For the use of a Registered Medical Practitioner, Hospital or Laboratory

Endogen® HP

Highly Purified FSH

Urofollitropin for Injection
For Subcutaneous / Intramuscular Injection only

Presentation :

Each ampoule of sterile freeze-dried product contains:

Urofollitropin (FSH) B.P.	75 I.U.
(As Highly Purified Human Follicle Stimulating Hormone)	
Mannitol I.P. 12 mg	
Potassium Dihydrogen orthophosphate B.P.	0.46 mg
Dipotassium Hydrogen orthophosphate B.P.	0.36 mg

Reconstitute with 1 ml of Sodium Chloride injection (0.9% w/v) I.P. provided with this pack.

Each ampoule of sterile freeze-dried product contains:

Urofollitropin (FSH) B.P.	150 I.U.
(As Highly Purified Human Follicle Stimulating Hormone)	
Mannitol I.P.	12 mg
Potassium Dihydrogen orthophosphate B.P.	0.46 mg
Dipotassium Hydrogen orthophosphate B.P.	0.36 mg

Reconstitute with 1 ml of Sodium Chloride injection (0.9% w/v) I.P. provided with this pack.

Drug Description

Endogen-HP is a product containing a highly purified preparation of human follicle stimulating hormone (hFSH) extracted from the urine of postmenopausal women. Human FSH 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.

Endogen-HP is a sterile, lyophilized powder intended for subcutaneous (SC) or intramuscular (IM) injection after reconstitution with Sodium Chloride 0.9% w/v Injection.

Indications & Usage

Ovulation Induction

Endogen-HP administered SC or IM in conjunction with hCG, (Pubergen JO 7500 IU) is indicated for ovulation induction in patients who have previously received pituitary suppression.

Multifollicular Development during ART

Endogen-HP administered SC in conjunction with hCG is indicated for multiple follicular development (controlled ovarian stimulation) during ART cycles in patients who have previously received pituitary suppression.

Selection of Patients

1.Before treatment with Endogen-HP is instituted, a thorough gynecologic and endocrine evaluation must be performed. Except for those patients enrolled in an in vitro fertilization program, this should include a hysterosalp in angiography (to rule out uterine and tubal pathology) and documentation of anovulation by means of basal body temperature, serial vaginal smears, examination of cervical mucus, determination of serum (or urine) progesterone, urinary pregnanediol and endometrial biopsy.

2.Primary ovarian failure should be excluded by the determination of gonadotropin levels.

3.Careful examination should be made to rule out the presence of an early pregnancy.

4.Patients in late reproductive life have a greater predilection to endometrial carcinoma as well as a higher incidence of anovulatory

Clinical Pharmacology

Endogen-HP administered for 7 to 12 days produces ovarian follicular growth in women who do not have primary ovarian failure. Treatment with Endogen-HP in most instances results only in follicular growth and maturation. When sufficient follicular maturation has occurred, hCG (Pubergen JO 7500 IU)must be given to induce ovulation.

Pharmacokinetics

Published clinical data reveals that there is a variation in AUC & Cmax depending on the route of administration. Pharmacokinetic data obtained by SC & IM routes are not bioequivalent.

Absorption

The maximum plasma concentration of FSH was attained at 20.5 and 17.4 hours following SC and IM single dose administration, respectively. However, following multiple dosing, it was attained at approximately 10 hours following both routes of administration.

Distribution

Human tissue or organ distribution of FSH has not been studied

Metabolism

Metabolism of FSH has not been studied for in humans.

Elimination

Published clinical studies have demonstrated the mean elimination half-lives of FSH for SC and IM single dosing are 31.8 and 37 hours, respectively. However, following multiple dosing (X 7 days) they are 20.6 and 15.2 hours for SC and IM, respectively.

Pediatric Populations

Endogen-HP is not indicated in pediatric populations.

Geriatric Populations

Endogen-HP is not indicated in geriatric populations.

Special Populations

The safety and efficacy of Endogen-HP in renal and hepatic insufficiency have not been studied.

Drug Interactions

No drug / drug interaction studies have been conducted for Endogen-HP in humans.

Storage Conditions

Store between 2° C - 8° C. Do not freeze.

Use Immediately after reconstitution.

After reconstitution of Endogen-HP, if the reconstituted solution is not used, do not store, discard the portion.

How Supplied

Box containing 1 Ampoule of sterile freeze-dried Highly Purified Urofollitropin 75 IU + 1 Ampoule of Sodium chloride injection I.P.(0.9 %w/v).

Box containing 1 Ampoule of sterile freeze-dried Highly Purified Urofollitropin 150 IU + 1 Ampoule of Sodium chloride injection I.P. (0.9 %w/v).

® -Regd.Trade Mark

Manufactured in india by :

SANGYO

A Healthcare Unit of UNI-SANKYO LTD

Gaganpahad, R.R. Dist. - 501 323, A.P., India

disorders. Cervical dilation and curettage should always be done for diagnosis before starting Endogen-HP therapy in such patients who demonstrate abnormal uterine bleeding or other signs of endometrial abnormalities.

5.Evaluation of the husband's fertility potential should be included in the workup.

Dosage:

Infertile patients with oligo-anovulation: The dose of Endogen-HP to stimulate development of ovarian follicles must be individualized for each patient. The lowest dose consistent with achieving good results based on clinical experience and reported clinical data should be used. The recommended initial dose of Endogen-HP for patients who have received GnRH agonist or antagonist pituitary suppression is 150 IU daily administered SC or IM for the first 5 days of treatment.

Based on clinical monitoring (including serum estradiol levels and vaginal ultrasound results) subsequent dosing should be adjusted according to individual patient response. Adjustments in dose should not be made more frequently than once every 2 days and should not exceed more than 75 to 150 IU per adjustment. The maximum daily dose of Endogen-HP should not exceed 450 IU and in most cases dosing beyond 12 days is not recommended.

If patient response to Endogen-HP is appropriate, hCG 7500 IU units, Pubergen JO should be given 1 day following the last dose of Endogen-HP .or the follicle attains a size greater than 18 mm. hCG should be withheld if the serum estradiol is greater than 2000 pg/mL, if the ovaries are abnormally enlarged or if abdominal pain occurs, and the patient should be advised to refrain from intercourse. These precautions may reduce the risk of Ovarian Hyperstimulation Syndrome and multiple gestations. Patients should be followed closely for at least 2 weeks after hCG administration. If there is inadequate follicle development or ovulation without subsequent pregnancy, the course of treatment with Endogen-HP may be repeated.

Assisted Reproductive Technologies:

The recommended initial dose of Endogen-HP for patients undergoing IVF and donor egg patients who have received GnRH agonist or antagonist pituitary suppression is 225 IU daily administered SC for the first 5 days of treatment. Based on clinical monitoring (including serum estradiol levels and vaginal ultrasound results) subsequent dosing should be adjusted according to individual patient response. Adjustments in dose should not be made more frequently than once every 2 days and should not exceed more than 75 to 150 IU per adjustment. The maximum daily dose of Endogen-HP given should not exceed 450 IU and in most cases dosing beyond 12 days is not recommended.

Once adequate follicular development is evident, highly purified hCG 7500 IU(Pubergen JO) should be administered to induce final follicular maturation in preparation for oocyte retrieval. The administration of hCG must be withheld in cases where the ovaries are abnormally enlarged on the last day of therapy. This should reduce the chance of developing OHSS.

Side-Effects

- Gastrointestinal Nausea, Vomitting, Abdominal Pain
- Other Symptoms Headache, Pain, Malaise
- In susceptible individuals Ovarian Hyperstimulation Syndrome (OHSS)

Warnings

Endogen-HP drug that should only be used by physicians who are thoroughly familiar with infertility problems.

Overstimulation of the Ovary During Endogen-HP Therapy

Ovarian Enlargement: Mild to moderate uncomplicated ovarian enlargement which may be accompanied by abdominal distension and/or abdominal pain occurs in susceptible individuals treated with follitropin and hCG, and generally regresses without treatment within two or three weeks. In order to minimize the hazard associated with the occasional abnormal ovarian enlargement, which may occur withFSH - hCG therapy, the lowest dose consistent with expectation of good results should be used.

Careful monitoring of ovarian response can further minimize the risk of over stimulation. If the ovaries are abnormally enlarged on the last day of Endogen HP therapy, hCG should not be administered in the course of therapy; this will reduce the chances of development of the Ovarian Hyperstimulation Syndrome. If severe OHSS occurs, treatment must be stopped and the patient should be hospitalized.

Multiple Pregnancies

Multiple pregnancies have occurred following treatment with Endogen-HP SC and IM. The patient and her partner should be advised of the potential risk of multiple births before starting treatment.

Hypersensitivity/Anaphylactic Reactions

Hypersensitivity/anaphylactic reactions associated with follitropins for injection, have been reported in some patients.

Precautions

Laboratory Tests

The combination of both estradiol levels and ultrasonography are useful for monitoring the growth and development of follicles, timing hCG administration, as well as minimizing the risk of the Ovarian Hyperstimulation Syndrome and multiple gestations.
The clinical confirmation of ovulation, is determined by:

a. Arise in basal body temperature,
b. Increase in serum progesterone, and
c. Menstruation following the shift in basal body temperature.

When used in conjunction with indices of progesterone production, sonographic visualization of the ovaries will assist in determining if ovulation has occurred. Sonographic evidence of ovulation may include the following:

a. Fluid in the cul-de-sac,
b. Ovarian stigmata, and
c. Collapsed follicle.

Because of the subjectivity of the various tests for the determination of follicular maturation and ovulation, it cannot be overemphasized that the physician should choose tests with which he/she is thoroughly familiar.

Carcinogenesis and Mutagenesis

Long-term toxicity studies in animals and in vitro mutagenicity tests have not been performed to evaluate the carcinogenic potential of urofollitropin for injection, purified.

Pregnancy & Lactation

Endogen-HP should not be administered during pregnancy. It is not known whether the drug is excreted in breast milk.

Geriatric Patients

Safety and effectiveness in geriatric patients have not been established.

Overdose

Aside from possible ovarian hyperstimulation and multiple gestations, little is known concerning the consequences of acute overdosage with Endogen-HP.

Contraindications

Endogen-HP is contraindicated in women who have:

Ahigh FSH level indicating primary ovarian failure.

- Uncontrolled thyroid and adrenal dysfunction.
- An organic intracranial lesion such as pituitary tumor.
- The presence of any cause of infertility other than anovulation.
- Abnormal bleeding of undetermined origin.
- Ovarian cysts or enlargement not due to polycystic ovary syndrome.
- Prior hypersensitivity to urofollitropins, purified.
- Endogen-HP is contraindicated in women who are pregnant and may cause fetal harm when administered to a pregnant woman. There are limited human data on the effects of Endogen-HP when administered during pregnancy.

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