

Package leaflet: Information for the user

Luveris 75 IU powder and solvent for solution for injection lutropin alfa

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Luveris is and what it is used for
2. What you need to know before you use Luveris
3. How to use Luveris
4. Possible side effects
5. How to store Luveris
6. Contents of the pack and other information

1. What Luveris is and what it is used for

What Luveris is

Luveris is a medicine containing lutropin alfa, a recombinant Luteinising Hormone (LH) which is essentially similar to the hormone found naturally in humans, but is made by means of biotechnology. It belongs to the family of hormones called gonadotropins, which are involved in the normal control of reproduction.

What Luveris is used for

Luveris is recommended for the treatment of adult women who have been shown to produce very low levels of some of the hormones involved in the natural reproductive cycle. The medicine is used together with another hormone called Follicle Stimulating Hormone, (FSH), to bring about the development of follicles which are in the ovary, the structures maturing the eggs (ova). It is followed by treatment with a single dose of human Chorionic Gonadotropin (hCG), which leads to the release of an egg from the follicle (ovulation).

2. What you need to know before you use Luveris

Do not use Luveris

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

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

Warnings and precautions

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

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

It is recommended not to use Luveris if you have any condition that usually makes a normal pregnancy impossible, such as ovaries that do not work because of a condition called primary ovarian failure, or malformations of sexual organs.

Porphyria

Tell your doctor before you start treatment, if you or any member of your family have porphyria (an inability to break down porphyrins that may be passed on from parents to children).

Ovarian hyperstimulation syndrome (OHSS)

This medicine stimulates your ovaries. This increases your risk of developing ovarian hyperstimulation syndrome or OHSS. This is when 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 if you have difficulty in breathing, talk to your doctor straight away who might ask you to stop using this medicine (see section 4 under "Serious side effects").

In case you are not ovulating, and if the recommended dose and schedule of administration are adhered to, the occurrence of OHSS is less likely. Luveris treatment seldom causes severe OHSS. This becomes more likely if the medicine that is used for final follicular maturation (containing human Chorionic Gonadotropin, hCG) is administered (see section 3 under "How much to use" for details). If you are developing OHSS your doctor may not give you any hCG in this treatment cycle and you may be told not to have sex or to use a barrier contraceptive method for at least four days.

Your doctor will ensure careful monitoring of ovarian response, based on ultrasound and blood sampling before and during the course of treatment.

Multiple pregnancy

When using Luveris, you have a higher risk of being pregnant with more than one child at the same time ("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 at the right times. When undergoing assisted reproductive technologies, the risk of having a multiple pregnancy is related to your age, the quality and the number of fertilised eggs or embryos placed inside you.

Miscarriage

When undergoing assisted reproductive technologies or stimulation of your ovaries to produce eggs, you are more likely to have a miscarriage than 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 obtained by spontaneous conception or with fertility treatments.

Blood clotting problems (thromboembolic events)

Talk to your doctor before using Luveris 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 with Luveris treatment.

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 drug regimens for infertility treatment.

Birth defects

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

Children and adolescents

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

Other medicines and Luveris

Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.

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

Pregnancy and breast-feeding

Do not use Luveris if you are pregnant or breast-feeding.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

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

Luveris contains sodium

Luveris contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium free”.

3. How to use Luveris

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

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.

How much to use

Luveris is usually used every day for up to three weeks simultaneously with injections of 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 physician may decide to extend your treatment up to 5 weeks.

When the desired response has been obtained, a single injection of hCG is given 24 to 48 hours after the last injections of Luveris and 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 medically assisted reproduction procedure may be performed based on your doctor’s judgment.

If an excessive response is obtained, 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 cycle.

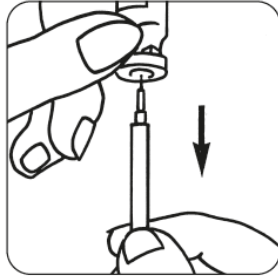
Method of administration

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

If you administer Luveris to yourself, please carefully read the following instructions:

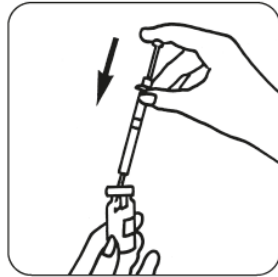
- Wash your hands. It is important that your hands and the items you use be as clean as possible.
- Assemble everything you need. Find a clean area and lay out everything:
 - one vial of Luveris,
 - one vial of solvent,
 - two alcohol swabs,
 - one syringe,
 - one reconstitution needle for dissolving 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. Then, 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.

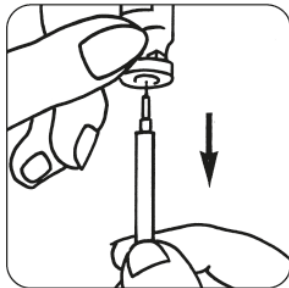


Carefully set the syringe down on the work-surface, taking care not to touch the needle.

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



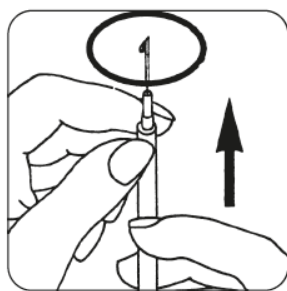
- After the powder has dissolved (which usually occurs immediately), check that the resulting solution is clear and does not contain any particles. Turn the vial upside down and gently draw the solution back into the syringe.



You may also mix Luveris and follitropin alfa as an alternative to injecting each product separately. After dissolving the Luveris powder, draw the solution back into the syringe and re-inject it into the container with the follitropin alfa powder. Once the powder has dissolved, draw the solution back into the syringe. Inspect for particles as before, and do not use if the solution is not clear.

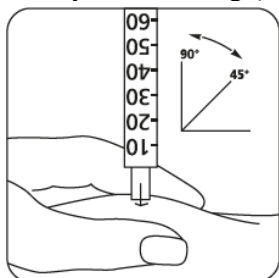
Up to 3 containers of powder may be dissolved in 1 mL of solvent.

- Change the needle for the **fine-bore needle** and remove any 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 chosen area with an alcohol swab. Firmly pinch the skin together and insert the needle at a 45° to 90° angle using a dart-like 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. Immediately withdraw the needle and clean the skin with an alcohol swab using a circular motion.



Dispose of all used items: Once you have finished your injection, immediately discard all needles and empty glass containers in the sharps container provided. Any unused solution must be discarded.

If you use more Luveris than you should

The effects of an overdose of Luveris are unknown, nevertheless there is a possibility that ovarian hyperstimulation syndrome may occur (see section 4). However, this will only occur if hCG is administered (see section 2 under “Warnings and precautions”).

If you forget to use Luveris

Do not use a double dose to make up for a forgotten dose. Please contact your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets 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 Luveris.

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 people).

Ovarian hyperstimulation syndrome (OHSS)

- Lower abdominal pain together with nausea or vomiting may be the symptoms of ovarian hyperstimulation syndrome (OHSS). Your ovaries may have over-reacted to the treatment and formed 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 people). 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 found very rarely. 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 have not been reported with Luveris, however, there have been rare cases reported following treatment with human menopausal gonadotropin (hMG), a urine-derived medication also containing LH.

Ectopic pregnancy (embryo implanted outside the womb) may occur especially in women with a history of prior tubal disease.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Luveris

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date, which is stated on the carton and the vials after EXP. The expiry date refers to the last day of that month.

Do not store above 25°C. Store in the original package in order to protect from light.

Do not use this medicine if you notice any visible signs of deterioration, such as discolouration of the powder or damage to the container.

The medicine should be administered immediately after dissolving the powder.

The solution should not be administered if it contains particles or is not clear.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Luveris contains

- The active substance is lutropin alfa. One vial of powder for injection contains 75 IU (International Units).
- Lutropin alfa is recombinant human Luteinising Hormone (r-hLH), produced by recombinant DNA technology.
- The other ingredients of the powder are polysorbate 20, sucrose, sodium dihydrogen phosphate monohydrate, disodium phosphate dihydrate, concentrated phosphoric acid, sodium hydroxide, L-methionine and nitrogen.
- The solvent is water for injections.

What Luveris looks like and contents of the pack

- Luveris 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 injections.
- Luveris is supplied in packs containing 1, 3 or 10 vials of powder, together with the same number of solvent vials.

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