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

HIGHLY PURIFIED MENOTROPHINS FOR INJECTION B.P.
(HUMAN MENOPAUSAL GONADOTROPHIN INJECTION)

karma-HMG (FREEZE DRIED)

for i.m. / s.c. Injection

COMPOSITION:
Each vial contains:
Highly Purified Menotrophins B.P. equivalent to activity of:
Follicle stimulating Hormone.....75 I.U. / 150 I.U.
Luteinizing Hormone.....75 I.U. / 150 I.U.

Added substance: Mannitol B.P.
Di-sodium Hydrogen Phosphate B.P.
Sodium Dihydreogen Phosphate B.P.

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.

PROPERTIES:
karma-HMG (Human Menopausal Gonadotrophin) is a hormonal substance containing FSH and LH in a ratio of 1:1. In the female, karma-HMG 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, karma-HMG stimulates the spermatogenesis by acting on the production of the androgen-binding protein in the seminiferous tubules of the sertoli cells.

INDICATIONS:
Women:
karma-HMG and subsequently karma-HCG (Chorionic Gonadotrophin Injection) are indicated for the induction of ovulation in the amenorrhoeic patient or anovulatory women with regular or irregular cycles.

Men:
karma-HMG with concomitant karma-HCG (Chorionic Gonadotrophin Injection) therapy is indicated for the stimulation of spermatogenesis in men who have primary or secondary Hypogonadotrophic hypogonadism.

DOSAGE & ADMINISTRATION:
karma-HMG is given by intramuscular injection. The powder for injection should be reconstituted with the Sodium Chloride Injection immediately prior to use. Upto 5 vials of karma-HMG may be dissolved in 1 ml of Sodium Chloride Injection. Discard any unused portion.

Women:
The object is to develop a single matured Graffian follicle with individually tailored doses of karma-HMG over several days and to give karma-HCG (Chorionic Gonadotrophin Injection) to release the ovum. Follicular development is judged by the concentration of oestrogen, measured in blood or urine. Clinical assessment of the response including pelvic examination and cervical mucus studies should also be performed. karma-HMG administration should continue until an adequate oestrogen level is achieved.

If the oestrogen values are less than either 180nmol/24hr. (50 µg/24hr) for tested urinary oestrogen or 1100 pmol/L (300pg/ml) for plasma 17β-oestradiol follicular development may be inadequate. Conversely, if the levels are higher than either 514nmol/24hr (140µg/24hr) for total urinary oestrogens or 3000 pmol/L (800pg/ml) for plasma 17β-oestradiol, there is an increased risk of ovarian hyperstimulation and karma-HCG should be withheld. The optimal time for karma-HCG (Chorionic Gonadotrophin Injection) administration is the day of the urinary oestrogen peak or the day after the plasma 17β-oestradiol peak. In the anovulatory patient the stimulated follicles will not liberate ova spontanously. Follicular rupture had to be achieved by injecting karma-HCG (Chorionic Gonadotrophin Injection) which stimulates the normal surge of LH at ovulation.

If the patient wishes to conceive, she is recommended to have coitus on the day when karma-HCG (Chorionic Gonadotrophin Injection) is given and on the following day. The dose of karma-HMG required to evoke the desired response is critical and varies both from patient to patient and in the same patient at different times. Monitoring by hormones assay is therefore essential.

Two dosage schedules may be employed:
Schedule 1: Alternate day therapy
Three equal doses of karma-HMG are given on alternate days. In menstruating woman the initial dose of karma-HMG should be given on day 7, 8 or 9 of the cycle. A single dose of karma-HCG (Chorionic Gonadotrophin Injection) 10000 I.U. is given one week after the first injection of karma-HMG provided the clinical and biochemical responses are adequate and not excessive.
Schedule 2: Daily therapy
Daily injections of karma-HMG are given until an adequate response is achieved. This is judged on the basis of daily oestrogen determinations. In the absence of a response, the dose of karma-HMG may be increased or the course abandoned. A single karma-HCG (Chorionic Gonadotrophin Injection) of 10000 I.U. is administered 24 - 28 hours after the last dose of karma-HMG. Schedule 2 is most commonly used.

Men:
Treatment should begin with karma-HCG (Chorionic Gonadotrophin Injection) 2000 I.U. 2–3 times a week to produce evidence of adequate masculinisation. If the response to karma-HCG (Chorionic Gonadotrophin Injection) is only androgenic, karma-HMG (1 vial 3 times a week) and karma-HCG (Chorionic Gonadotrophin Injection) 2000 I.U. (twice a week) are required to be administered.

CONTRA-INDICATIONS AND WARNINGS:
Women:
karma-HMG therapy is precluded when an effective response cannot be obtained e.g. Ovarian dysgenesis, Absence of uterus, Premature menopause, Tubular occlusion.

Men:
Patients with elevated endogenous FSH levels indicative of primary testicular failure are usually unresponsive to karma-HMG and karma-HCG (Chorionic Gonadotrophin Injection) therapy.

Appropriate treatment should first be given for hypothyroidism, adrenocortical deficiency, hyperprolactinaemia or pituitary tumour. An acceptable semen analysis should be available before karma-HMG treatment.

Adherence to the recommended dosage and monitoring schedules will minimise the possibility of ovarian hyperstimulation. Excessive oestrogenic response to karma-HMG do not generally give rise to significant side effects unless karma-HCG (Chorionic Gonadotrophin Injection) is given to induce ovulation. Hormone assays will detect an excessive oestrogen response to karma-HMG and karma-HCG (Chorionic Gonadotrophin Injection). In such cases karma-HMG administration should be withheld. The incidence of multiple births following karma-HMG / karma-HCG (Chorionic Gonadotrophin Injection) therapy has been variously reported between 10% and 40%. However, the majority of multiple conceptions are twins. Pregnancy wastes by abortion is higher than in a normal population but comparable with the rates in woman with other fertility problems. The risks of congenital abnormalities are not increased by karma-HMG.

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 karma-HMG and karma-HCG (Chorionic Gonadotrophin Injection) may cause gynecomastia.

STORAGE:
Vials of karma-HMG should be stored between 2°C - 8°C. Do not freeze. Solution reconstituted should be used immediately. Discard any unused portion.

PRESENTATION:
karma-HMG is available in sterile freeze dried form as a white powder in vials containing 75 I.U. / 150 I.U. of each FSH and LH activity.

SHELF LIFE:
Sealed and unopened containers, when stored as recommended have a shelf life of 36 months from date of manufacturing.

Keep out of reach of children.

Manufactured by:
BSV BioScience GmbH
Germany

Marketed by:
karma Pharmatech GmbH
Germany