Foligen™

Follicle Stimulating Hormone (Urofollitropin BP) for Injection

DESCRIPTION

Foligen™ is a preparation of highly purified human follicle stimulating hormone (FSH). Human FSH is a gonadotrophin and consists of two non-covalently linked glycoproteins designated as the α and β subunits. The α subunit has 92 amino acids of which two are modified by attachment of carbohydrates. The β subunit has 111 amino acids of which two are modified by attachment of carbohydrates. Follicle Stimulating Hormone (FSH) is essential for normal female and male gamete growth and maturation, and gonadal steroid production. Deficiencies in the endogenous production of FSH may lead to infertility. FSH is critical at the onset and duration of follicular development, and consequently for the timing and number of follicles reaching maturity in females. Follicle stimulating hormone produces its effect by binding to its specific receptors present on the ovarian cell membrane. Binding of FSH to its receptor leads to the formation of hormone receptor complex. The formation of this complex leads to biochemical changes in the ovarian follicle, present in the ovary. The ovarian follicles mature and release a mature ovum in the fallopian tube for fertilization. **Foligen™** administered for 7 to 12 days produce ovarian follicular growth in women who do not have primary ovarian failure. Treatment with **Foligen™** in most instances result only in follicular growth and maturation. When sufficient follicular maturation has occurred, hCG must be given to induce ovulation. FSH may also be used to cause the ovary to produce several follicles, which can then be harvested for use in Gamete Intrafallopian Transfer (GIFT) or In Vitro Fertilization (IVF).

INDICATIONS

In the female:

- Induction of ovulation & pregnancy in the anovulatory infertile patient in whom the cause of infertility is functional and not due to primary ovarian failure.
- Development of multiple follicles in the ovulatory patient participating in an Assisted Reproductive Technology (ART) program.
- Used to treat Polycystic Ovarian Syndrome (PCOS) related infertility.

In the male:

- Induction of spermatogenesis in men with primary and secondary hypogonadotrophic hypogonadism in whom the cause of infertility is not due to primary testicular failure.

DOSAGE AND ADMINISTRATION

Method: To prevent painful injections and minimize leakage from the injection site, **Foligen™** should be slowly administered intramuscularly or subcutaneously. The subcutaneous injection site should be alternated to prevent lipoathropy. Any unused solution should be discarded. Subcutaneous injection of **Foligen™** may be carried out by patient or partner, provided that proper instructions are given by the physician. Self-administration of **Foligen™** should only be performed by patients who are well-motivated, adequately trained and with access to expert advice.

Reconstitution: To prepare the solution, inject 1 mL of sterile saline for injection into the vial of 75 IU **Foligen™**. Do not shake, but gently swirl until the solution is clear. Generally **Foligen™** dissolves immediately. Check the liquid in the container; if it is not clear or contains particles, do not use it. For patients requiring a single injection from multiple vials of **Foligen™**, up to 4 vials can be reconstituted with 1 mL sterile saline for injection. This can be accompanied by reconstituting a single vial as described above. Then draw the entire contents of the first vial into a syringe and inject the contents into a second vial of lyophilized Urofollitropin. Gently swirl the second vial, once again checking to make sure the solution is clear and free of particles. This step can be repeated with 2 additional vials for a total of up to 4 vials (300 IU) of 75 IU **Foligen™**.

Dosage in the female:

Infertile patients with oligo-anovulation/ Ovulation Induction:

- Initial starting 150 IU per day for 5 days, administered subcutaneously or intramuscularly
- Individualization of dosing after 5 days
- Dosage adjustments not to occur more frequently than once every 2 days and not to exceed 75 to 150 IU per adjustment
- Do not administer greater than 450 IU per day
- Dosing beyond 12 days is not recommended

Assisted Reproductive Technologies (ART)/In Vitro Fertilization (IVF):

- Initial starting dose of the first cycle – 225 IU per day for 5 days, administered subcutaneously
- Individualization of dosing after 5 days
- Dosage adjustments not to occur more frequently than once every 2 days and not to exceed 75 to 150 IU per adjustment
- Do not administer greater than 450 IU per day
- Dosing beyond 12 days is not recommended

Polycystic Ovarian Syndrome (PCOS) Related Infertility:

Conventional Protocol

Initial daily doses of 75–150 IU FSH are administered intramuscularly with increases of 75 IU FSH every 5–7 days, when needed. Treatment should be discontinued after 35 days of treatment or if the patient was at risk of OSS.

Chronic Low-Dose Protocols

- **Low-dose step-up protocol:** The initial dose of 75 IU/day is maintained for up to 14 days. If no ovarian response is noted after 14 days of 75 IU/day therapy, the daily FSH dose is increased by 37.5 IU. Any further FSH increment thereafter is made by 37.5 IU at weekly intervals to a maximum of 225 IU/day.
- **Low-dose step-down protocol:** The initial dose is 150 IU FSH daily. The dose is then decreased to 112.5 IU per day followed by a further decrease to 75 IU per day 3 days later, which is continued until hCG is administered to induce ovulation.
- **Sequential low-dose protocol, combining step-up and step-down regimens:** The initial dose is 300 IU of FSH on cycle day 3 and no treatment is given for the next 3 days (cycle days 4–6). FSH therapy is reinitiated on cycle day 7 (treatment day 5) by administering 75 IU/day after pertinent ultrasound scanning of the ovaries had been performed. This dose is maintained until cycle day 9 (i.e., 1 week after treatment was initiated) and then follows the low-dose step-up approach.

OR AS DIRECTED BY THE PHYSICIAN.

Dosage in male:

Induction of Spermatogenesis in Men:

- Pretreat with hCG until serum testosterone is in normal range
- Administer 450 IU per week (225 IU twice weekly or 150 IU three times weekly) with hCG 3 times per week
- Do not administer greater than 300 IU 3 times per week
- May administer for up to 18 months

CONTRAINDICATIONS

Human follicle stimulating hormone (hFSH) is contraindicated who exhibit:

- Prior hypersensitivity to hFSH or urofollitropins
- High levels of FSH indicating primary ovarian failure
- Pregnancy
- Presence of uncontrolled non-gonadal endocrinopathies
- Sex hormone dependent tumors of the reproductive tract and accessory organ
- Tumors of pituitary gland or hypothalamus
- Abnormal uterine bleeding of undetermined origin
- Ovarian cysts or enlargement of undetermined origin, not due to polycystic ovary syndrome

SIDE EFFECTS

The most common adverse reactions in ovulation induction include: headache, hot flashes, OHSS, pain, and respiratory disorder.

The most common adverse reactions in ART include: abdominal cramps, abdominal fullness/enlargement, headache, nausea, pelvic pain, and post retrieval pain.

The most common adverse reactions in PCOS include: high levels of activity in the ovaries, pain in the abdomen, swelling in the abdomen, nausea, vomiting, diarrhea, weight gain, difficulty breathing and decreased urination.

The most common adverse reactions in spermatogenesis include: headache, acne, injection site reaction, injection site pain, gynecomastia, rash and dermoid cyst.

PRECAUTIONS AND WARNINGS

Careful attention should be given to the diagnosis of infertility in candidates for follicle stimulating hormone (FSH) therapy. FSH is a potent gonadotrophic substance capable of causing Ovarian Hyperstimulation Syndrome (OHSS) in women with or without pulmonary or vascular complications and multiple births.

- Abnormal Ovarian Enlargement
- Ovarian Hyperstimulation Syndrome
- Pulmonary and Vascular Complications
- Ovarian Torsion
- Multi-fetal Gestation and Birth
- Congenital Malformations
- Ectopic Pregnancy
- Spontaneous Abortion
- Ovarian Neoplasms

Gonadotrophin therapy requires a certain time commitment by physicians and supportive health professionals, and requires the availability of appropriate monitoring facilities. Safe and effective use of FSH in women require monitoring of ovarian response with serum estradiol and vaginal ultrasound on a regular basis. The lowest effective dose should be used.

USE IN PREGNANCY AND LACTATION

Follicle stimulating hormone is contraindicated in pregnancy. It is not known whether this drug is excreted in human milk. Therefore, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

PEDIATRIC USE

Safety and effectiveness in pediatric patients have not been established.

DRUG INTERACTION

No drug/drug interaction studies in humans have been performed.

OVERDOSE

Aside from possible ovarian hyperstimulation and multiple gestations, there is no information on the consequences of acute overdosage with follicle stimulating hormone.

STORAGE CONDITION

Foligen™ sterile lyophilized powder for injection should be stored in refrigerator (2°C-8°C temperature). Do not freeze. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Foligen™ for Injection: Each box contains 1 vial of highly purified human follicle stimulating hormone (Urofollitropin BP) 75 IU (International Unit) and 1 ampoule of 1 mL sterile 0.9% NaCl injection with sterile disposable syringe, ampoule breaker, alcohol pad and first aid band.

SK+F
Manufactured by
ESKAYEF PHARMACEUTICALS LTD.
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