PART III: CONSUMER INFORMATION

PrPERGOVERIS®
follitropin alfa/lutropin alfa injection (150 IU:75 IU)
Solution for Injection in a Pre-filled Pen

This information is part III of a three-part "Product Monograph" published when PERGOVERIS was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about PERGOVERIS. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What is PERGOVERIS?
PERGOVERIS is a combination of GONAL-f and LUVERIS at a fixed dose of 150 IU FSH and 75 IU LH. Prior to therapy with PERGOVERIS, patients should be informed of the duration of treatment and need for monitoring.

What is the medication used for:
PERGOVERIS is indicated for the stimulation of follicular development in hypogonadotropic hypogonadal women with severe LH deficiency (LH< 1.2 IU/L) and FSH deficiency (≤ 5.0 IU/L) who are candidates for concurrent therapy with FSH and LH.

The medicinal product should only be used under the strict supervision of a doctor.

What it does:
Women with hypogonadotropic hypogonadism have pituitary glands that do not release follicle stimulating hormone (FSH) or luteinizing hormone (LH). This means that the follicles are unable to develop and mature, so ovulation cannot take place.

PERGOVERIS contains FSH and LH and is used to stimulate follicular growth for ovulation.

When it should not be used:
Do not use PERGOVERIS if you have:

- Hypersensitivity to the active substances follitropin alfa and lutropin alfa or to any of the excipients or component of the container. For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section of the Product Monograph
- Primary ovarian failure or anovulation with normal levels of LH and FSH
- Uncontrolled thyroid or adrenal dysfunction
- Tumours of the hypothalamus or pituitary gland
- Ovarian enlargement or cyst of undetermined origin
- Gynecological hemorrhages of undetermined origin
- Sex hormone dependent tumors of the reproductive tract and accessory organs
- Current pregnancy or lactation

PERGOVERIS should not be used when a condition exists which would make a normal pregnancy impossible, such as:
- premature menopause,
- malformation of reproductive organs,
- specific tumours of the uterus, including severe uterine fibroids.

What the medicinal ingredients are:
PERGOVERIS is fixed dose combination of 150 IU follitropin alfa (GONAL-f) and 75 IU lutropin alfa (LUVERIS). These hormones belong to the gonadotropin family and are made in laboratories by special recombinant DNA techniques.

What the important nonmedicinal ingredients are:
Sucrose, arginine monohydrochloride, phenol, disodium phosphate dihydrate, sodium dihydrogen phosphate monohydrate, poloxamer 188, methionine, phosphoric acid and sodium hydroxide for pH adjustment

For a full listing of nonmedicinal ingredients see Part 1 of the Product Monograph.

What dosage forms it comes in:
PERGOVERIS is a clear, colorless to slightly yellow solution for injection available in pre-filled pens that can deliver 2 doses, 3 doses or 6 doses of 150 IU follitropin alfa and 75 IU lutropin alfa. Not all pack sizes may be marketed.

PERGOVERIS also comes as a powder and diluent for solution for injection (see Product Monograph for information)

WARNINGS AND PRECAUTIONS

BEFORE YOU USE PERGOVERIS:

If you have porphyria, which is a group of inherited disorders (a disorder that may be passed on from parents to children), you should inform your doctor as the use of certain medications may trigger an attack of the illness. If you notice your skin becoming fragile and blisters easily (especially areas that are frequently exposed to sunlight) and/or you have stomach or limb pain you should tell your doctor who may recommend that you stop treatment.

This treatment increases your risk of developing ovarian hyperstimulation syndrome (OHSS) (see Section SIDE EFFECTS). PERGOVERIS treatment seldom gives rise to significant OHSS unless the medicine used to induce final follicular maturation (containing human chorionic gonadotropin - hCG) is administered. It is therefore prudent to withhold administration of hCG in cases where OHSS is developing and not to have sexual intercourse. You should use barrier methods for at least four days.

If you are at risk of thromboembolic events (formation of a blood clot in vein or artery), because of your personal or family history, treatment with gonadotropins, like pregnancy itself, may further increase the risk. If you think you may have such a risk, please talk to your doctor.
In patients undergoing induction of ovulation, the incidence of a multiple pregnancy and births is increased compared with natural conception.

The frequency of miscarriages is higher than in the normal population, but similar to the rate found overall in women with fertility problems.

Women with a history of tubal disease are at a 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.

There have been reports of tumours of 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.

INTERACTIONS WITH THIS MEDICATION

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, but may be given at the same time as follitropin alfa in a separate injection, if prescribed by your doctor.

PROPER USE OF THIS MEDICATION

Usual dose:
Always take PERGOVERIS exactly as your doctor or Healthcare Professional (HCP) has instructed you. You should check with your doctor or HCP if you are not sure. With professional guidance, you can learn to inject yourself, in the comfort and privacy of your own home.

It is recommended that you inject PERGOVERIS at around the same time each day.

A treatment regimen commences with the recommended dose of PERGOVERIS containing 150 IU follitropin alfa and 75 IU lutropin alfa. This is one dose from your pre-filled pen. According to your response, your doctor may increase your dose of follitropin alfa usually by 37.5-75 IU at 7 to 14-day intervals.

When the desired response has been obtained, a single injection of hCG is given 24-48 hours after the last injection of PERGOVERIS. It is recommended that you have sexual intercourse on the day of, and the day following administration of the hCG. Alternatively, intrauterine insemination (IUI) or *in vitro* fertilization (IVF) may be performed.

If an excessive response occurs, treatment should be stopped and hCG withheld (see section SIDE EFFECTS). For the following cycle, your doctor may prescribe follitropin alfa at a lower dose than that used in the previous cycle.

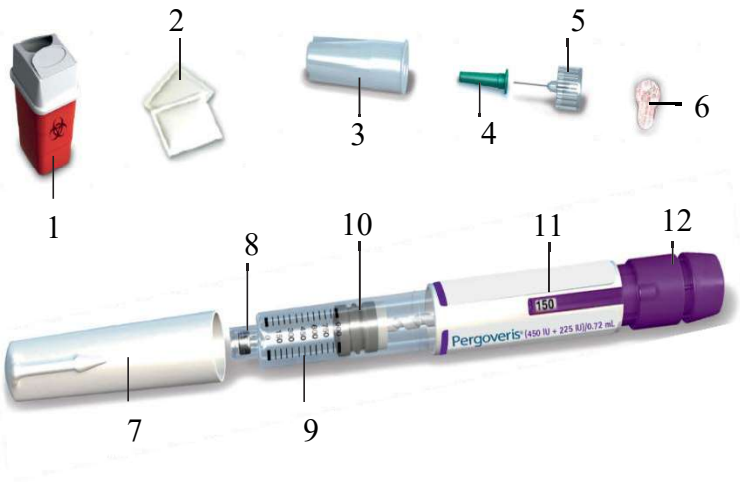
Every treatment is individualized. Yours has been carefully designed for you by your doctor according to your own specific needs. It is very important that you keep your appointments and follow your doctor's instructions, particularly with regard to the amount and frequency of the medication you are taking.

Route of administration

PERGOVERIS is intended for subcutaneous use that means given by injection just under the skin.

If you self-administer PERGOVERIS, please read the following instructions carefully:

PERGOVERIS Pre-filled Pen and other materials you may need for injection.



1. Sharps disposal container
2. Alcohol swabs
3. Outer needle cap
4. Inner needle shield
5. Removable needle
6. Peel-off seal tab
7. Pen cap
8. Threaded needle connector
9. Reservoir holder
10. Plunger piston
11. Dose Display
12. Dose setting knob

1. Before you start using PERGOVERIS pre-filled pen:

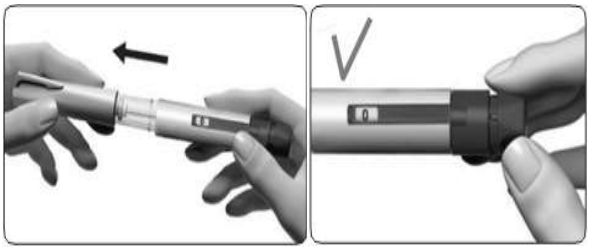
- Wash your hands with soap and water. It is important that your hands and items you use be as clean as possible.

- On a clean surface, e.g., clean table or kitchen surface, lay out everything you will need:
  - PERGOVERIS pre-filled pen
  - One removable injection needle
  - Alcohol swabs
  - Sharps disposal container

- Verify the **expiration date** on the label. Do not use expired medication.

2. Getting your PERGOVERIS pen ready for injection

- Take off the pen cap.
- Wipe the end of the threaded tip (containing the rubber centre) using an alcohol swab.
- Verify that the Dose Display is set to "0". The numbers in the dose feedback window represent the number of International Units or IU and show the dose of follitropin alfa. Your doctor will tell you how many IUs of follitropin alfa to inject each day.



- Prepare your needle for injection:
  - Get a new needle – only use the "single-use" needles supplied
  - Hold the outer needle cap firmly
  - Check that the peel-off seal on the outer needle cap is not damaged or loose:

Example of a good seal

Example of a bad seal

- Remove the peel-off seal

CAUTION: If the peel-off seal is damaged or loose, do not use the needle. Throw it away in a sharps disposal container. Get a new needle.

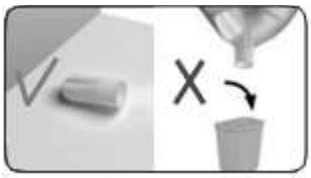
3. Attach the needle

- Screw the threaded tip of the PERGOVERIS pen into the outer needle cap until you feel a light resistance.

  - Important Note: Do not attach the needle too tightly; the needle could be difficult to remove after the injection.

- Remove the outer needle cap by pulling it gently. Put it aside for later use.

- Do not throw away the outer needle cap; you will need it for removing the needle from the pen.



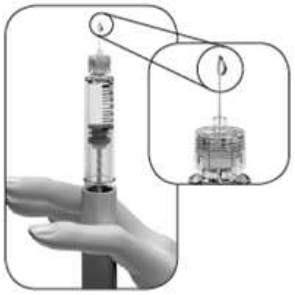
- Hold the PERGOVERIS pen with the needle pointing upwards.

- Carefully remove the green inner shield by pulling it straight off and discard it.
  - Warning: Do not recap the needle with the green inner shield as this can lead to needle stick.

- **Please note: if this is NOT a brand new PERGOVERIS pen (you have done previous injections with this pen), then proceed to Section 4: "Setting the dose prescribed by your doctor".**

- **If this IS A BRAND NEW PEN that you are using for the first time**, look closely at the tip of the needle for a tiny drop of fluid.
  - If you see a tiny drop(s) of fluid, proceed to Section 4 "Setting the dose prescribed by your doctor".
  - If you do not see a tiny drop(s), please see to Section 7 "Preparing your new PERGOVERIS Pre-filled Pen for first time use".

- **Important Note: Only check for drop(s) with a brand new pen. This step is not required if you are doing additional injections using the same pen.**

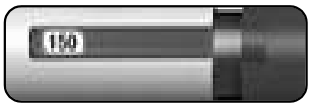


4. Setting the dose prescribed by your doctor

- Turn the dose setting knob forward (or clockwise) until your prescribed dose shows in the Dose Display. Do not push or pull the dose setting knob while you turn it.
  - In this example below, it is 150 IU.

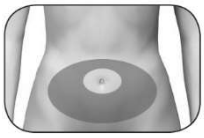
  - If you have turned the knob past your prescribed dose, turn the knob backwards (or counter-clockwise) to correct the dose.

- Important Note: Check that the Dose Display shows your prescribed dose before you move on to the next step.



5. Injecting the dose

- Choose an injection site in the area your doctor or nurse has told you to give the injection.
  - Note: To minimize skin irritation, select a different injection site each day.



- Clean the skin by wiping the area with an alcohol swab. Allow the site to dry.
- Set the alcohol wipe to the side.
- Verify once more that the Dose Display is showing the correct dose. If it is not the correct dose, you must adjust it by turning the dose setting knob either clockwise or counter-clockwise (see Step 4 "Setting your dose prescribed by your doctor").
- Inject the dose as you were trained to do by your doctor or nurse
  - Holding the pen in one hand, use your other hand to gently squeeze the skin together to make a raised area at the injection site.
  - Insert the needle at a 90º angle into the skin. You might bend the needle if you do not insert it at a 90º angle.
  - Press the dose knob down as far as it will go and hold it to complete the full injection.

- Hold the dose knob down for a minimum of 5 seconds to ensure you inject the full dose. The larger the dose, the longer it will take to inject.

- **Do not release the dose setting knob until you remove the needle from your skin.**

- Remove the needle from your skin, release the dose setting knob.

- The dose number shown in the Dose Display will turn back to 0 to indicate that the complete dose was delivered. If you see a number higher than 0, proceed to Section 6 "After the Injection – Complete a Partial Injection" (only when needed).

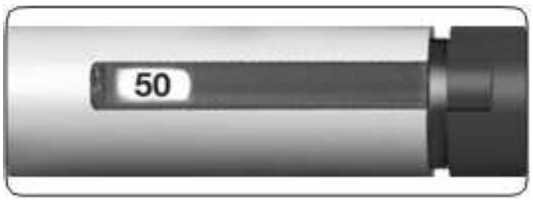
6. After the injection

- Verify you have given a complete injection.
- Check that the dose Display shows 0.

Important Note: If the Dose Display shows a number higher than 0, the PERGOVERIS pen is empty and you have not received your full prescribed dose.

Complete a Partial Injection (only when needed):

- The Dose Display will indicate the missing amount (in the example below, it is 50 IU), you need to inject using a new pen.



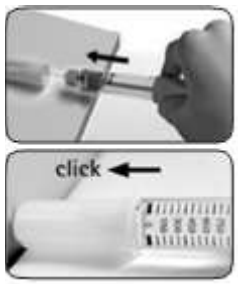
- Repeat Section 1 "Before you start using PERGOVERIS" through Section 2 "Getting your PERGOVERIS pen ready for injection" with a second pen.

- **For a brand new pen that you are using for the first time**, look closely at the tip of the needle for a tiny drop of fluid.
  - If you see a tiny drop(s) of fluid, proceed to Section 4 "Setting the dose prescribed by your doctor".
  - If you do not see a tiny drop(s), please see Section 7 "Preparing your new PERGOVERIS pen for first time use".
- Once your pen is ready, set the dose as described in Section 4 to the missing amount indicated in the Dose Display on your previous pen. Complete your prescribed dose by following steps outlined in Section 5 "Injecting the dose".

Important Note: Always make sure to use a new needle for each injection.

Removing the needle after each injection:

- Place the outer needle cap on a flat surface.
- Hold the PERGOVERIS pen firmly with one hand, and slip the needle into the outer needle cap. Be careful not to prick yourself with the needle.
- Continue by pushing the capped needle against a firm surface until you hear a "click."



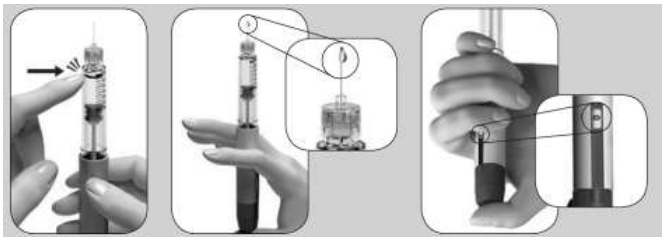
- Grip the outer needle cap and unscrew the needle by turning counter clockwise. Dispose of the used needle safely.

- Never reuse any used needle. Never share needles.
- Recap the pen.

7. <u>Preparing your new PERGOVERIS pen for first time use</u>

- If you do not see a tiny drop(s) at or near the needle tip the first time you use a new pen, you must perform the steps below:
  - Gently turn the dose setting knob clockwise until it reads 25 in the Dose Display. You can turn the dose knob backwards if you turn it past 25.

- Hold the pen with the needle pointing upward.
- Tap the reservoir holder gently.
- Press the dose setting knob as far as it will go. A tiny drop of fluid will appear at the tip of the needle. The amount of fluid seen at the needle tip is part of the overfill from the pre-filled pen.
- Verify that the Dose Display reads "0".



- You may need to repeat this step if you do not see a tiny drop of liquid appearing at the tip of the needle.
- Proceed to Section 4 "Setting the dose prescribed by your doctor".

Storing the PERGOVERIS pen:

CAUTION: Never store the pen with the needle attached. Always remove the needle from the PERGOVERIS pen before replacing the pen cap.

- Store the pen in its original packaging in a safe place
- When the pen is empty, ask your pharmacist how to dispose of it.

Important Note: Medicine should not be disposed of via wastewater or household waste.

Overdose:
The effects of an overdose of PERGOVERIS are unknown, nevertheless one might expect ovarian hyperstimulation syndrome to occur, which is further described in section SIDE EFFECTS. However this will only occur if hCG is administered.

If you have accidentally injected too much PERGOVERIS, contact your physician, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:
If you missed a dose of PERGOVERIS, do not take a double dose, please contact your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, PERGOVERIS may cause side effects, although not everyone gets them.

The most commonly reported side effects are abdominal pain, pelvic pain, breast pain, constipation, dysmenorrhea (painful menstruation), flatulence (stomach or intestinal gas), headache, nausea, and local reactions at the injection site (pain, redness, itching, bruising, swelling and/or irritation).

When taking PERGOVERIS, there is a risk of developing ovarian hyperstimulation syndrome (OHSS). The early warning signs of development of OHSS are severe abdominal pain, nausea, vomiting and weight gain. Since OHSS develops rapidly, if you experience any of these symptoms, contact your doctor immediately.

In serious, but rare cases, ovarian hyperstimulation syndrome with clearly enlarged ovaries can include accumulation of fluid in the abdomen or thorax as well as more serious thromboembolic (abnormal blood clotting) complications. In rare cases, thromboembolic complications 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 should be discontinued by your doctor and treatment with hCG abandoned.

Isolated cases of non-serious allergic reactions to PERGOVERIS have been reported.

Ectopic pregnancy (embryo implanted outside the uterus) may occur especially in women with a history of prior disease/scarring in their Fallopian tubes.

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

This is not a complete list of side effects. For any unexpected effects while taking PERGOVERIS, contact your doctor or pharmacist.

HOW TO STORE IT

Store in a refrigerator (2°-8°C). Avoid freezing. 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 or below 25°C).

Never store the pen with the needle still attached. Always remove the needle from the PERGOVERIS pre-filled pen before replacing the pen cap. Dispose of the used needles safely.

Keep out of the reach of children.

Do not use PERGOVERIS after the expiry date which is stated on the pen after EXP. The expiry date refers to the last day of that month.

Do not use PERGOVERIS if you notice any visible signs of deterioration, if the liquid 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.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Report Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to:
    Canada Vigilance Program
    Health Canada
    Postal Locator 1908C
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Website at: www.healthcanada.gc.ca/medeffect

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice

MORE INFORMATION

This document plus the full Product Monograph, prepared for health care professionals can be obtained by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php), http://www.emdserono.ca, or by calling EMD Serono at 1-800-387-8479.

This leaflet was prepared by EMD Serono, A Division of EMD Inc., Canada

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