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

Urofollitropin for Injection B.P.

FOLICULIN

75 I.U. / 150 I.U

(Freeze Dried)

For Subcutaneous / Intramuscular Injection only

Composition:
Each vial contains:
Urofollitropin B.P..... 75 I.U. / 150 I.U.
Excipients :
Mannitol B.P., Sucrose B.P., Sodium Ascorbate B.P., Anhydrous Di-sodium Hydrogen Phosphate B.P. and Phosphoric Acid B.P.

Each vial of ***FOLICULIN*** is accompanied by an ampoule of Sodium Chloride Injection B.P. 1ml.

Properties :
FOLICULIN contains a purified hormone urofollitropin, obtained from Human Menopausal urine having FSH activity of 75 I.U. / 150 I.U. and less than 1 I.U. / 2 I.U. Luteinizing Hormone activity per vial. (Human menopausal gonadotrophins (HMG) exerts both FSH and LH activities. For this reason, HMG is indicated in Hypogonadotropic hypopituitarism (WHO Group I patients), where both gonadotrophin stimulations are needed.)

Patients showing normal or high LH levels (WHO Group II), require preparations without LH activity, this character belongs to FSH.

Pharmacodynamics:
FOLICULIN 75 I.U. contains purified hormone urofollitropin, obtained from Human Menopausal urine having FSH activity of 75 I.U./150 I.U. and less than 1 IU/2 IU Luteinizing Hormone activity per vial Patients showing normal or high LH levels (WHO Group II) , require preparations without LH activity, this character belongs to FSH.

FSH stimulates both the growth and maturation of follicles, it induces secretion of oestrogens and proliferation of the endometrium.

Pharmacokinetics*:*
After multiple intramuscular dosing of Urofollitropin, the maximum plasma concentration of Follicle-stimulating hormone occurs about 10 hours after a dose, and has an elimination half-lifer of about 15 or 20 hours respectively.
Because there are no longer ovarian steroids and inhibin to inhibit LH and FSH secretion, gonadotropin secretion is greatly increased, and the levels of FSH are higher than those of LH in postmenopausal women.
FSH and LH are eliminated in two phases. In both phases the biological half-life of FSH is longer than that of LH.
The gonadotropins of either pituitary or placental origin are effective only if given by injection, usually intramuscularly. The rate at which gonadotropins are cleared from plasma is difficult to measure accurately because of their structural heterogeneity and the background of pulsatile secretion of the endogenous hormones.
The prolonged circulatory life of these glycoprotein hormone relative to many other peptide hormones is a result of their resistance to metabolic degradation in most tissue beds.
Clearance of injected (and presumably of endogenous) glycoprotein hormones is by glomerular

filtration, followed by degradation in the proximal renal tubule or excretion (unchanged) in the urine. Removal of the sialic acid residues results in their rapid and complete clearance by the hepatic reticuloendothelial system.

Indications :
FOLICULIN is indicated for stimulation of follicular growth in infertile women. A course of ***FOLICULIN*** is usually followed by human chorionic gonadotrophin (HCG) to induce ovulation.

FOLICULIN is used :
a) For single follicular development in cases such as hypothalamic pituitary dysfunction (WHO Group II classification), include patients with polycystic ovarian disease.
b) For multiple follicular development (assisted conception techniques); in cases such as tubal occlusion, unexplained infertility and male factor infertility.

Contra-indications :
FOLICULIN is contra-indicated in women who exhibit :
1. High levels of FSH, indicating primary ovarian failure.
2. Uncontrolled thyroid or adrental dysfunction.
3. An organic intracranial lesion such as pituitary tumor.
4. The presence of any cause of infertility other than anovulation unless they are candidates for in vitro fertilization.
5. Ovarian cysts or enlargement not due to ovarian polycystic Ovarian Disease.
6. Prior hypersensitivity to Urofollitropin.
7. ***FOLICULIN*** is contra-indicated in women who are pregnant. There are limited human data on the effects of ***FOLICULIN*** when administered during pregnancy.

Contraindicated for safety reasons in Gynecological hemorrhages of unknown aetiology.'

Warning and Precautions :
Before starting treatment the couple's infertility should be assessed as appropriate and putative contra-indications for pregnancy evaluated.

Adherence to the recommended dosage and monitoring schedules will minimize the possibility of ovarian hyper stimulation syndrome.

Excessive ovarian response to ***FOLICULIN*** treatment does generally not induce significant adverse effects except if HCG is administered for ovulation induction or if pregnancy occurs; ovarian hyper stimulation syndrome occurs usually 1 to 2 weeks following HCG administration and ovulation.

In case of symptoms such as pelvic pain, abdominal distension or ovarian enlargement or if oestrogen assays or ultrasound examinations suggest an excessive oestrogenic response, ***FOLICULIN*** administration should be discontinued and HCG should not be administered and intercourse avoided in order to prevent ovarian hyper stimulation.

Ascites, pericardial effusion, hydrothorax, hemo-concentration, secondary hyperaldosteronism or hypercoagulability might appear. These symptoms should be controlled through appropriate medical measure, including avoidance of unnecessary pelvic examination. In the absence of pregnancy they usually resolve spontaneously with the onset of the menses.

Dosage and Administration :

Dosage:

The dose of ***FOLICULIN*** to produce maturation of Follicle must be individualized for each patient.

It is recommended that initial dose to any patient should be 75 I.U. of ***FOLICULIN*** per day administered subcutaneous for at least 7 days followed by HCG 5000 I.U. to 10000 I.U. one day after last dose of ***FOLICULIN*.**

Courses of treatment should be no longer than 12 days.

If there is evidence of ovulation but no pregnancy, repeat above dosage regimen for atleast 2 or more courses before increasing the dose to ***FOLICULIN*** 150 I.U. per day for 7 days. As stated above this dose should be followed by HCG 5000 I.U. to 10000 I.U. one day after last dose of ***FOLICULIN.*** If evidence of ovulation is present but pregnancy is not sure repeat the same dose for 2 more courses. Doses larger than this are not routinely recommended.

In-vitro Fertilization :

In-vitro Fertilization therapy with ***FOLICULIN*** should be initiated in the early follicular phase (cycle day 2 or 3) at a dose of 150 I.U. per day until sufficient Follicular development is attained. In most cases therapy should not exceed beyond 10 days.

Administration :

Reconstitute the contents of vial containing ***FOLICULIN*** in 1ml of Sodium Chloride Injection and administer subcutaneous immediately. Any unused portion of reconstituted solution should be discarded.

Interaction :

No clinically significant adverse drug/drug or drug/food interactions have been reported during ***FOLICULIN*** therapy. Concomitant use of ***FOLICULIN*** and Clomifene citrate may potentiate the follicular response, where as concurrent use of GnRH agonist induced pituitary desensitization may increase the dosage of ***FOLICULIN*** needed to elicit an adequate ovarian response.

Side Effects :

Local reactions at the injection site, fever and arthralgias have been reported following urofollitropins and Menotropins administration.

Gastrointestinal symptoms may occur as well as bloating of the stomach, pelvic pain or sore breasts. Mild to moderate ovarian enlargement, ovarian cysts may be observed. Severe hyper stimulation syndrome is rare . In rare instances, arterial thromboembolisms have been associated with menotropin human chorionic gonadotrophin therapy.

Pregnancy wastage by miscarriage or abortion is comparable with the rates in women with other fertility problems. Ectopic pregnancy may occur in women with a history of prior tubal disease.

Overdose :

There are no reports of toxic effects occurring as a result of overdosage. However an ovarian hyperstimulation syndrome cannot be ruled out. Aside from possible ovarian overstimulation and multiple gestations, little is known concerning the consequence of acute overdosage with ***FOLICULIN***.

Incompatibilities :
No drug incompatibilities have been reported for ***FOLICULIN*** 75 I.U./150 I.U. It should not be mixed with other drugs in the same ampoules or syringe.

Storage :
Vials of ***FOLICULIN*** Injection packed with 1ml Sodium Chloride Injection B.P. as solvent should be stored between 2^0C - 8^0C. Do not freeze. Protect from light. Reconstituted solution of ***FOLICULIN*** should be used immediately after preparation. Discard any unused portion.

Presentation :
FOLICULIN is supplied in vial containing sterile, freeze dried white to off white powder having FSH activity of 75 I.U. / 150 I.U. Each vial is accompanied by an ampoule containing 1ml of Sodium Chloride Injection B.P.

Date of Revision : April 2011 shelf Life :: 36 months

Marketing Authorization Holder :
FIRSTLINE PHARMACEUTICAL SDN BHD
No.3, JLN 19/1, 46300, P.J, Selangor.

Manufactured in India by :
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