in the male: Hypogonadotropic hypogonadism 1000-2000 I.U. **HuCoG** two to three times per week. If the main complaint is subfertility, Pregnyl may be given with an additional follitropin (FSH)-containing preparation two to three times a week. This treatment should be continued for at least three months before any improvement in spermatogenesis can be expected.

During this treatment testosterone replacement therapy should be suspended. Once achieved, the improvement may sometimes be maintained by **(HCG)** alone. Delayed puberty associated with insufficient gonadotropic pituitary function 1500 I.U. two to three times weekly for at least six months Cryptorchidism, not due to anatomical obstruction - Under 2 years of age: 250 I.U. twice weekly for six weeks - Under 6 years of age: 500-1000
I.U. twice weekly for six weeks - Over 6 years of age: 1500 I.U. twice weekly for six weeks. If necessary, this treatment can be repeated.

ADVERSE EFFECTS :
Immune system disorders: In rare cases generalized rash or fever may occur. General disorders and administrative site conditions: Local site reactions such as bruising, pain, redness, swelling and itching. Oedema. Occasionally allergic reactions have been reported, mostly manifesting as pain and/or rash at the injection site. Tiredness. Nervous system disorders: Headache. Psychiatric disorders: Mood changes. In the female:- Reproductive system and breast disorders: Unwanted ovarian hyperstimulation, mild or severe ovarian hyperstimulation syndrome (OHSS): Mild OHSS: Painful breasts, Mild to moderate enlargement of ovaries, Ovarian cysts, Abdominal pain, Abdominal discomfort, Gastrointestinal symptoms such as nausea, diarrhoea and bloating Severe OHSS: Large ovarian cysts (prone to rupture), Acute abdominal pain, Ascites,Weight gain, Hydrothorax In rare instances, thromboembolism has been associated with FSH/**(HCG)** therapy Not all symptoms described are always associated to OHSS. In the male:- Metabolism and nutrition disorders: Water and sodium retention is occasionally seen after administration of high dosages; this is regarded as a result of excessive androgen production. Reproduction system and breast disorders: **(HCG)** treatment may sporadically cause gynaecomastia. Skin and subcutaneous tissue disorders: Acne may occur occasionally during **(HCG)** therapy.

CONTRA-INDICATION :
Hypersensitivity to human gonadotropins or any of the excipients. Known or suspected sex hormone-dependent tumours, such as ovary, breast and uterine carcinoma in female and prostatic or breast carcinoma in the male. Malformations of the sexual organs incompatible with pregnancy Fibroid tumours of the uterus incompatible with pregnancy.

WARNING AND PRECAUTIONS :
(HGC) should be given with care to patients in whom fluid retention might be a hazard, as in asthma, epilepsy, migraine or cardiac or renal disorders. **(HCG)** preparations should only be used under the supervision of a specialist having available adequate facilities for appropriate laboratory monitoring.

In the female:
Use in induction of ovulation may result in ovarian enlargement or cysts, acute abdominal pain, superovulation or multiple pregnancies, particularly if endocrine monitoring is inadequate. Since infertile women undergoing assisted reproduction, and particularly IVF, often have tubal abnormalities the incidence of ectopic pregnancies might be increased. Early ultrasound confirmation that a pregnancy is intrauterine is therefore important. Rates of pregnancy loss in women undergoing assisted reproductive technologies (ART) are higher than in the normal population. Prior to treating patients for inadequate endogenous stimulation of the gonads, an examination should be performed to exclude anatomical abnormalities of the genital organs or nongonadal endocrinopathies (e.g. thyroid or adrenal disorders, diabetes). Primary ovarian failure should be excluded by the determination of gonadotrophin levels. Unwanted hyperstimulation During treatment of female patients, determinations of oestrogen levels and assessment of ovarian size and if possible, ultrasonography should be performed prior to treatment and at regular intervals during treatment. High dosages may cause oestrogen levels to rise excessively rapidly,
e.g. more than doubling on 2 or 3 consecutive days, and possibly reaching excessively high pre-ovulatory values. The diagnosis of unwanted ovarian hyperstimulation may be confirmed by ultrasound examination. If unwanted hyperstimulation occurs (i.e. not as part of a treatment preparing for IVF/ET or GIFT or other assisted reproduction techniques), the administration of (HMG) should be discontinued immediately. **(HCG)** must not be given, because the administration of an hLH active gonadotrophin at this stage may induce, in addition to multiple ovulations, the ovarian hyperstimulation syndrome. This warning is particularly important with respect to patients with polycystic ovarian disease. The severe form of ovarian hyperstimulation syndrome may be life-threatening and is characterized by large ovarian cysts (prone to rupture), acute abdominal pain, ascites, very often hydrothorax and occasionally thrombo-embolic pnenomena. In the male? Treatment for cryptochidism not due to anatomical obstruction may produce precocious puberty; use should cease immediately. Gynaemastia has been reported. A growth spurt may also be associated with use and this should be kept in mind particularly where epiphyseal growth is still potentially active.

- Women with generally recognised risk factors for thrombosis, such as a personal or family history, severe obesity (Body Mass Index > 30 kg/m2) or thrombophilia, may have an increased risk of venous or arterial thromboembolic events, during or following treatment with gonadotrophins. In these women the benefits of IVF treatment need to be weighed against the risks. It should be noted, however, that pregnancy itself also carries an increased risk of thrombosis. - There have been reports of ovarian and other reproductive system neoplasms, both benign and malignant, in women who have undergone multiple drug regimens for infertility treatment. It is not yet established whether or not treatment with gonadotrophins increases the baseline risk of these tumours in infertile women. - **HuCoG** should not be used for body weight reduction. **(HCG)** has no effect on fat metabolism, fat distribution or appetite.

In the male:
Treatment with **(HCG)** leads to increased androgen production. Therefore: - Patients with latent or overt cardiac failure, renal dysfunction, hypertension, epilepsy or migraine (or a history of these conditions) should be kept under close medical supervision, since aggravation or recurrence may occasionally be induced as a result of increased androgen production. - **(HCG)** should be used cautiously in prepubertal boys to avoid premature epiphyseal closure or precocious sexual development. Skeletal maturation should be monitored regularly.

INTERACTIONS WITH OTHER MEDICAMENTS :
Interactions of **HuCoG** with other medicines have not been investigated; interactions with commonly used medicinal products can therefore not be excluded. Following administration, **HuCoG** may interfere for up to ten days with the immunological determination of serum/urinary **(HCG)**, leading to

a false positive pregnancy test.

PREGNANCY AND LACTATION :
HuCoG may be used for luteal phase support only, but must not be used afterwards during pregnancy. It must not be used during lactation.

SYMPTOMS & TREATMENT OF OVERDOSE :
The acute toxicity of urinary gonadotropin preparations has been shown to be very low. Nevertheless, there is a possibility that too high a dosage of **(HCG)** may lead to ovarian hyperstimulation syndrome.

INCOMPATIBILITY :
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

STORAGE :
Vials of **HuCoG** should be stored between 2°C-8°C. Do not freeze. Protect from light. Reconstituted solution should be used immediately after preparation, any unused portion should be discarded. Storage condition for solvent - Store between 2°C-8°C.

PRESENTATION :
HuCoG is supplied in vials containing sterile, powder for Injection having activity of 5000 I.U. Each vial is accompanied by an ampoule containing 1ml of Sodium Chloride Injection B.P.

SHELF LIFE :
36 months.

DATE OF REVISION :
September 2017.

Marketing Authorization Holder :
FIRSTLINE PHARMACEUTICAL SDN BHD
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Manufactured in India by :
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