APPROVED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

Schedule 4

PRODUCT NAME, STRENGTH AND PHARMACEUTICAL FORM

PERGOVERIS® (300 IU + 150 IU)/0,48 mL solution for injection in pre-filled pen

PERGOVERIS® (450 IU + 225 IU)/0,72 mL solution for injection in pre-filled pen

PERGOVERIS® (900 IU + 450 IU)/1,44 mL solution for injection in pre-filled pen

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 Pergoveris is and what it is used for

What Pergoveris is

Pergoveris contains two different active substances called “follitropin alfa” and “lutropin alfa”. Both belong to the family of hormones called “gonadotropins”, which are involved in reproduction and fertility.

What Pergoveris is used for

This medicine is used to stimulate the development of follicles (each containing an egg) in your ovaries. This is to help you get pregnant. It is for use in adult women (18 years old or above) who have low levels (severe deficiency) of “follicle stimulating hormone” (FSH) and “luteinising hormone” (LH). These women are usually infertile.

How Pergoveris works

The active substances in Pergoveris are copies of the natural hormones FSH and LH. In your body:

- FSH stimulates the production of eggs
- LH stimulates the release of the eggs.

By replacing the missing hormones, Pergoveris allows women with low levels of FSH and LH to develop a follicle. This will then release an egg, after an injection of the hormone “human chorionic gonadotropin (hCG)”. This helps the women to become pregnant.

2. What you need to know before you use Pergoveris

You and your partner's fertility should be evaluated before the treatment is started by a doctor experienced in treating fertility problems.

Do not use Pergoveris

- if you are allergic to follicle stimulating hormone (FSH), luteinising hormone (LH) or any of the other ingredients of this medicine (listed in section 6)
- if you have a brain tumour (in your hypothalamus or pituitary gland)
- if you have large ovaries or sacs of fluid within your ovaries (ovarian cysts) of unknown origin
- if you have unexplained vaginal bleeding
- if you have cancer in your ovaries, womb or breasts
- if you have a condition that would make a normal pregnancy impossible, such as an early menopause, malformed sex organs or benign tumours of the womb.

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

Warnings and precautions

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

Porphyria

Talk to your doctor before you start your treatment. If you or any member of your family have porphyria (an inability to breakdown porphyrins that may be passed on from parents to children).

Tell your doctor straight away if:

- your skin becomes fragile and easily blistered, especially skin that has been frequently exposed to sunlight.
- you have stomach, arm or leg pain.

In case of above events your doctor may recommend that you stop treatment.

Ovarian hyperstimulation syndrome (OHSS)

This medicine stimulates your ovaries. This increases your risk of developing ovarian hyperstimulation syndrome (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. They might ask you to stop using this medicine (see in section 4. under “Most serious side effects”).
In case you are not ovulating and if the recommended dose and schedule of administration are adhered to, the occurrence of severe OHSS is less likely. Pergoveris treatment seldom causes severe OHSS.
This becomes more likely if the medicine that is used for final follicular maturation (containing human chorionic gonadotrophin, hCG) is administered (see in 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 that you should use a barrier contraceptive method for at least four days.
Your doctor will ensure, careful monitoring of the ovarian response, based on ultrasound and blood tests (oestradiol measurements) before and during the course of treatment.

Multiple pregnancy

When using Pergoveris, 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 Pergoveris at the right times.
To minimise the risk of multiple pregnancy, ultrasound scans as well as blood tests are recommended.

Miscarriage

When undergoing stimulation of your ovaries to produce eggs, you are more likely to have a

miscarriage than the average woman.

Ectopic pregnancy

Women who have ever had blocked or damaged fallopian tubes (tubal disease) are at risk of pregnancy where the embryo is implanted outside the womb (ectopic pregnancy). This is whether the pregnancy is obtained by spontaneous conception or with fertility treatments.

Blood clotting problems (thromboembolic events)

Talk to your doctor before using Pergoveris 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 Pergoveris treatment.

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, talk to your doctor before using Pergoveris.

Children and adolescents

Pergoveris is not for use in children and adolescents below 18 years old.

Other medicines and Pergoveris

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. (This includes all complementary or traditional medicines).

Do not use Pergoveris with other medicines in the same injection.

You can use Pergoveris with a licensed follitropin alfa preparation as separate injections, if prescribed by your doctor.

Pregnancy and breastfeeding

Do not use Pergoveris if you are pregnant or breastfeeding.

Driving and using machines

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

It is not always possible to predict to what extent Pergoveris may interfere with your daily activities.

Pergoveris contains sodium

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

3. How to use Pergoveris

Do not share medicines prescribed for you with any other person.

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

Using this medicine

- Pergoveris is intended to be given by injection just under the skin (subcutaneously). To minimise skin irritation, select a different injection site each day.
- Your doctor or nurse will show you how to use the Pergoveris pre-filled pen to inject the medicine.

- If they are satisfied that you can administer Pergoveris safely, you can then prepare and inject the medicine yourself at home.
- If you administer Pergoveris to yourself, please carefully read and follow section "Instructions for Use".

Your doctor will tell you how long your treatment with Pergoveris will last.

How much to use

A treatment regimen commences with the recommended dose of Pergoveris containing 150 International Units (IU) of follitropin alfa and 75 IU of lutropin alfa every day.
According to your response, your doctor may decide to add every day a dose of a licensed follitropin alfa preparation 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 you get the desired response. This is when you have developed a suitable follicle, as assessed using ultrasound scans and blood tests.
- This may take up to 5 weeks.

When you get the desired response, you will be given a single injection of human chorionic gonadotropin (hCG) 24 to 48 hours after your last Pergoveris injection.
The best time to have sex is on the day of the hCG injection and the day after. Alternatively, intrauterine insemination (IUI) may be performed.
If your body responds too strongly, your treatment will be stopped and you will not be given any hCG (see in section 2. under "Ovarian hyperstimulation syndrome (OHSS)"). In this case, your doctor will give you a lower follitropin alfa dose in the following cycle.

If you use more Pergoveris than you should

The effects of an overdose of Pergoveris are unknown, nevertheless one could expect OHSS to occur.
However this will only occur if hCG is administered (see in section 2. under "Ovarian

hyperstimulation syndrome (OHSS)").

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to use Pergoveris

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

If you have any further question 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.

Not all side effects reported for Pergoveris are included in this leaflet. Should your general health worsen or if you experience any untoward effects while using Pergoveris, please consult your health care provider for advice.

Most 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 Pergoveris.

Allergic reactions

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.

Ovarian hyperstimulation syndrome (OHSS)

- Lower abdominal pain together with nausea or vomiting. These 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 in 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.

- The OHSS may become severe with clearly enlarged ovaries, decreased urine production, weight gain, difficulty in breathing and/or possible fluid accumulation in your stomach or chest.

This side effect is uncommon (may affect up to 1 in 100 people).

- Complications of OHSS such as twisting of ovaries or blood clotting occur rarely (may affect up to 1 in 1,000 people).
- Serious blood clotting problems (thromboembolic events) usually with severe OHSS are found very rarely. This could cause chest pain, breathlessness, stroke or heart attack. In rare cases this can also happen independently of OHSS (see in section 2. under “Blood clotting problems (thromboembolic events)”).

Other side effects

Very common (may affect more than 1 in 10 people):

- 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 people):

- diarrhoea
- breast pain
- feeling sick or vomiting
- abdominal or pelvic pain

- abdominal cramp or bloating.

Very rare (may affect up to 1 in 10,000 people):

- Your asthma may get worse.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on safety of Pergoveris.

5. How to store Pergoveris

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 label and the carton after EXP.
The expiry date refers to the last day of that month.
Store in a refrigerator (2 °C - 8 °C). Do not freeze.
Store in the original package in order to protect from light.
Once opened, the pre-filled pen may be stored for a maximum of 28 days outside of the refrigerator (at 25 °C).
Do not use Pergoveris if you notice any visible signs of deterioration, if the liquid contains particles or is not clear.
Return all unused medicine to your pharmacist.
After the injection, dispose of the used needle safely.
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 Pergoveris contains

The active substances are follitropin alfa and lutropin alfa.

- Each pre-filled pen of Pergoveris (300 IU + 150 IU)/0,48 mL contains 300 IU (International Units) of follitropin alfa and 150 IU of lutropin alfa in 0,48 mL and can deliver two doses of Pergoveris 150 IU/75 IU.
- Each pre-filled pen of Pergoveris (450 IU + 225 IU)/0,72 mL contains 450 IU (International Units) of follitropin alfa and 225 IU of lutropin alfa in 0,72 mL and can deliver three doses of Pergoveris 150 IU/75 IU.
- Each Pergoveris (900 IU + 450 IU)/1,44 mL pre-filled pen contains 1,44 mL of solution for injection and can deliver six doses of Pergoveris 150 IU/75 IU.

The other ingredients are

- Sucrose, arginine monohydrochloride, poloxamer 188, methionine, phenol, disodium phosphate dihydrate, sodium dihydrogen phosphate monohydrate and water for injections. Tiny amounts of concentrated phosphoric acid and sodium hydroxide are added to keep acidity levels (pH levels) normal.

What Pergoveris looks like and contents of the pack

Pergoveris is presented as a clear, colourless to slightly yellow solution for injection, free from visible particulate matter, in a mulitidose pre-filled pen:

- Pergoveris (300 IU +150 IU)/0,48 mL is supplied in packs of 1 multidose pre-filled pen and 5 disposable injection needles.
- Pergoveris (450 IU + 225 IU)/0,72 mL is supplied in packs of 1 multidose pre-filled pen and 7 disposable injection needles.

- Pergoveris (900 IU + 450 IU)/1,44 mL is supplied in packs of 1 multidose pre-filled pen and 14 disposable injection needles.

Holder of Certificate of Registration

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