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

Menotrophin for Injection B.P.

HuMoG

75 I.U./ 150 I.U.

Powder for Injection

For Subcutaneous / Intramuscular Injection

COMPOSITION :

Each vial contains :
Menotrophin B.P. equivalent to activity of
Follicle Stimulating Hormone……75 I.U. / 150 I.U.
Luteinizing Hormone……75 I.U. / 150 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 **HuMoG** is accompanied by an ampoule of Sodium Chloride Injection B.P. 1ml.

One I.U. of human urinary FSH and one I.U. of human urinary LH are defined as the activities contained in 0.11388 mg and 0.13369 mg of the 1st International Standard respectively.

PHARMACOLOGICAL PROPERTIES :

Pharmacodynamic Properties:

HuMoG (Human Menopausal Gonadotropin) is a hormonal substance containing FSH and LH in ration of 1:1.
In female, **HuMoG** stimulates both the growth and the maturation of follicles. It induces an increase in the oestrogen levels and a proliferation of the endometrium.
In the male **HuMoG** stimulates the spermatogenesis by acting on the production of the androgen-binding protein in the seminiferous tubules of the sertoli cells.

Pharmacokinetic Properties:

Human Menopausal Gonadotrophins (HMG) is not effective when taken orally and is injected intra-muscularly. The HMG biological effectiveness is mainly due to its FSH content. The pharmacokinetics of HMG following IM administration shows great individual variations. The maximum serum level of FSH is reached 6 - 24 hours after IM injection, 6 - 36 hours after SC injection, resp. After that the serum level decreases by a half-life of 56 (i.m.), resp. 51 (SC) hours. Administered HMG is predominantly discharged renally.

INDICATIONS :

Women :

Sterility in females with hypo- or normogonadotrophic ovarian insufficiency: Stimulation of follicle growth.

Men :

Sterility in males with hypo- or normogonadotrophic hypogonadism: in combination with HCG to stimulate spermatogenesis.

DOSAGE AND ADMINISTRATION :

HuMoG is given by subcutaneous / intramuscular injection only.
Reconstitute powder of vial in 1ml of Sodium Chloride Injection B.P. provided in the pack immediately prior to use. Upto 5 vials of **HuMoG** may be reconstituted in 1ml of Sodium Chloride Injection B.P. Reconstituted solution should be used immediately after preparation. Any unused portion of solution should be discarded.

RECOMMENDED DOSAGE :

Sterility in females:

The dosage of HMG for the induction of follicle growth in normo-or hypogonadotrophic women varies according to the individual. The amount depends on ovarian reaction and should be checked by ultrasound examinations of the ovaries and measuring estradiol levels. If the HMG dosage is too high for the treated individual, multiple uni- and bilateral follicle growth can occur.

HMG is administered intramuscularly or subcutaneously and in general, the therapy is begun with a daily dosage corresponding to 75-150 I.U. FSH. If the ovaries do not respond, the dosage can slowly be increased until a rise in estradiol secretion and follicle growth is evident. Treatment with the same dosage of HMG continues until the preovulatory estradiol serum level is attained. If the level rises too quickly, the dosage should be reduced. To induce ovulation, 5000 or 10000 I.U. HCG are injected i.m. 1 to 2 days after the last HMG administration.

Note: After administering a HMG dosage which is too high for the corresponding individual, a subsequent HCG administration can cause an unintentional hyperstimulation of the ovaries.

Sterility in males:

In men with infertility due to hypogonadotrophic hypogonadism, spermatogenesis is stimulated with chorionic gonadotrophin and then human menopausal gonadotrophin are added In a dose of 75 IU or 150 IU of FSH, two or three times weekly by intramuscular or subcutaneous injection. Treatment should be continued for at least 3 or 4 months.

MODE OF ADMINISTRATION :

HuMoG is given by subcutaneous / intramuscular injection only.

CONTRAINDICATIONS :

In females:

- Pregnancy,
- Enlargement of the ovaries or cysts that is not caused by polycystic ovarian syndrome,
- Gynaecological bleeding of unknown cause,
- Tumours in the uterus, ovaries and breasts.

In males:

- Carcinoma of the prostate,
- Tumours in the testes.

The following conditions should be properly treated before HMG-therapy is begun: dysfunction of the thyroid gland and of the cortex of the suprarenal gland, a rise in the serum level of prolaction with different causes (hyperprolactinaemia), tumours in the pituitary gland (hypophysis) or in part of the diencephalons (hypothalamus).

WARNING AND PRECAUTIONS :

The following conditions should be properly treated and excluded as the cause of infertility before menotrophin therapy is initiated:

- Dysfunction of the thyroid gland and cortex of the suprarenal gland.
- Hyperprolactinaemia.
- Tumours in the pituitary or hypothalmic glands.

In the treatment of female infertility, ovarian activity should be checked (by ultrasound and plasma 17 beta- oestradiol measurement) prior to **HuMoG** administration. During treatment, these tests and urinary oestrogen measurement should be carried out at regular intervals, until stimulation occurs. Close supervision is imperative during treatment. See “posology and administration” for optimum

response levels of urinary oestrogens and plasma 17 beta-oestradiol. Values below these ranges may indicate inadequate follicular development. If urinary oestrogen levels exceed 540 nmol (150 micrograms)/24 hours, or if plasma 17 beta-oestradiol levels exceed 3000 pmol/L (800 picograms/ml), or if there is any steep rise in values, there is an increased risk of hyperstimulation and **HuMoG** treatment should be immediately discontinued and human chorionic gonadotrophin withheld. Ultrasound will reveal any excessive follicular development and unintentional hyperstimulation. In the event of hyperstimulation, the patient should refrain from sexual intercourse until they are no longer at risk.

If during ultrasound, several mature follicles are visualised, human chorionic gonadotrophin should not be given as there is a risk of multiple ovulation and the occurrence of hyperstimulation syndrome.

Patients undergoing superovulation may be at an increased risk of developing hyperstimulation in view of the excessive oestrogen response and multiple follicular development. Aspiration of all follicles, prior to ovulation, may reduce the incidence of hyperstimulation syndrome.

The severe form of hyperstimulation syndrome may be life-threatening and is characterised by large ovarian cysts (prone to rupture), acute abdominal pain, ascites, very often hydrothorax and occasionally thromboembolic phenomena.

Prior to treatment with **HuMoG**, primary ovarian failure should be excluded by the determination of gonadotrophin levels.

There have been reports of ectopic pregnancy in women receiving Menotrophin who have undergone assisted conception. One predisposing factor for ectopic pregnancy is tubal disease/occlusion, which women undergoing assisted conception may have. No causal relationship between ectopic pregnancy and the use of menotrophin has been established.

Special precautions for the physician:
HuCoG should not be administered to induce ovulation in females whose ovaries have unintentionally been hyperstimulated.

When treating sterile women, ovarian activity should be checked (ultrasound and estradiol levels in serum resp.) prior to **HuMoG** administration. During treatment, these tests should be carried out every one to two days until stimulation occurs. Ovarian reaction can also be measured using a cervix index.
Close supervision is imperative during treatment. Treatment should be immediately discontinued if unintentional hyperstimulation occurs.

DRUG INTERACTION :
Interactions with other medications are unknown. HMG can be injected together with HCG when treating infertile males.

PREGNANCYAND LACTATION :
HuMoG should not be given if pregnancy is suspected or to lactating mothers.

SIDE EFFECTS :
In the female, a local reaction at the injection site, fever and arthralgia have been observed in rare cases. In the male, a combined treatment with **HuMoG** and HuCoG may cause gynecomastia.

Occasionally, nausea and vomiting can occur.

In single cases, hypersensitivity reactions and fever can occur during treatment with **HuMoG**. The administration of **HuMoG** may lead to reactions at the injection site: reddening, pain, swelling and itching. In very rare cases, long-term usage can lead to the formation of anti-bodies, making the therapy ineffective.

Treatment with **HuMoG** can often lead to ovarian hyperstimulation that first becomes clinically relevant after the administration of HuCoG (pregnancy hormone) to induce ovulation. This can lead to the formation of large ovarian cysts that tend to rupture, and to intraabdominal bleeding. In addition, the accumulation of fluids in the abdominal cavity (ascites), the accumulation of fluid in the chest cavity (hydrothorax), a decrease in the excretion of urine (oliguria), lowering of the blood pressure (hypotension), and occlusion of blood vessels by blood clots (thromboembolic phenomena) can occur.
Treatment should be immediately discontinued when the first signs of hyperstimulation appear: abdominal pain and a palpable (by the physician) enlargement in the lower abdomen, which can be detected sonographically.
If abdominal pain occurs, please see your physician.
If pregnancy occurs, these side effects can intensify, continues over a long period of time, and be life-threatening. Unintentional multiple pregnancies occur more often during treatment with **HuMoG**.

SYMPTOMS AND TREATMENT OF OVERDOSE :
The acute toxicity of menotrophin has been shown to be very low. However, too high a dosage for more than one day may lead to hyperstimulation, which is categorised as mild, moderate or severe. Symptoms of overdosage usually appear 3-6 days after treatment with human chorionic gonadotrophin.

Mild hyperstimulation - Symptoms include some abdominal swelling and pain; ovaries enlarged to about 5 cm diameter. Therapy - rest; careful observation and symptomatic relief. Ovarian enlargement declines rapidly.

Moderate hyperstimulation - Symptoms include more pronounced abdominal distension and pain; nausea; vomiting; occasional diarrhoea; ovaries enlarged up to 12 cm diameter. Therapy - bed rest; close observation especially in the case of conception occurring, to detect any progression to severe hyperstimulation. Pelvic examination of enlarged ovaries should be gentle in order to avoid rupture of the cysts. Symptoms subside spontaneously over 2-3 weeks.

Severe hyperstimulation - This is a rare but serious complication - symptoms include pronounced abdominal distension and pain; ascites; pleural effusion; decreased blood volume; reduced urine output; electrolyte imbalance and sometimes shock; ovaries enlarge to in excess of 12 cm diameter. Therapy - hospitalisation; treatment should be conservative and concentrate on restoring blood volume and preventing shock. Acute symptoms subside over several days and ovaries return to normal over 20-40 days if conception does not occur - symptoms may be prolonged if conception occurs.

INCOMPATIBILITIES :
No drug incompatibilities have been reported for **HuMoG**. It should not be mixed with other drugs in the same ampoule or syringe.

STORAGE :
Vials of **HuMoG** should be stored between 20C - 80C. Do not freeze.Protect from light.Reconstituted solution of **HuMoG** should be used immediately after preparation. Discard any unused portion.

a) **PRESENTATION :**

HuMoG is supplied in vial containing sterile, freeze dried white powder having 75 I.U. / 150 I.U. activity of each FSH and LH. Each vial is accompanied by an ampoule containing 1ml of Sodium Chloride Injection B.P.

b) **PRODUCT DESCRIPTION :**

Before reconstitution :

Almost white or slightly yellow powder or cake.

After reconstitution :

Clear colourless solution.

Sodium Chloride - clear, colourless solution.

SHELF LIFE :

36 months.

Marketing Authorization Holder :

FIRSTLINE PHARMACEUTICAL SDN BHD

No.3, JLN 19/1, 46300, P.J, Selangor.

Manufactured in India by :

BHARAT SERUMS AND VACCINES LIMITED

Plot No. K-27, Additional M.I.D.C, Ambernath (E) -421 501