

Patient leaflet in accordance with the Pharmacists' Regulations
(Preparations) – 1986

This medicine is dispensed with a doctor's prescription only

Luveris[®] 75 IU

Powder and solvent for solution for subcutaneous injection

Active ingredient: lutropin alfa 75 IU
(*International units - IU)

Solvent: Water for injection

Inactive ingredients and allergens in this medicine: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine.

This leaflet contains concise information about the medicine. If you have any further questions, consult your doctor or pharmacist. Keep this leaflet, you may need to read it again. This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. WHAT IS THIS MEDICINE INTENDED FOR

Luveris in association with a follicle stimulating hormone (FSH) preparation is intended for the stimulation of follicular development in women with severe gonadotropin deficiency (FSH and LH).

Therapeutic group: Gonadotropin hormone involved in regulation of the reproductive system.

Luveris 75 is a medicine containing lutropin alfa, a recombinant luteinising hormone (LH) which is essentially similar to the hormone found naturally in the human body but is made by means of biotechnology. It belongs to the group of hormones called gonadotropins, which are involved in the normal regulation of reproduction.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to gonadotropins (such as luteinising hormone, follicle stimulating hormone or human chorionic gonadotropin), or to any of the other ingredients in this medicine (see section 6).
- You have cancer of ovaries, uterus or breast.
- You have had a brain tumour diagnosed.
- You have ovarian enlargement or sacs of fluid within the ovaries (ovarian cyst) of unknown origin.
- You have unexplained vaginal bleeding.

- You have a condition that makes a normal pregnancy impossible, such as inactivity of the ovaries due to a condition called primary ovarian failure, or defects (anomaly, malformation) in the reproductive organs or uterine muscle tumour.

Do not use Luveris 75 if any of the above conditions applies to you. If you are not sure, talk to your doctor before using this medicine.

Special warnings about using this medicine

Talk to your doctor, pharmacist or nurse before using Luveris 75.

You and your partner's fertility should be evaluated before the treatment is started.

Porphyria

Tell your doctor before you start treatment, if you or any member of your family have porphyria (a hereditary disease that may be passed on from parents to children, in which porphyrins cannot be broken down).

Ovarian hyperstimulation syndrome (OHSS)

This medicine stimulates your ovaries and increases your risk of developing ovarian hyperstimulation syndrome (OHSS). In this condition, your follicles develop too much and become large cysts. If you get lower abdominal pain, gain any weight rapidly, feel sick or are vomiting or you have difficulty in breathing, contact your doctor straight away. Your doctor may instruct you to stop using this medicine (see section 4 under 'Serious side effects').

In case you are not ovulating and are adhering to the recommended dose and schedule of administration, the occurrence of OHSS is less likely. Luveris 75 treatment seldom causes severe OHSS. The risk of the syndrome increases if the medicine for final follicular maturation (containing human chorionic gonadotropin – hCG) is used (see section 3 under 'Dosage'). If you are developing OHSS, your doctor may not give you any treatment with hCG in this treatment cycle and ask you not to have sex or to use a barrier contraceptive method for at least 4 days.

Your doctor will monitor ovarian response, based on an ultrasound and blood test before and during the course of the treatment cycle.

Multiple pregnancy

When using Luveris 75, you have a higher risk of a pregnancy with more than one child ("multiple pregnancy", mostly twins), than if you conceived naturally. Multiple pregnancy may lead to medical complications for you and your babies. You can reduce the risk of multiple pregnancy by using the right dose of Luveris 75 at the right times. When using reproductive technologies, the risk of a multiple pregnancy is related to your age, the quality and the number of fertilised eggs or embryos transferred.

Miscarriage

When using reproductive technologies or stimulation of your ovaries to produce eggs, the risk of miscarriage is higher than for the average woman.

Ectopic pregnancy

Women with a history of tubal disease are at risk of ectopic pregnancy (pregnancy where the embryo is implanted outside the womb), whether the pregnancy is spontaneous or due to fertility treatments.

Blood clotting problems (thromboembolic events: thromboembolism)

Consult your doctor before using Luveris 75 if you or a member of your family have ever had blood clots in the leg or in the lung, or a heart attack or stroke. You may be at a higher risk of serious blood clots or existing clots might become worse during treatment with Luveris 75.

Tumours of sexual organs

There have been reports of tumours in the ovaries and other sex organs, both benign and malignant, in women who have undergone multiple treatment regimens for infertility.

Birth defects

Birth defects after use of reproductive technologies may be slightly higher than after spontaneous conception. This could be due to differences in parental factors like maternal age, genetics, as well as the assisted reproductive technology and multiple pregnancy.

Children and adolescents

Luveris 75 not intended for use in children and adolescents below 18 years of age.

Interactions with other medicines

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

Do not use Luveris 75 in combination with other medicines in the same injection, except for follitropin alfa, if prescribed by your doctor.

Pregnancy and breast-feeding

Do not use Luveris 75 if you are pregnant or breast-feeding. If you are pregnant or breast-feeding, ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Luveris 75 has no or negligible influence on the ability to drive and use machines.

Important information about some of this medicine's ingredients

Luveris 75 contains less than 1 mmol sodium (23 mg) per dose - considered 'sodium-free'.

3. HOW TO USE THE MEDICINE

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Using this medicine

Your doctor will decide on the dose and schedule of administration, which are most appropriate for you during this course of treatment.

Dosage

Luveris 75 is usually used every day for up to three weeks in combination with injections of follicle stimulating hormone (FSH).

- **The usual starting dose is 75 IU (1 vial) of Luveris together with 75 IU or 150 IU of FSH.**
- **According to your response**, your doctor may increase your dose of FSH by preferably 37.5 to 75 IU at 7-to-14-day intervals.

Your doctor may decide to extend your treatment up to 5 weeks.

When the desired response has been obtained, a single injection of human chorionic gonadotropin – hCG is given within 24 to 48 hours after the last injection of Luveris 75 and follicle stimulating hormone (FSH). You are recommended to have sexual intercourse on the day of, and the day following, administration of the hCG. Alternatively, intrauterine insemination or another assisted reproductive technology may be used based on your doctor's judgment.

If an excessive response is obtained, the treatment should be stopped and hCG withheld (see section 4 under 'Ovarian hyperstimulation syndrome (OHSS)'). For the following cycle, your doctor will prescribe FSH at a lower dose than that of the previous treatment cycle.

Do not exceed the recommended dose.

Method of administration

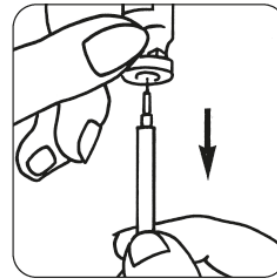
Luveris 75 is intended for subcutaneous use, which means it is given by injection under the skin. Each vial is for single use only.

If you inject Luveris 75 yourself, please carefully read the following instructions:

- Wash your hands. It is important that your hands and the items you use be as clean as possible.
- Assemble everything you need and place on a clean surface:
 - one vial of Luveris 75
 - one vial of solvent
 - two alcohol swabs
 - one syringe
 - one reconstitution (mixing) needle for dissolving the powder in the solvent
 - a fine-bore needle for subcutaneous injection
 - a sharps container for safe disposal of glass and needles

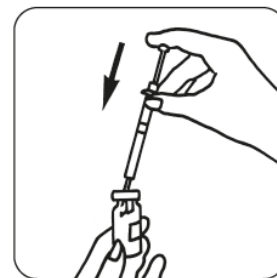
- Remove the protective cap from the **solvent vial**.

Attach the **reconstitution needle** to the syringe and draw up some air into the syringe by pulling the plunger to approximately the 1 mL mark. Insert the needle into the vial, push the plunger to expel the air, turn the vial upside down and gently draw up all the solvent.

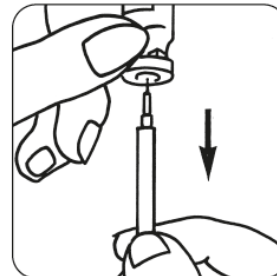


Carefully set the syringe down on the work surface, taking care not to touch the needle.

- Prepare the injection solution: Remove the protective cap from the **Luveris 75 powder vial**, pick up your syringe and slowly inject the solvent into the vial of Luveris 75. Swirl gently without removing the syringe. **Do not shake**.



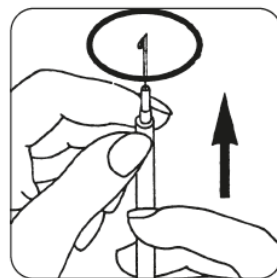
- After the powder has dissolved (which usually occurs immediately), check that the solution is clear and does not contain any particles. Turn the vial upside down, and gently draw the solution back into the syringe.



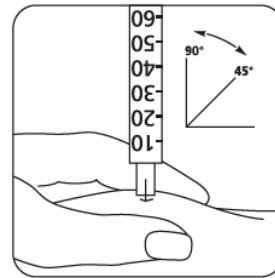
You may mix Luveris 75 and follitropin alfa instead of injecting each product separately. After dissolving the Luveris 75 powder, draw the solution back into the syringe and re-inject it into the vial that contains the follitropin alfa powder. Once the powder has dissolved, draw the solution back into the syringe. Once again, check that there are no particles, and do not use the solution if it is not clear.

Up to 3 containers of powder may be dissolved in 1 mL of solvent.

- Change the reconstitution needle for the **fine-bore needle** and remove the air bubbles. If you see air bubbles in the syringe, hold the syringe with the needle pointing upwards and gently flick the syringe until all the air collects at the top. Gently push the plunger until the air bubbles are gone.



- Immediately inject the solution: Your doctor or nurse will have already advised you where to inject (e.g. tummy, front of thigh). Wipe the area you have chosen with an alcohol swab. Firmly pinch the skin together and insert the needle at a 45° to 90° angle with a rapid motion. Inject under the skin, as you were taught. Do not inject directly into a vein. Inject the solution by pushing gently on the plunger. Take as much time as you need to inject all the solution. When done, withdraw the needle, and clean the skin with an alcohol swab using a circular motion.



Dispose of all the items you used: Once you have finished your injection, immediately discard all the needles and empty glass vials in the container intended for this purpose. Any solution you have not used should be discarded.

If you have accidentally taken a higher dose or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you. The effects of an overdose of Luvris 75 are unknown, nevertheless there is a possibility that ovarian hyperstimulation syndrome may occur (see section 4). However, this will only occur if you received human chorionic gonadotropin (hCG) (see section 2 under 'Special warnings about using this medicine').

If you forget to take the medicine

Do not use a double dose to make up for the forgotten dose. Contact your doctor.

Adhere to the treatment as recommended by your doctor.

Do not take medicines in the dark! Check the label and dose every time you take a medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, using Luvris 75 may cause side effects in some users. Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

Serious side effects

Contact your doctor straight away if you notice any of the below listed side effects. The doctor might ask you to stop using Luvris.

Allergic reaction

Allergic reactions such as rash, red skin, hives, swelling of your face with difficulty breathing can sometimes be serious. This side effect is very rare (may affect up to 1 in 10,000 patients).

Ovarian hyperstimulation syndrome (OHSS)

- Lower abdominal pain together with nausea or vomiting may be symptoms of ovarian hyperstimulation syndrome (OHSS). This may indicate that your ovaries have over-reacted to the treatment and development of large sacs of fluid or cysts (see section 2 under 'Ovarian hyperstimulation syndrome (OHSS)'). This side effect is common (may affect up to 1 in 10 patients). If this happens, your doctor will need to examine you as soon as possible.
- Serious blood clotting complications (thromboembolic events) usually with severe OHSS are very rare side effects. This could cause chest pain, breathlessness, stroke or heart attack (see section 2 under 'Blood clotting problems').

Other common side effects

- Headache
- Feeling sick, vomiting, diarrhoea, abdominal discomfort or abdominal pain
- Sacs of fluid within the ovaries (ovarian cysts), breast pain and pelvic pain
- Local reactions at the injection site, such as pain, itching, bruising, swelling or irritation

Torsion of the ovary and bleeding into the abdomen due to the use of Luvris 75 have not been reported, however, there have been rare cases reported following treatment with human menopausal gonadotropin (hMG), a urine-derived medication also containing LH.

Ectopic pregnancy may occur especially in women with a history of prior tubal disease.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Side effects can be reported to the Ministry of Health by clicking on the link 'Report Side Effects of Drug Treatment' found on the Ministry of Health home page (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <http://sideeffects.health.gov.il>

5. HOW TO STORE THE MEDICINE

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place, out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- Store below 25°C.

- Store in the original package in order to protect from light.
- Do not use Luveris 75 if you notice any visible signs of deterioration, such as discolouration of the powder or damage to the container.
- The medicine should be used immediately after dissolving the powder.
- The solution should not be administered if it contains particles or is not clear.
- Do not throw away medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, this medicine also contains:

Sucrose, disodium phosphate dihydrate, L-methionine, sodium dihydrogen phosphate monohydrate, polysorbate 20, concentrated phosphoric acid, sodium hydroxide, nitrogen

Solvent: Water for injection

What the medicine looks like and contents of the pack:

- Luveris 75 comes as a powder and solvent for solution for injection.
- Each vial of powder contains 75 IU of lutropin alfa, and each vial of solvent contains 1 mL of water for injection.
- The package contains 1, 3 or 10 vials of powder, together with the same number of solvent vials.

Not all pack sizes may be marketed.

Registration holder's name and address: Merck Serono Ltd., 18 HaKishon St., Yavne 81220.

Manufacturer's name and address: Merck Serono S.A., Aubonne, Switzerland.

This leaflet was revised in January 2025.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 124 27 30373 00