Fostimon®

Highly purified Human urofollitrophin (FSH) for intramuscular injections

IBSA

Composition

1 vial of active ingredient contains:

Active ingredient:
human follicle stimulating hormone (Urofollitrophin, FSH) 75 or 150 I.U.

Excipients: Mannitol.

Solvent: Physiological solution.

Properties/Effects

Urofollitrophin (FSH) is a hormone secreted by the gonadotropic cells of the anterior lobe of the pituitary gland.
Human urofollitrophin is a hormone preparation containing highly purified FSH. The active ingredient is extracted from the urine of postmenopausal women and then freed of its contents of LH.
The secretion of FSH is permanent in men and cyclic in women, occurring during both the follicular and luteal phases of a normal menstrual cycle.
FSH stimulates the maturation and functioning of somatic cells associated with gametogenesis (Sertoli and granulose cells). Hence, the endometrium is induced to proliferate and enables the implantation and nidation of a fertilized ovum.

Pharmacokinetic

After intramuscular administration, FSH is excreted in two phases.
The half–life of the first phase is of 4 hours, whereas that of the second phase is of about 70 hours.
The renal excretion of FSH in its intact biological and immunological form is irrelevant.

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Indications/Directions for use

A treatment with FSH, followed by the administration of human chorionic gonadotrophin (HCG) is indicated to induce ovulation in infertile women with hormone imbalance, characterized by an abnormal and persistent increase of LH level in comparison with that of FSH:

- polycystic ovary syndrome
- amenorrhea
- anovulatory cycles
- luteal insufficiency (with a high LH: FSH ratio).

FSH offers good therapeutic prospects for patients whose imbalance of LH: FSH ratio has to be adjusted, avoiding an exogenous supply of LH.
FSH may be used alone or in concomitance with human menopausal gonadotrophin (HMG) in order to stimulate a multiple follicular growth in patients enrolled in a medically assisted conception program (IVF-ET, GIFT).

Administration
Fostimon is administered as intramuscular injections only.
The solution should be reconstituted immediately before use with an ampoule of solvent.

Dosage/Usage

A treatment with gonadotrophins should be performed only by a specialist physician, with experience in the diagnosis and treatment of fertility problems. Any other possible cause of infertility should be excluded first (mechanical, immunological and andrological).

Ovulation induction: the aim of the treatment is to bring a single Graaf follicle to maturation within a few days, by means of individually adapted doses of Fostimon. Subsequently, ovulation is induced with an injection of human chorionic gonadotrophin (HCG).

The treatment involves 2 phases:

First phase: administration by i.m. route of 1 to 2 vials of Fostimon 75 I.U. daily.
The follicular maturation is assessed by hormonal controls and a clinical examination. Hormonal controls include the assay of blood (or urinary) oestrogens. The clinical examination includes the basal body temperature curve, ferning of the cervical mucus and the determination of the follicle size by ultrasonography. The administration of Fostimon must be pursued until the oestrogen ratio and the follicle size show that the patient is in the pre–ovulatory phase:
Plasmatic oestrogens 300–800 pg (1,1–2,9 pMol)/ml.
Average diameter of the dominant follicle 18–22 mm.
Cervical score according to Insler ≥ 8 points out of 12.
However, it is unadvisable to administer Fostimon for more than 10 to 12 consecutive days.
In case of excessive response, the treatment must be discontinued and HCG must not be injected (see "Precautions").
The treatment will be resumed in the following cycle, at a lower dosage than in the previous one.

Second phase: once the pre–ovulatory phase is evident, ovulation is induced with an injection of 5000 to 10000 I.U. of HCG, given a day after the last injection of Fostimon.
Ovulation generally takes place 32 to 48 hours later. In case of failure, the administration of HCG can be repeated a day after the first injection.
However, a total administration of 3 injections for 3 consecutive days must not be exceeded.
The patient should be recommended to have daily intercourse, beginning on the day prior to the administration of HCG, until ovulation occurs. The rise of basal temperature should confirm it. If pregnancy does not ensue in spite of ovulation, the treatment can be repeated following the same scheme for at least two courses of treatment.
A course of treatment at higher doses should be carried out only in case of persistent failure and under a strict ultrasonographic and endocrinologic monitoring. The highest daily dose should not exceed 450 I.U. of FSH (6 vials of Fostimon 75 I.U. or 3 vials of 150 I.U.)

Induction of a multiple follicular growth, during a medically assisted conception program:
The dose of Fostimon has to be adapted to each patient according to the results given daily by the hormone controls and by the echography.

1st phase: inject 150 to 300 I.U. of Fostimon i.m. daily, starting on the 3rd day of the cycle and until a sufficient follicle growth is obtained. If Fostimon is used alongside HMG, the dose of the former will be reduced accordingly.

2nd phase: the ovulation is induced by an injection of 5000 to 10000 I.U. of HCG.

Use restrictions

Contraindications
The patients must be carefully selected, in order to rule out all cases whose pathology or particular conditions do not guarantee a successful therapy.

This is applicable in the following cases:

- pregnancy,

- premature menopause,
- sterility without any impairment of normal follicular maturation (e.g. due to tubal or cervical factors), except patients who take part in an in-vitro fertilization program,
- ovarian cysts not due to polycystic ovary syndrome,
- gynecological bleeding of undetermined origin,
- hypergonadotropic ovarian insufficiency,
- hyperprolactinaemia,
- endocrinopathy of thyroidal or adrenal origin,
- ovarian, uterine or breast carcinoma,
- pituitary gland or hypothalamus tumor.

The partner's fertility potential should be assessed prior to the start of the treatment.

Precautions:
FSH (Fostimon) and HCG are highly effective drugs.
They must be administered with caution and at an appropriate dosage, in order to avoid ovarian hyperstimulation and multiple pregnancies.
Since the presence of LH in FSH is extremely low, the risk of hyperstimulation is comparable to the possible risk (very low) of a treatment with HMG.
However, the patient should be submitted to an endocrinologic and clinical examination at least every other day during the whole course of treatment and for two weeks following the end of it.
An excessive oestrogen reaction due to FSH does not generally cause any symptom of hyperstimulation.
It is only after the administration of HCG that hyperstimulation may occur.
If the hormone dosage shows an excessive oestrogen reaction or if clinical or ultrasonographic signs of ovarian hyperstimulation should occur, the treatment with Fostimon must be immediately stopped and HCG must not be injected (see "Dosage/Usage").
The clinical signs of ovarian hyperstimulation in mild cases are: abdominal pain or abdominal tension with ovarian enlargement. In moderate to severe cases the clinical signs are: sudden and marked ovarian hypertrophy, ascites with or without pleural effusion and haemodynamic disorders, rupture of ovarian cysts followed by peritonitis.
Symptoms of hyperstimulation generally appear 4 to 8 days after the administration of HCG.
For this reason the patient must be kept under control for at least 2 weeks after the last injection.
However, if symptoms similar to those of hyperstimulation should occur only 3 weeks or more after the end of the therapy, their origin should be ascribable to an imminent abortion or to an extra-uterine pregnancy.
In case of a mild hyperstimulation, a careful examination of the patient should be sufficient.
On the other hand, in case of ascites or severe complications, the patient must be hospitalized and submitted to an electrolythic and haemodinamic control.
In rare cases, an ovarian hyperstimulation syndrome with acute ovarian hypertrophy can be accompanied by fluid loss in the abdomen and thorax, as well as by more serious thromboembolic complications.
The latter may occur in rare cases, independently from an ovarian hyperstimulation syndrome.
Women in superovulation treatment have a higher risk of developing a hyperstimulation, due to an excessive oestrogen response or a multifollicular development.
The ponction of all follicles before ovulation may reduce the onset of hyperstimulation.
The risk of hyperstimulation is insignificant if the recommended posology is followed and the necessary precautions taken.
The patient should be informed, before the treatment with gonadotrophins that such therapy increases the risk of multiple pregnancy and spontaneous abortion.
However, there is no evidence that the risk of foetus malformations is higher, in comparison with births issued from spontaneous pregnancies.

Pregnancy/Lactation
Pregnancy category: X.
There is evidence of a foetal risk, based on human or animal experience, and the administration of this drug to pregnant women is too risky, in comparison with the possible benefits.
The drug is contraindicated for pregnant women.
It is unknown whether FSH penetrates into milk and the effects it can have on breast-fed babies.
This drug is contraindicated for lactating women.

Side effects
Nausea, vomit, fever, articular pain, cutaneous rash, breast tenderness and irritation at the site of the injection have been observed in very rare cases.
All severe complications occasioned by a treatment with gonadotrophins are generally due to ovarian hyperstimulation (see paragraph "Precautions" and "Contraindications").

Interactions
No clinically significant interactions have been reported with the use of Fostimon. The concomitant treatment of Fostimon and clomiphene citrate can increase the follicular response whereas the concomitant use of a hypophisary desensibilisation with a GnRH agonist may require the increase of the posology of Fostimon in order to obtain an adequate ovarian response.
No drug interaction has been reported.
Fostimon must not be mixed with other drugs in the same syringe.

Overdosage
The effects of an overdosage with Fostimon are unknown.
However, ovarian hyperstimulation syndrome cannot be ruled out (see "Precautions").

Other information
Storage
Ampoules of Fostimon must be stored at a temperature lower than 25°C.
Fostimon must not be used beyond the expiry date indicated on the package.
Once reconstituted in solution, Fostimon must be used immediately.

Package presentation
Vials 75 I.U. with the lyophilized substance + ampoule of solvent:
1 and 10.
Vials 150 I.U. with lyophilized substance + ampoule of solvent:
1 and 10.

Information update
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