Merck Serono

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PACKAGE LEAFLET: INFORMATION FOR THE USER

Pergoveris® 150 IU/75 IU

powder and solvent for solution for injection
Follitropin alfa/Lutropin alfa

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others.
  It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell you doctor or pharmacist.

In this leaflet:

1. WHAT PERGOVERIS IS AND WHAT IT IS USED FOR

Pergoveris belongs to the family of hormones called gonadotrophins, which are involved in the normal control of reproduction.

Pergoveris is a medicine containing follitropin alfa and lutropin alfa, which is made in laboratories by special recombinant DNA techniques.

The medicine should only be used under the strict supervision of a physician.

In women who are not ovulating due to very low production of the fertility hormones (FSH and LH) by their pituitary gland, Pergoveris is used to cause ovulation.

2. BEFORE YOU USE PERGOVERIS

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

Do not use Pergoveris
- if you are allergic (hypersensitive) to follicle stimulating hormone, luteinising hormone or any of the other ingredients of Pergoveris,
- if you have tumours of the hypothalamus and pituitary gland,
- if you have ovarian enlargement or cyst not due to polycystic ovarian disease,
- if you have gynaecological bleeding of unknown cause,
- if you have ovarian, uterine or breast cancer.

The medicine must not be used when a condition exists which would make a normal pregnancy impossible, such as :
- premature menopause,
- malformation of sexual organs,
- specific tumours of the womb.

Take special care with Pergoveris

Inform you doctor if you have porphyria or a family history of porphyria (a disorder that may be passed on from parents to children). The use of certain medications may trigger an attack of the illness.

Tell your doctor if you notice the following:
- your skin becoming fragile and easily blistered (especially areas that are frequently exposed to sunlight)
- and/or you have stomach or limb pain.

Your doctor may recommend that you stop treatment.

This treatment stimulates your ovaries sometimes leading to excessive growth of the follicles, which may be associated with the risk of excessive increase of ovarian size. This can lead to the so called ovarian hyperstimulation syndrome (OHSS) (see 4. Possible side effects). However, if you are not ovulating and the recommended dose and schedule of administration are adhered to, the occurrence of severe OHSS is uncommon (likely to occur in fewer than 1 in 100 patients). Pergoveris treatment seldom gives rise to significant OHSS unless the medicine used to induce final follicular maturation (containing human chorionic gonadotrophin - hCG) is administered. It is therefore prudent to withhold administration of hCG in cases where OHSS is developing (see 4. Possible side effects) and not to have sexual intercourse or use barrier methods for at least four days.

In patients undergoing induction of ovulation, the incidence of multiple pregnancies and births is increased compared with natural conception. However, this can be minimised by using the recommended dose and schedule of administration.

To minimise the risk of OHSS or of multiple pregnancy, ultrasound scans as well as oestradiol measurements are recommended.

Miscarriages are higher than in the normal population, but comparable with the rates found in women with fertility problems.

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

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

There have been isolated reports of non-serious allergic reactions to Pergoveris. If you had this type of reaction to similar medicines, inform your doctor.

Using other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pergoveris should not be administered as a mixture with other medicinal products in the same injection, except for follitropin alfa, if prescribed by your doctor.

Pregnancy and breast-feeding

Pergoveris is not indicated if you are pregnant or are breast-feeding.

Driving and using machines

No studies on the effects on the ability to drive and use machines have been performed.

Important information about some of the ingredients of Pergoveris

Pergoveris contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially "sodium-free".

Pergoveris contains 30 mg of sucrose per dose. This should be taken into account in patients with diabetes mellitus.

3. HOW TO USE PERGOVERIS

Always use Pergoveris exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Pergoveris is intended for subcutaneous use, that means it is given by injection just under the skin. It is for single use only.

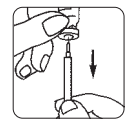
The usual dose is one vial of Pergoveris used every day for up to three weeks. According to your response, your doctor may increase your dose of follitropin alfa by preferably 37.5-75 IU at 7 to 14-day intervals.

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 24-48 hours after the last injections of Pergoveris. You are recommended to have sexual intercourse on the day of, and the day following administration of the hCG. Alternatively, intrauterine insemination (IUI) may be performed.

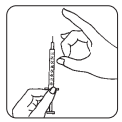
If an excessive response is obtained, treatment should be stopped and hCG withheld (see 4. Possible side effects). For the following cycle, your doctor will prescribe follitropin alfa at a lower dose than that of the previous cycle.

If you administer Pergoveris 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 and lay out on a clean surface everything you need:
- one vial containing Pergoveris powder
- one solvent vial
- two alcohol swabs
- one syringe
- one needle for reconstitution and a fine bore needle for subcutaneous injection
- sharps container
- 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

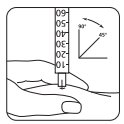


the needle into the vial, push the plunger to expel the air, turn the vial upside down and gently draw up all the solvent. Set the syringe down carefully on the work-surface taking care not to touch the needle.

- Prepare the injection solution: Remove the protective cap from the Pergoveris powder vial, pick up your 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 any particles. Turn the vial upside down, gently draw the solution back into the syringe.
- 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. 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 Pergoveris than you should

The effects of an overdose of Pergoveris are unknown, nevertheless one could expect ovarian hyperstimulation syndrome to occur, which is further described in the Possible side effects Section. However this will only occur if hCG is administered (see 2. Before you use Pergoveris).

If you forget to take Pergoveris

Do not take a double dose to make up for a forgotten dose, please contact your doctor.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Pergoveris can cause side effects, although not every body gets them.

The very common (likely to occur in more than 1 in 10 patients) reported side effects are:

- ovarian cysts
- headache
- local reactions at the injection site (pain, redness, itching, bruising, swelling and/or irritation)

Other common (likely to occur in fewer than 1 in 10 patients) side effects are:

- abdominal pain
- pelvic pain
- breast pain
- nausea
- vomiting
- diarrhoea
- abdominal cramp
- bloating
- somnolence (sleepiness).

Following treatment with Pergoveris when human chorionic gonadotrophin is administered, a condition called ovarian hyperstimulation syndrome (see 2. Before you use Pergoveris) can occur. This syndrome is characterised by large ovarian cysts. The following are first symptoms of ovarian hyperstimulation:

- pain in the lower abdominal region, possibly in combination with nausea
- vomiting and weight gain.

Should the above mentioned symptoms occur, a careful medical examination is indicated as soon as possible. In serious, but rare cases (likely to occur in fewer than 1 in 1,000 patients), an ovarian hyperstimulation syndrome with clearly enlarged ovaries, can go hand in hand with possible accumulation of fluid in the abdomen or thorax as well as ovarian torsion or more serious thromboembolic complications. In rare cases the latter can also be found independently of ovarian hyperstimulation syndrome.

In view of the above, to prevent such events, when the ovarian response is excessive, treatment with Pergoveris could be discontinued by your physician and the treatment with hCG abandoned.

Very rarely (likely to occur in fewer than 1 in 10,000 patients) blood clots in blood vessels (abnormal blood clottings) have been seen to occur with similar medicines.Therefore, this could possibly occur with Pergoveris / hCG therapy.

Very rare (likely to occur in fewer than 1 in 10,000 patients) cases of allergic reactions to follitropin alfa have occurred causing redness of the skin, rash, swelling, hives and difficulty in breathing. These reactions can sometimes be serious.

Very rarely (likely to occur in fewer than 1 in 10,000 patients) patients with asthma may experience worsening of their condition.

Pregnancy where the embryo is implanted outside the womb (ectopic pregnacy) may occur especially in women with a history of prior tubal disease.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE PERGOVERIS

Keep out of the reach and sight of children.

Do not use Pergoveris after the expiry date which is stated on the vials and the carton 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.

The medicine must be administered immediately after reconstitution.

Do not use Pergoveris if you notice any visible signs of deterioration.

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

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Pergoveris contains

The active substances are follitropin alfa and lutropin alfa . One vial of powder contains 150 IU follitropin alfa and 75 IU lutropin alfa.

The other ingredients are sucrose, disodium phosphate dihydrate, sodium dihydrogen phosphate monohydrate, methionine, polysorbate 20, concentrated phosphoric acid and sodium hydroxide.

The solvent is water for injections.

What Pergoveris looks like and contents of the pack

Pergoveris is presented as a powder and solvent for solution for injection.

The powder is a white lyophilised pellet.

The solvent is a clear colourless solution.

One vial of powder contains 150 IU of follitropin alfa and 75 IU of lutropin alfa. One vial of solvent contains 1 ml of Water for Injections.

The medicine is supplied in packs of 1, 3 and 10 vials with the corresponding number of 1, 3 and 10 vials of solvent. Not all pack sizes may be marketed.

THIS IS A MEDICINE

- A medicine is a product which aff ects your health and its consumption, contrary to instructions, is dangerous for you.
- Closely follow your doctor's prescription, the method of use and the instructions of the pharmacist who sold the product.
- Your doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not interrupt the period of treatment prescribed without your doctor's permission.
- Do not repeat the same prescription without consulting your doctor.

Keep medicines out of reach of children.

Council of Arab Health Ministers

Union Arab Pharmacists

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