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

This medicine is dispensed with a doctor's prescription only

Pergoveris®

Powder and solvent for preparation of solution for subcutaneous injection

Active ingredients:
follitropin alfa 150 IU*
lutropin alfa 75 IU
*IU - International units

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 this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to the 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 the medicine intended for?

The medicine is intended for stimulation of follicles and their maturation in the ovaries in adult women with severe gonadotropin hormone deficiency (FSH and LH).

Therapeutic group: Gonadotropin hormones involved in regulating the reproductive system.

The medicine contains 2 active ingredients called follitropin alfa and lutropin alfa. Both of the ingredients belong to a group of hormones called gonadotropins, which are involved in regulation of the reproductive system.

The active ingredients in the medicine are copies of the natural hormones FSH and LH in the body:
Follicle stimulating hormone (FSH) - stimulates maturation of eggs.
Luteinizing hormone (LH) - encourages release of the eggs.

The medicine allows women with low levels of FSH and LH to develop a follicle. The injection of another hormone - human chorionic gonadotropin (hCG) - leads to the release of the egg from the follicle.
This process helps achieve pregnancy.

2. Before using this medicine

You and your partner to the fertility process must be examined by a doctor specializing in treatment of fertility problems before starting treatment.

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredients (FSH and/or LH) or to any of the other ingredients in this medicine (for the list of inactive ingredients, see section 6).
- you are suffering from a brain tumour (in the hypothalamus or pituitary gland [hypophysis]).
- you are suffering from enlarged ovaries or sacs of fluid within the ovaries (ovarian cysts) of unknown origin.
- you are suffering from unexplained vaginal bleeding.
- you have ovarian, uterine or breast cancer.
- you are suffering from a condition that makes normal pregnancy impossible, for example, early menopause, sex organ defect (malformation) or a benign tumour in the womb.

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

Special warnings regarding use of this medicine
Talk to your doctor, pharmacist or nurse before using Pergoveris.

Porphyria
Talk to your doctor before you start treatment if you or any member of your family have porphyria (a hereditary disease in which there is no ability to break down porphyrins).

Tell your doctor immediately if:

- Your skin becomes fragile and easily blistered, especially after frequent exposure to sunlight.
- You have stomach, arm or leg pain.

In these cases, your doctor may recommend that you stop treatment.

Ovarian hyperstimulation syndrome (OHSS)
This medicine stimulates the ovaries and increases the risk of developing ovarian hyperstimulation syndrome (OHSS). In this condition, your follicles develop too much and become large cysts. If you suffer from lower abdominal pain, rapid weight gain, nausea, vomiting or if you have difficulty breathing, contact your doctor straight away. Your doctor might instruct you to stop using this medicine (see section 4 under ‘Most serious side effects’).

In case you are not ovulating and are adhering to the recommended dose and schedule of administration, the occurrence of severe OHSS is less likely. Pergoveris treatment seldom causes severe OHSS. The risk of appearance of the syndrome increases if a medicine for final follicular maturation is used (containing human chorionic gonadotropin – hCG) – 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 will ask you not to have sex or to use a barrier contraceptive method for at least 4 days.
Your doctor will carefully monitor the ovarian response, based on an ultrasound and blood test (oestradiol levels) before and during the course of the treatment cycle.

Multiple pregnancy
When using Pergoveris, there is a higher risk of a pregnancy with more than one foetus ("multiple pregnancy", mostly twins), compared to a pregnancy resulting from natural conception. 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 Pergoveris and by administration at the right times.
To minimise the risk of multiple pregnancy, ultrasound scans and blood tests are recommended.

Miscarriage
When undergoing stimulation of the ovaries to produce eggs, the risk of miscarriage is higher than in the general population.

Ectopic pregnancy
Women with a history of blocked or damaged fallopian tubes (tubal disease) are at risk of pregnancy where the embryo is implanted outside the womb (ectopic pregnancy), both in the case of spontaneous pregnancy and pregnancy following fertility treatments.

Blood clotting problems (thromboembolic events: thromboembolism)
Consult your doctor before using this medicine if you or a member of your family have ever had blood clots in the leg or 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 Pergoveris.

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

Allergic reactions
There have been isolated reports of non-serious allergic reactions to Pergoveris. If you have ever had this type of reaction to a similar medicine, tell your doctor before using Pergoveris.

Girls and adolescents
Pergoveris is not intended for use in girls and adolescent girls below the age of 18.

Interactions with other medicines
If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell your doctor or pharmacist.
Do not use Pergoveris 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 Pergoveris if you are pregnant or breast-feeding.

Driving and using machines
This medicine is not expected to affect your ability to drive or use dangerous machines.

Important information about some of this medicine's ingredients
Pergoveris contains less than 1 mmol (23 mg) sodium per dose - that is to say essentially "sodium-free".

3. How to use this 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 use this medicine.

Using this medicine
- Pergoveris is intended to be given by injection under the skin. To minimise skin irritation, select a different injection site each day.
- The medicine comes as a powder and solvent, which you need to mix together and use straight away.
- Your doctor or nurse will show you how to prepare and inject this medicine. They will supervise your first injection.
- When they confirm that you are able to administer the medicine safely, you can then prepare and inject the medicine yourself at home. When you self-inject, carefully read and follow the instructions under 'How to prepare and use Pergoveris (powder and solvent)'.

Dosage
Only your doctor will determine your dose and how you should take this medicine.

The treatment regimen begins with one vial of Pergoveris every day.
- According to your response, your doctor may decide to add a dose of a follitropin alfa every day in addition to your Pergoveris injection. In this case, the follitropin alfa dose is usually increased every 7 or every 14 days by 37.5 to 75 IU.
- Treatment is continued until the desired response is achieved. This is when you have developed a suitable follicle, as confirmed by ultrasound scans and blood tests.
- This may take up to 5 weeks.

When the desired response is achieved, you will be given a single injection of human chorionic gonadotropin (hCG) 24 to 48 hours after your last Pergoveris injection. It is recommended to have sex on the day of the hCG injection and the day after. Alternatively, intrauterine insemination (IUI) can be performed or other assisted reproductive technologies used according to your doctor's judgment.

If your body responds too strongly, your treatment will be stopped and human chorionic gonadotropin (hCG) will not be given (see in section 2 under 'Ovarian hyperstimulation syndrome'). In this case, your doctor will prescribe a lower follitropin alfa dose in the following treatment cycle.

Do not exceed the recommended dose.

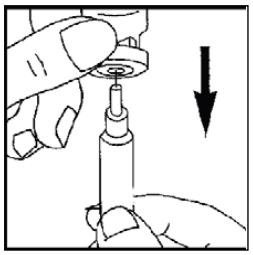
How to prepare and use Pergoveris (powder and solvent)
Before starting the preparation, please carefully read the following instructions the whole way through: Inject the medicine at the same time each day.

1. **Wash your hands, and find a clean area**
- It is important that your hands and the items you use be as clean as possible
- A clean table or kitchen surface are places that can be suitable

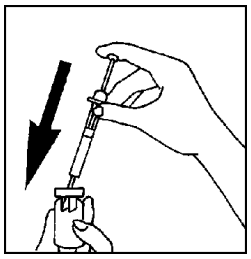
2. **Prepare everything needed in advance on the clean surface**
- 1 vial containing Pergoveris powder
- 1 vial containing water for injection (solvent)

Additional supplies not in the medicine pack:
- 2 alcohol swabs
- 1 empty syringe for injection
- 1 needle for preparation
- 1 fine bore needle for injection under the skin
- 1 sharps container for safe disposal of glass and needles

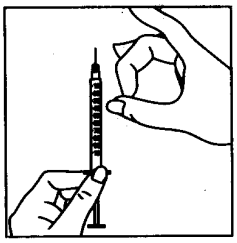
3. **Preparing the solution**
- Remove the protective cap from the vial that contains water (solvent vial).
- Attach the needle for preparation to the empty syringe for injection.
- Draw up some air into the syringe by pulling the plunger to the 1 mL mark.
- Insert the needle into the vial of solvent, push the plunger to expel the air.
- Turn the vial upside down and gently draw up all the solvent.
- Remove the syringe from the vial and set it down carefully on a clean surface. Do not touch the needle and do not allow the needle to touch any surface.



- Remove the protective cap from the vial of Pergoveris powder.
- Take the syringe and slowly inject the solvent into the vial of powder.
- 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 particles.
- Turn the vial upside down, and carefully draw the solution back into the syringe. Check that the solution does not contain particles as before, and do not use if the solution is not clear.

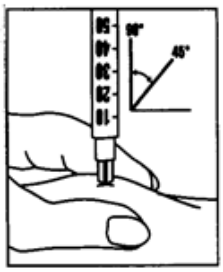


4. Preparing the syringe for injection



- Change the needle for the fine bore needle for injection under the skin.
- Remove the air bubbles: If you see air bubbles in the syringe, hold the syringe with the needle pointing upwards, gently flick the syringe until all the bubbles collect at the top.
  Push the plunger until the air bubbles disappear.

5. Injecting



- Immediately inject the solution. Your doctor or nurse have already instructed you where to inject (e.g. tummy, front of thigh). To minimise skin irritation, select a different injection site each day.
- Clean and disinfect the chosen area with an alcohol swab (using a circular motion).
- 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.
- Then withdraw the needle and clean the skin with a new alcohol swab using a circular motion.

6. After the injection

- 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

The effects of an overdose of Pergoveris are unknown, although OHSS might occur. However, this will only occur if hCG is administered (see section 2 under 'Ovarian hyperstimulation syndrome (OHSS)').

If you have taken an overdose or if a child has accidentally swallowed some medicine, immediately refer to a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine

Do not take a double dose to make up for a 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 <u>every time</u> you take a medicine. Wear glasses if you need them.
If you have any further questions regarding use of the medicine, consult your doctor, pharmacist or nurse.

4. Side effects

As with any medicine, using Pergoveris may cause side effects in some users. Do not be alarmed by this list of side effects. You may not suffer from any of them.

Most serious side effects
Contact your doctor immediately if you notice any of the side effects listed below. The doctor might ask you to stop using Pergoveris.

Allergic reactions
Allergic reactions such as rash, red skin, hives, swelling of your face with difficulty breathing can sometimes be serious. These side effects are rare.

Ovarian hyperstimulation syndrome (OHSS)
- Lower abdominal pain together with nausea or vomiting may be symptoms of ovarian hyperstimulation syndrome (OHSS). This may indicate an over-reaction to the treatment of the ovaries and development of sacs filled with fluid or cysts (see section 2 under 'Ovarian hyperstimulation syndrome (OHSS)'). This side effect is common. If this happens, your doctor will need to examine you as soon as possible.
- OHSS may become severe when there is significant enlargement of the ovaries, decreased urine production, weight gain, breathing difficulties and/or possible fluid accumulation in your stomach or chest. This side effect is uncommon (may affect up to 1 in 100 patients).
- Complications of OHSS such as twisting of ovaries or development of blood clots are rare (may affect up to 1 in 1,000 patients).
- Serious blood clotting complications (thromboembolic events) usually with severe OHSS are very rare. This complication could cause chest pain, breathlessness, stroke or heart attack. In rare cases this can happen independently of OHSS (see section 2 under 'Blood clotting problems [thromboembolic events: thromboembolism]').

Additional side effects

Very common (may affect more than 1 in 10 patients):
- sacs of fluid within the ovaries (ovarian cysts)
- headache
- local reactions at the injection site such as pain, itching, bruising, swelling or irritation.

Common (may affect up to 1 in 10 patients):
- diarrhoea
- breast pain
- feeling sick or vomiting
- abdominal or pelvic pain
- abdominal cramps or bloating.

Very rare (may affect up to 1 in 10,000 patients):
- Your asthma may get worse.

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.

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or by entering the link: https://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 your 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.
- Do not store above 25°C. Store in the original package to protect from light.
- The medicine should be used immediately after dissolving the powder.
- Do not use the medicine if you see it has been damaged.
- The solution should not be administered if it contains particles or is not clear.
- Do not throw away any medicine via wastewater (sewer) or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredients, this medicine also contains:
Sucrose, disodium phosphate dihydrate, sodium dihydrogen phosphate monohydrate, methionine, polysorbate 20, o-phosphoric acid, sodium hydroxide
Solvent: Water for injections

What the medicine looks like and contents of the pack:
- Pergoveris is presented as a powder and solvent for solution for injection.
- The powder is white to off-white in a glass vial with a rubber stopper containing 150 IU (equivalent to 11 micrograms) of follitropin alfa and 75 IU (equivalent to 3 micrograms) of lutropin alfa.
- The solvent is a clear colourless liquid in a glass vial containing 1 mL of water for injection.
- The pack contains one vial of powder and one vial of solvent.

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: 145 07 33159 00