Alfagon™

Recombinant Human Follicle Stimulating Hormone
(Follitropin Alfa) Injection

Presentation
Alfagon™ 75 Injection: Each pre-filled syringe contains Recombinant Human Follicle Stimulating Hormone (Follitropin Alfa) INN 75 IU in 0.12 mL solution for injection.
Alfagon™ 150 Injection: Each pre-filled syringe contains Recombinant Human Follicle Stimulating Hormone (Follitropin Alfa) INN 150 IU in 0.24 mL solution for injection.

Description
Alfagon™ is a human follicle stimulating hormone (FSH) preparation of recombinant DNA origin which consists of two non-covalently linked, non-identical glycoproteins designated as the α- and β-subunits. The α- and β-subunits have 92 and 111 amino acids, respectively, and their primary and tertiary structure are indistinguishable from those of human follicle stimulating hormone. Recombinant FSH production occurs by genetical modification in bioreactors. Purification by immunochromatography using an antibody specifically binding FSH results in a highly purified preparation with a consistent FSH isoform profile, and a high specific activity. The in vivo biological activity of follitropin alfa has been calibrated against the first International Standard for Recombinant Human Follicle Stimulation Hormone established in 1995 by the Expert Committee on Biological Standards of the World Health Organization.

Indications and Usage
Alfagon™ is a gonadotropin indicated for:
Women:
- Induction of ovulation and pregnancy in oligo-anovulatory infertile women for whom the cause of infertility is functional and not due to primary ovarian failure.
- Development of multiple follicles in ovulatory infertile women as part of Assisted Reproductive Technology (ART) cycles.

Men:
- Induction of spermatogenesis in infertile men with primary and secondary hypogonadotropic hypogonadism for whom the cause of infertility is not due to primary testicular failure.

Dosage and Administration:
Induction of Ovulation
- Initial starting dose of the first cycle: 75 International Units of Alfagon™ per day for 14 days, administered subcutaneously
- Individualize doses after 14 days
- Do not administer doses greater than 300 International Units per day

Development of Multiple Follicles in Assisted Reproductive Technology (ART)
- Initial starting dose of the first cycle: 150 International Units per day, administered subcutaneously
- Dosage adjustments after 3 to 5 days and by 75 to 150 International Units at each adjustment
- Do not administer doses greater than 450 International Units per day

Males with Hypogonadotropic Hypogonadism and Azoospermia
- Use in conjunction with Human Chorionic Gonadotropin.
- Prior to concomitant therapy with Alfagon™ and Human Chorionic Gonadotropin, pretreat with 1,000 to 2,250 units of Human Chorionic Gonadotropin alone 2-3 times per week to achieve normal serum testosterone levels, which may take 3 to 6 months.
- After normalization of serum testosterone, administer 150 International Units of Alfagon™ subcutaneously three times a week and 1,000 units of Human Chorionic Gonadotropin (or the dose required to maintain serum testosterone levels within the normal range) three times a week.

Side Effects:
- The most common adverse reactions (≥5%) in ovulation induction include: ovarian cyst, headache, abdominal pain, Ovarian Hyperstimulation Syndrome (OHSS), nausea, flatulence, pain and intermenstrual bleeding.
- The most common adverse reactions (≥5%) in development of multiple folllicles in ART include: headache, nausea,pelvic pain and abdominal pain.
- The most common adverse reactions (>5%) in hypogonadotropic hypogonadal men participating in induction of spermatogenesis include: acne, injection site pain, fatigue, gynecomastia and seborrhea.

Precautions:
- Hypersensitivity Reactions and Anaphylaxis: If occurs, initiate appropriate therapy including supportive measures and discontinue
- Ovarian Hyperstimulation Syndrome: If serious, stop gonadotropins including hCG and determine if the woman needs to be hospitalized. Treatment is primarily symptomatic and consists of bed rest, fluid and electrolyte management and analgesics
- Pulmonary and Vascular Complications: In women with recognized risk factors, the benefits of induction of ovulation and ART need to be weighed against the risks. During or after use of discontinued Alfagon™, monitor for venous or arterial thromboembolic events
- Ovarian Torsion: Early diagnosis and immediate detorsion limit damage to the ovary due to reduced blood supply
- Abnormal Ovarian Enlargement: If the ovaries are abnormally enlarged on the last day of discontinue Alfagon™ therapy, inform women not to administer hCG and to avoid intercourse
- Multi-fetal Gestation and Births: The rate of multiple births is dependent on the number of embryos transferred. Advise the woman and her partner of the potential risk of multi-fetal gestation and birth before beginning therapy with Alfagon™
- Embryofetal Toxicity: Inform women that the incidence of congenital malformations (birth defects) after some Assisted Reproductive Technology [(ART) specifically in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI)] may be slightly higher than after spontaneous conception. There is no evidence that the use of gonadotropins during IVF or ICSI is associated with an increased risk of congenital malformations
- Ectopic Pregnancy: Advise women who become pregnant following ART and have: abdominal/pelvic pain (particularly on one side); shoulder, neck or rectal pain; and nausea and vomiting to seek immediate medical attention. Confirm the presence of an intrauterine pregnancy early by β-hCG testing and transvaginal ultrasound
- Spontaneous Abortion: The risk of spontaneous abortion (miscarriage) is increased with gonadotropin products however, causality has not been established
- Ovarian Neoplasm: Both benign and malignant ovarian neoplasms are reported in women who have had multiple drug therapy for controlled ovarian stimulation however, causality has not been established

Contraindications
Alfagon™ is contraindicated in women and men who exhibit:
- Prior hypersensitivity to recombinant FSH products
- High levels of FSH indicating primary gonadal failure
- Uncontrolled non-gonadal endocrinopathies
- Sex hormone dependent tumors of the reproductive tract and accessory organs
- Tumors of pituitary gland or hypothalamus

Alfagon™ is also contraindicated in women who exhibit:
- Abnormal uterine bleeding of undetermined origin
- Ovarian cyst or enlargement of undetermined origin

Drug Interactions
No drug-drug interaction studies have been conducted.

Use in Pregnancy & Lactation
Pregnancy Category: X
Recombinant FSH must not be used during pregnancy and lactation.

Overdosage
Ovarian hyperstimulation syndrome (OHSS) and multiple gestations have been observed in women with Alfagon™ overdosage

Storage
- **Store at 2°C-8°C.**
- Do not keep in deep freeze.
- Keep out of reach of children.

Commercial Pack
Alfagon™ 75 Injection: Each pack contains 1 pre-filled syringe of 75 IU Recombinant Human Follicle Stimulating Hormone (Follitropin Alfa).
Alfagon™ 150 Injection: Each pack contains 1 pre-filled syringe of 150 IU Recombinant Human Follicle Stimulating Hormone (Follitropin Alfa).

Manufactured by
Incepta Pharmaceuticals Ltd
Dhamrai Unit, Dhaka, Bangladesh

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