



Merck Serono



PATIENT PACKAGE INSERT IN ACCORDANCE
WITH THE PHARMACISTS' REGULATIONS
(PREPARATIONS) – 1986

The medicine is dispensed with a doctor's
prescription only

PERGOVERIS®
150 IU/75 IU

Powder and solvent for preparation of
solution for subcutaneous injection

One vial containing powder – the active ingredients:
Follitropin Alfa (r-hFSH) 150 IU (international units),
equivalent to 11 micrograms.

Lutropin Alfa (r-hLH) 75 IU, equivalent to
3 micrograms.

One vial containing solvent: 1 ml of water for
injection.

* Inactive ingredients and allergens in the
preparation – see section 6.

**Read this leaflet carefully in its entirety before
using this medicine.** This leaflet contains concise
information about the medicine. If you have further
questions, refer to the doctor or pharmacist. Keep
this leaflet as 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.
The medicine is not intended for young girls and
female adolescents below 18 years of age.

1. WHAT IS THE MEDICINE INTENDED FOR?

This medicine is intended for stimulation and
maturation of follicles in women who have very
low production levels of gonadotropin hormones
(FSH and LH).

In clinical trials, the patients were defined by blood
levels of LH (luteinizing hormone) lower than 1.2 IU
per liter.

Therapeutic group: Gonadotropin hormones
involved in the regulation of the reproductive system.
The medicine contains 2 active ingredients
called – follitropin alfa and lutropin alfa. Both
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:
FSH, Follicle stimulating hormone – stimulates
maturation of the eggs.

LH, Luteinizing hormone – stimulates the release of
the egg.

The medicine enables women with low levels of FSH
and LH to develop a follicle. Injection of an additional
hormone – human chorionic gonadotropin (hCG)
leads to release of the egg from the follicle.

This process helps achieve pregnancy.

2. BEFORE USING THE MEDICINE

You and your partner to the fertilization process
must be examined by a fertility specialist before
commencing treatment.

☒ Do not use the medicine if:

- You are sensitive (allergic) to the active
ingredients (FSH and LH) or to or any of
the additional ingredients contained in the
medicine (for a list of the inactive ingredients,
see section 6).
- You are suffering from a brain tumor – in
the hypothalamus or in the pituitary gland
(hypophysis).
- You are suffering from enlarged ovaries or
sacs of fluids in the ovaries (ovarian cysts) of
unknown origin.
- You have unexplained vaginal bleeding.
- You have ovarian, uterine or breast cancer.
- You are suffering from a condition where
pregnancy is not possible, e.g.: primary ovarian
failure, sexual organ defect (malformation) or a
benign uterine tumor.

Do not use this medicine if any of the above conditions
apply to you. If you are unsure, consult with a doctor
or pharmacist before using the medicine.

Special warnings regarding use of the medicine
Porphyria

Inform your doctor before commencing treatment if
you or any of your family members has porphyria
(a hereditary metabolic disease in which there is no
ability to metabolize porphyrins).

Tell your doctor straight away if:

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

In such cases, your doctor may recommend to stop
treatment.

Blood clotting problems (thromboembolic events)

Consult with your doctor before using the medicine
if you or a member of your family has 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 Pergoveris.

Allergic reactions

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

Additional warnings:

Treatment must be done under medical supervision.

Ovarian Hyperstimulation Syndrome (OHSS)

This medicine stimulates your ovaries and increases
your risk of developing a situation called ovarian
hyperstimulation syndrome (OHSS). This is when your
follicles develop too much and become large cysts.

If you are suffering from lower abdominal pains,
rapid weight gain, nauseous feeling, vomiting or if
you have difficulty in breathing, refer to the doctor
straight away. He might tell you to stop using this
medicine (see section 4, Side Effects).

In case you are not ovulating and if the recommended
dose and schedule of administration are adhered
to, the risk of severe OHSS is less likely. Pergoveris
treatment seldom causes severe OHSS. The risk of
having this syndrome increases when using a
medicine for final follicular maturation (which
contains human chorionic gonadotropin – hCG) – see
section 3, How Should You Use The Medicine.

If you developed OHSS, your doctor may not give
you human chorionic gonadotropin – hCG in this
treatment cycle and will ask you not to have sex or
that you use a barrier contraceptive method for at
least 4 days.

Your doctor will carefully monitor the ovarian
response, based on ultrasound and blood tests
(estradiol levels) before and during the treatment cycle.

Multiple pregnancy

When using Pergoveris, there is a higher risk
of being pregnant with more than one fetus
("multiple pregnancy", mostly twins), when
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 at the right times. To
minimize the risk of multiple pregnancy, ultrasound
scans as well as blood tests are recommended.

Miscarriage

When undergoing ovarian stimulation, the risk of
miscarriage is higher than in the average population.

Ectopic pregnancy

Women who have a history of blocked or damaged
fallopian tubes (tubal disease) are at higher risk of
pregnancy in which the embryo is implanted outside
the womb (ectopic pregnancy), in both spontaneous
pregnancy and pregnancy achieved following
fertility treatments.

Tumors of sex organs

There have been reports of tumors in the ovaries
and other sex organs, both benign and malignant,
in women who underwent multi-drug treatment
regimens of infertility treatment.

Children and adolescents

Pergoveris is not intended for use in young girls and
female adolescents below 18 years old.

**If you are taking, or have recently taken, other
medicines, including non-prescription medicines
and nutritional supplements, tell the doctor or
pharmacist.**

In particular, inform the doctor or pharmacist if you
are taking:

Do not administer Pergoveris with other medical
preparations mixed in the same injection, except in
combination with follitropin alfa (FSH), if prescribed
by the doctor.

Pregnancy and breast-feeding

The medicine is not intended for use in pregnancy or
breastfeeding.

Driving and using machines

It is not expected that this medicine will affect your
ability to drive or operate dangerous machines.

**Important information about some of the
ingredients of the medicine**

Pergoveris contains less than 1 mmol sodium (23 mg)
per dose. It is essentially "sodium-free".

Pergoveris contains 30 mg sucrose per dose; this
information is for diabetic patients.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain.
The dosage and treatment regimen will be determined
by the doctor only.

When the desired response is achieved, a single
injection of hCG should be added within 24-48 hours
of completion of treatment. It is recommended to
have sex on the day of and the day after the hCG
injection. Alternatively, intrauterine insemination
(IUI) may be performed. If a hyper-reaction occurs
(OHSS, see section 2, Special warnings regarding use
of the medicine), the treatment will be stopped and
administration of human chorionic gonadotropin
(hCG) should be discontinued. In this case, refer
to the doctor immediately, and in the following
treatment, your doctor will prescribe for you a lower
follitropin alfa dose.

Do not exceed the recommended dose.

Directions for use:

- Pergoveris is intended for subcutaneous
administration, i.e., injection under the skin. In
order to minimize skin irritation, select a different
injection site each day. Each vial is intended for
single use.
- The medicine comes as a powder and solvent,
which you need to mix together and then use
straight away.
- The doctor or nurse will show you how to prepare
and inject this medicine. They will supervise your
first injection. Once they confirm that you can

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 in the following section – How to
prepare and use Pergoveris (powder and solvent).

**How to prepare and use Pergoveris (powder and
solvent)**

Before preparing the solution for injection, carefully
read the instructions first.

Inject the medicine at the same time every day.

1. Wash your hands and find a clean area:

- It is important that your hands and all the items
you use be as clean as possible.
- A clean table or kitchen surface may be suitable
areas.

**2. Prepare in advance everything you need on a
clean surface:**

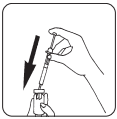
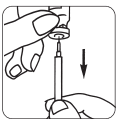
- A vial containing Pergoveris powder
- A vial containing water for injection (solvent)

Additional necessary items not provided in the
medicine pack:

- 2 alcohol swabs
- 1 empty syringe for injection
- 1 needle for suspension
- 1 fine bore needle suitable for subcutaneous
injection
- 1 sharps container for safe disposal of glass and
needles

3. Preparing the solution for injection:

- Remove the protective cap from the vial filled
with water (solvent vial).
- Attach the needle for suspension to the empty
injection syringe.
- Draw up some air into the syringe by pulling the
plunger back to the 1 ml mark.
- Insert the needle into the solvent vial, 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 filled
with Pergoveris powder.
- Pick up the syringe you have prepared and slowly inject the
solvent into the vial of powder.
- Swirl gently without removing the
syringe. Do not shake.
- After the powder has dissolved (this usually occurs
immediately), check that the resulting solution is
clear and does not contain any particles.
- Turn the vial upside down and carefully draw the
solution into the syringe
- Check the solution as previously and do not use
the solution if it is not clear.



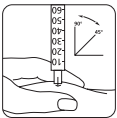
4. Preparing for injection:

- Change the needle to the fine bore needle suitable
for subcutaneous injection.
- Expel the air bubbles: If you see
air bubbles in the syringe, hold the
syringe with the needle pointing
upwards and flick the syringe with
your finger, until all the bubbles
collect at the top. Push the plunger until the air
bubbles are expelled.



5. The injection:

- Inject the solution immediately: Your doctor or
nurse will have already advised you on where to
inject (e.g. tummy, front of thigh); to minimize
skin irritation, choose a different injection site
every day.
- Clean (with a circular motion) and disinfect the
selected area with an alcohol swab.
- Firmly pinch the skin and insert the
needle at a 45°-90° angle.
- Inject under the skin, as you were
trained. Do not inject directly into
a vein.
- Inject the solution by gently pushing on the
plunger. Take as much time as you need to inject
all the solution.
- When you have finished, withdraw the needle
and clean the skin with a new alcohol swab, using
a circular motion.



After the injection:

- Discard all items you have used. When you
have finished the injection, immediately discard
the needles and empty glass vials in the sharps
container. Discard any unused solution.

Tests and follow-up – see subsections: Ovarian
hyperstimulation syndrome (OHSS) and Multiple
pregnancy in section 2, Special warnings regarding
use of the medicine.

If you accidentally took a higher dosage

The effects of an overdose of Pergoveris are
unknown, nevertheless, OHSS may occur. However,
this will only occur if human chorionic gonadotropin
(hCG) is administered (see section 2, Special warnings
regarding use of the medicine).

If you took an overdose, or if a child has accidentally
swallowed the medicine, refer immediately to a
doctor or proceed to a hospital emergency room,
and bring the package of the medicine 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 regimen recommended by
the doctor.

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

If you have further questions regarding use of the
medicine, consult the doctor, pharmacist or nurse.

4. SIDE EFFECTS

As with any medicine, use of Pergoveris may cause
side effects in some users. Do not be alarmed when
reading the list of side effects. You may not suffer
from any of them.

Most serious side effects

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

Allergic reactions

Allergic reactions such as: rash, red skin, hives,
swelling of the face with difficulty breathing, which
sometimes can be serious. This side effect is very rare.

Ovarian Hyperstimulation Syndrome (OHSS)

- Lower abdominal pain together with nausea or
vomiting, may be the symptoms of OHSS. This
may indicate a hyper-reaction of the ovaries to
the treatment and formation of fluid-filled sacs
or a large ovarian cyst (see section 2, Special
warnings regarding use of this medicine). This side
effect is common. If this effect occurs, the doctor
will need to examine you as soon as possible.
- The OHSS becomes serious when there is
significant enlargement of ovaries, decreased
urine production, weight gain, difficulty in
breathing and/or possible fluid accumulation
in the stomach or chest. This side effect is
uncommon (may affect up to 1 in 100 patients).
- Complications of OHSS, e.g.: 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 also happen independently
of OHSS (see Section 2, Special warnings
regarding use of the medicine).

Additional side effects

*Side effects occurring very commonly (may affect
more than 1 in 10 patients):*

- sacs of fluid within the ovaries (cysts)
- headache
- local reactions at the injection site such as: pain,
itching, bruising, swelling or irritation

*Side effects occurring commonly (may affect up to 1
in 10 patients):*

- diarrhea
- chest pain
- nausea and vomiting
- abdominal or pelvic pain
- abdominal cramps or bloating

*Side effects occurring very rarely (may affect
up to 1 in 10,000 patients):*

- in patients with asthma, the condition may
deteriorate

If a side effect occurs, if one of the side effects
worsens, or if you are suffering from a side effect
not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of
Health by clicking on the link "Reporting Side Effects
of Drug Treatment" found on the Ministry of Health
homepage (www.health.gov.il) that directs you to an
online form for reporting side effects, or by entering
the link:

[https://forms.gov.il/globaldata/getsequence/
getsequence.aspx?formType=AdversEffectMedic@
moh.gov.il](https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il)

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other
medicine, must be kept in a safe place out of the
sight and reach 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) that appears on the package. The expiry
date refers to the last day of that month.

Do not store at a temperature above 25°C. Store in
the original packaging to protect from light.

Use this medicine immediately after reconstitution.

Do not use the preparation if you see that it has been
damaged.

Do not use if the resulting solution is not clear or
contains particles.

Do not discard medicines into the sewage drainage
system or household waste. Ask the pharmacist how
to dispose of medicines you no longer use. These
measures will help protect the environment.

6. FURTHER INFORMATION

**In addition to the active ingredients, the medicine
also contains –**

Sucrose, Disodium phosphate dihydrate, Sodium
dihydrogen phosphate monohydrate, Methionine,
Polysorbate 20, Phosphoric acid concentrated (for pH
adjustment), Sodium hydroxide (for pH adjustment).
Solvent: Water for injections.

Pergoveris contains less than 1 mmol (23 mg) of
sodium per dose – considered "sodium free".

Pergoveris contains 30 mg of sucrose per dose.

**What the medicine looks like and the contents of
the package –**

The package contains one vial containing powder
and one vial containing solvent.
The powder is white to off-white in color.

Each vial of solvent contains 1 ml of water for
injection.

Registration holder and address – Merck Serono
Ltd., 18 Hakishon St., Yavne 81220

Manufacturer and address – Merck Serono S.A.,
Aubonne, Switzerland

**Registration number of the medicine in the
National Drug Registry of the Ministry of
Health** – 145-07-33159-00

This leaflet was checked and approved by the
Ministry of Health in February 2016

