אוגוסט 2022

Luveris 75 IU לובריס 75

powder and solvent for solution for injection

רופא/ה, רוקח/ת וצוות רפואי נכבדים,

אנו מבקשים להודיעכם כי העלון לרופא של התכשיר **Luveris 75 IU** עודכן.

<u>ההתוויה המאושרת:</u>

Luveris in association with a follicle stimulating hormone (FSH) preparation is recommended for the stimulation of follicular development in adult women with severe luteinising hormone (LH) and FSH deficiency. In clinical trials these patients were defined by an endogenous serum LH level <1.2 IU/L.

השינויים בעלון לרופא הינם

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sex hormones and modulators of the genital system, gonadotropins.
ATC code: G03GA07

<u>Mechanism of action</u>
~~Lutropin alfa is a recombinant human Luteinising Hormone (r-hLH), a glycoprotein composed of non-covalently bound α- and β-subunits. Luteinising Hormone (LH) binds on the ovarian theca (and granulosa) cells and testicular Leydig cells, to a receptor shared with human chorionic gonadotropin hormone (hCG). This LH/CG transmembrane receptor is a member of the super-family of G protein-coupled receptors; specifically, it has a large extra-cellular domain. *In vitro* the affinity binding of recombinant hLH to the LH/CG receptor on Leydig tumour cells (MA-10) is between that for hCG and that of pituitary hLH, but within the same order of magnitude.~~

~~In the ovaries, during the follicular phase, LH stimulates theca cells to secrete androgens, which will be used as the substrate by granulosa cell aromatase enzyme to produce estradiol, supporting FSH-induced follicular development. At mid-cycle, high levels of LH trigger corpus luteum formation and ovulation. After ovulation, LH stimulates progesterone production in the corpus luteum by increasing the conversion of cholesterol to pregnenolone.~~

Merck Serono Ltd.
18 Kishon St.
Yavne, Israel 81220
Tel: +972 8 9382610
Fax: +972 8 9403152
office.israel@merckgroup.com

www.merckserono.co.il

Luteinising hormone (LH) and follicle stimulating hormone (FSH) are secreted from the anterior pituitary gland in response to gonadotropin-releasing hormone (GnRH) and play a complementary role in follicle development and ovulation. In theca cells, LH stimulates the secretion of androgens that are transferred to granulosa cells to be converted to estradiol (E2) by aromatase. In granulosa cells, FSH stimulates the development of ovarian follicles, while LH action is involved in follicle development, steroidogenesis and maturation.

Pharmacodynamic effects

~~In the stimulation of follicular development in anovulatory women deficient in LH and FSH, the primary effect resulting from administration of lutropin alfa is an increase in estradiol secretion by the follicles, the growth of which is stimulated by FSH.~~

The primary effect resulting from administration of r-hLH is a dose-related increase of E2 secretion, enhancing the effect of FSH administration on follicular growth.

Clinical efficacy

In clinical trials, patients were defined by an endogenous serum LH level < 1.2 IU/L as measured in a central laboratory. ~~However, it should be taken into account that there are variations between LH measurements performed in different laboratories.~~

In these trials the ovulation rate per cycle was 70 ~~-~~ to 75%. However, it should be taken into account that there are variations between LH measurements performed in different laboratories.

In one clinical study of women with hypogonadotropic hypogonadism and an endogenous serum LH concentration below 1.2 IU/L the appropriate dose of r-hLH was investigated. A dose of 75 IU r-hLH daily (in combination with 150 IU r-hFSH) resulted in adequate follicular development and estrogen production. A dose of 25 IU r-hLH daily (in combination with 150 IU r-hFSH) resulted in insufficient follicular development.

5.2 Pharmacokinetic properties

The pharmacokinetics of lutropin alfa have been studied in pituitary desensitised female volunteers from 75 IU up to 40,000 IU. The pharmacokinetic profile of lutropin alfa is similar to that of ~~urinary-derived~~ endogenous LH.

There is no pharmacokinetic interaction with follitropin alfa when administered simultaneously.

~~Absorption~~

~~Following subcutaneous administration, the absolute bioavailability is approximately 60%.~~

Distribution

Following intravenous administration, lutropin alfa is rapidly distributed with an initial half-life of approximately one hour and eliminated from the body with a terminal half-life of about 9 to 11 hours. The steady state volume of distribution is ~~around 10~~ in the range of 5 ~~-~~ to 14 L. ~~The mean residence time is approximately 5 hours.~~

Lutropin alfa shows linear pharmacokinetics, as assessed by area under curve (AUC) which is directly proportional to the dose administered.

Following subcutaneous administration, the absolute bioavailability is 56% and the apparent terminal half-life is in the range of 8 to 21 hours. Dose proportionality after subcutaneous administration was demonstrated up to 450 IU. The lutropin alfa pharmacokinetics following single and repeated administration of Luveris are comparable and the accumulation ratio of lutropin alfa is minimal. ~~There is no pharmacokinetic interaction with follitropin alfa when administered simultaneously.~~

Elimination

~~Following~~ intravenous ~~administration of Luveris, lutropin alfa is eliminated from the body with a terminal half-life of about 10-12 hours. Following subcutaneous administration, the terminal half-life is slightly prolonged.~~ Total body clearance is around ~~2~~ 1.8 L/~~h with~~ h and less than 5% of the dose ~~being~~ is excreted in the urine.

למידע המלא יש לעיין בעלון לרופא כפי שאושר על ידי משרד הבריאות.

העלון לרופא מפורסם במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום מרק סרונו בע"מ, רח' הקישון 18 , יבנה 81220 , טל' 09-9510737

בברכה,

אורית פוקס
רוקחת ממונה