LPIS00227C-1

# Follitropin alfa Rx

## Follitrope™

(Recombinant Human Follicle Stimulating Hormone(FSH))

**COMPOSITION**

Each syringe of Follitropin alfa (Follitrope™) Inj. contains :

| Active ingredient : Recombinant human follitropin alfa : | 75 IU /0.15 mL | 150 IU /0.3 mL | 225 IU /0.45 mL | 300 IU /0.6 mL |
|---|---|---|---|---|

Excipients : Glycine, Methionine, Polysorbate 20, Monobasic sodium phosphate, Dibasic sodium phosphate, Sodium hydroxide, Phosphoric acid, Water for injection.

**DESCRIPTION**

Colorless or light yellow solution for injection in prefilled syringe.

**INDICATIONS**

Treatment of female infertility in the following clinical situations:
Controlled ovarian hyperstimulation to induce the development of multiple follicles in medically assisted reproduction program (e.g. in vitro fertilization (IVF), gamete intra-fallopian transfer (GIFT) and zygote intra-fallopian transfer (ZIFT), intracytoplasmic sperm injection (ICSI)).
Anovulation in Clomiphene-resistant anovulatory infertility women (WHO Group II, including polycystic ovarian disease(PCOD))

**DOSAGE AND MODE/ROUTE OF ADMINISTRATION**

Treatment with Follitropin alfa (Follitrope) should be initiated under the supervision of a physician experienced in the treatment of fertility problems.
Follitropin alfa (Follitrope) is intended for subcutaneous or intramuscular administration.
*Women undergoing ovarian stimulation for multiple follicular development prior to in vitro fertilization or other assisted reproductive technologies:*
Various stimulation protocols are applied in order to suppress the endogenous LH surge and to control tonic levels of LH. A commonly used regimen for hyperovulation involves the administration of 150~300 IU of Follitropin alfa (Follitrope) daily, commencing on days 2 to 5 of the cycle. Treatment is continued until adequate follicular development has been achieved (as assessed by monitoring of serum oestrogen levels and/or ultrasound examination), with the dose adjusted according to the patients' response, to usually not higher than 450 IU daily. In general, adequate follicular development was achieved on average by the tenth day of treatment. A single injection of up to 10,000 IU hCG is administered 48 hours after the last Follitropin alfa (Follitrope) injection to induce final follicular maturation.

*Women with anovulation (including PCOD):*
The object of Follitropin alfa (Follitrope) therapy is to develop a single mature Graafian follicle from which the ovum will be liberated after the administration of hCG.
Follitropin alfa (Follitrope) may be given as a course of daily injections. In menstruating patients treatment should commence within the first 7 days of the menstrual cycle.
Treatment should be tailored to the individual patient's response as assessed by measuring follicle size by ultrasound and/or oestogen secretion. A commonly used regimen commences at 75-150 IU FSH daily and is increased by 75 IU at 7 or preferably 14 day intervals if necessary, to obtain an adequate, but not excessive, response. The maximal daily dose is usually not higher than 225 IU FSH. If a patient fails to respond adequately after 4 weeks of treatment, that cycle should be abandoned and the patient should recommence treatment at a higher starting dose than in the abandoned cycle.
When an optimal response is obtained, a single injection of 5,000 IU or up to 10,000 IU hCG should be administered 24-48 hours after the last Follitropin alfa (Follitrope) injection. The patient is recommended to have coitus on the day of, and the day following, hCG administration. Alternatively intrauterine insemination (IUI) may be performed.
If an excessive response is obtained, treatment should be stopped and hCG withheld. The treatment should recommence in the next cycle at a dosage lower than that of the previous cycle.

**WARNINGS AND PRECAUTIONS**

**1. Contra-indications**

1) Tumors of the ovary, breast, uterus, hypothalamus or pituitary gland
2) Pregnancy and lactation
3) Undiagnosed vaginal bleeding
4) Hypersensitivity to the active substance or to any of the excipients
5) Primary ovarian failure
6) Ovarian cysts or enlarged ovaries, not related to polycystic ovarian disease (PCOD)
7) Malformations of the sexual organs incompatible with pregnancy
8) Fibroid tumors of the uterus incompatible with pregnancy
9) The presence of uncontrolled non-gonadal endocrinopathies (e.g. thyroid, adrenal or pituitary disorders).

**2. Warnings**

1) 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.
2) The diagnosis of ovarian hyperstimulation may be confirmed by ultrasound examination. Ultrasonographic assessment of follicular development, and determination of oestradiol levels should be performed prior to treatment and at regular intervals during treatment. If unwanted ovarian hyperstimulation occurs, the administration of FSH should be discontinued and hCG must be withheld, because it may induce the ovarian hyperstimulation syndrome (OHSS). Clinical symptoms and sign of mild ovarian hyperstimulation syndrome are abdominal pain, nausea, vomitting and weight gain. In rare cases, severe ovarian hyperstimulation syndrome can happen characterized by large ovarian cysts (prone to rupture), ascites, often hydrothorax, which may be life-threatening. In rare instances, venous or arterial thromboembolism may occur in association with OHSS. But if hCG administration is withheld and intercourse is avoided at least for 4 days, excessive estrogen response does not cause ovarian hyperstimulation.
The combination of both ultrasound and serum estradiol measurement are useful for monitoring the development of follicles, for timing of the ovulatory trigger, as well as for detecting ovarian enlargement and minimizing the risk of the Ovarian Hyperstimulation Syndrome and multiple gestation.
In anovulation, the risk of OHSS and multiple pregnancy is increased by high concentration of serum oestradiol and a number of matured follicles. Prior to therapy with Follitropin alfa (Follitrope), patients should be informed of the duration of treatment and monitoring of their condition that will be required. To minimize ovarian hyperstimulation and multiple pregnancy, monitoring is required.
3) There were no reports of hypersensitivity of human FSH, but the possibility of anaphylaxis response is present. The first injection of Follitropin alfa (Follitrope) should be performed under direct medical supervision.
4) Rates of pregnancy loss in women undergoing assisted reproduction techniques, patients treatmented with FSH are higher than in the normal population.

**3. Adverse Drug Reactions**

1) Unwanted ovarian hyperstimulation is observed.
2) Clinical use of Follitropin alfa (Follitrope) by the intramuscular or subcutaneous routes may lead to local reactions at the site of injection such as bruising, pain, swelling and itching, the majority of which are mild and transient in nature. Systemic reaction was not observed.
3) A slightly increased risk of ectopic pregnancy and multiple pregnancies can be seen.
4) In rare instances, thromboembolism can be associated with hMG/hCG therapy. This may also occur with Follitropin alfa (Follitrope)/hCG therapy.
5) Most common undesirable effects during the clinical test are headache, abdomen enlarged and displeasure. And fatigue, dizziness, nausea, side abdomen pain, ovarian hyperstimulation and fever are also reported.

**4. Interaction**

1) Concomitant use of Follitropin alfa (Follitrope) and Clomiphene citrate may enhance the follicular response.
2) After pituitary desensitization induced by a Gonadotropin Release Hormone(GnRH) analogue, a higher dose of Follitropin alfa (Follitrope) may be necessary to achieve an adequate follicular response.
3) No drug/drug interaction studies have been performed.

**5. Pregnancy and lactation**

Follitropin alfa (Follitrope) must not be used during pregnancy and lactation.

**6. Effects on ability to drive and use machines**

No effects on ability to drive and use machines have been observed.

**7. Overdose and Treatment**

No data on acute toxicity of Follitropin alfa (Follitrope) in humans is available, but the acute toxicity of Follitropin alfa (Follitrope) and of urinary gonadotropin preparations in animal studies has been shown to be very low. Very high dose of FSH may lead to hyperstimulation of the ovaries.

**8. Instruction for use, handling and disposal**

1) Do not use if the solution contains particles or the solution is not clear.
2) Once the syringe opened, it should be administered immediately.
3) Self-administration Instruction
Inject the amount of medication that was prescribed by your doctor. The next injection should be done at the same time the next day.
① Wash your hands with water.
② Prepare alcohol swabs, the prefilled syringe of Follitropin alfa (Follitrope) for administration.
③ Choose an injection site. Your doctor or nurse will advise you where to inject. You should vary the injection site with each injection.
④ Clean the injection site with an alcohol swab. Let the alcohol dry before proceeding. Hold the syringe in the hand you will use to inject Follitropin alfa (Follitrope). Use the other hand to pinch the skin a little.
⑤ Insert the needle at an angle (45-90 degrees) into the skin. Slowly push down on the plunger all the time until all the Follitropin alfa (Follitrope) is injected.
⑥ Immediately withdraw the needle and press the injection site with an alcohol swab for several seconds.
⑦ Discard used syringes immediately after injection.
⑧ Any remaining solution should be discarded.

**HOW SUPPLIED**

75 IU, 150 IU, 225 IU, 300 IU prefilled syringe / pack

**STORAGE CONDITION**

Store between 2~8℃ in hermetic container protected from light. Avoid freezing.

**SHELF LIFE**

36 months

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
Keep out of reach of children.
For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.
Registration number: BR-1247 (75 IU), BR-1248 (150 IU), BR-1249 (225 IU), BR-1250 (300 IU)
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