

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

^{Pr}PERGOVERIS®

follitropin alfa/lutropin alfa for injection (150 IU:75 IU)

Powder and diluent for solution for injection

Solution for Injection in a Pre-filled Pen

Read this carefully before you start taking **PERGOVERIS** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **PERGOVERIS**.

What is PERGOVERIS used for?

- PERGOVERIS is indicated for the stimulation of follicular development in hypogonadotropic hypogonadal women with severe luteinizing hormone (LH) deficiency (LH < 1.2 IU/L) and follicle stimulating hormone (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 healthcare professional.

How does PERGOVERIS work?

The active substances in PERGOVERIS are follicle stimulating hormone (FSH) and luteinizing hormone (LH). FSH and LH are natural hormones in women:

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

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

What are the ingredients in PERGOVERIS?

Medicinal ingredients: 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.

Non-medicinal ingredients: Sucrose, disodium phosphate dihydrate, sodium dihydrogen phosphate monohydrate, methionine, polysorbate 20, concentrated phosphoric acid and sodium hydroxide.

The diluent is Water for Injection.

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

PERGOVERIS comes in the following dosage forms:

PERGOVERIS comes as a powder and diluent for solution for injection, or as a pre-filled pens (see Product Monograph for information).

Powder and diluent for solution for injection: PERGOVERIS powder is a white lyophilized pellet. The diluent is a clear colourless solution. One vial of powder contains 150 IU of follitropin alfa and 75 IU of lutropin alfa. One vial of diluent contains 1 ml of Water for Injection. The product is supplied in packs of 1, 3 and 10 vials with the corresponding number of diluent vials. Not all pack sizes may be marketed.

Solution for injection in a pre-filled pen: PERGOVERIS is a clear, colourless 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

300 IU r-hFSH/150 IU r-hLH in 0.48 mL;

450 IU r-hFSH/225 IU r-hLH in 0.72 mL;

900 IU r-hFSH/450 IU r-hLH in 1.44 mL.

Do not use PERGOVERIS if:

- you are allergic to FSH, LH or any of the other ingredients of this medicine
- your ovaries stop functioning or egg doesn't release with normal levels of LH and FSH
- you have an uncontrolled thyroid or adrenal function
- you have a brain tumour (in your hypothalamus or pituitary gland)
- you have large ovaries or sacs of fluid within your ovaries (ovarian cysts) of unknown origin
- you have unexplained vaginal bleeding
- you have sex hormone dependent tumours of the reproductive system and accessory organs
- you are currently pregnant or breast feeding

The medicine 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.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take PERGOVERIS. Talk about any health conditions or problems you may have, including:

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 healthcare professional 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 healthcare professional who may recommend that you stop treatment.

This treatment increases your risk of developing ovarian hyperstimulation syndrome (OHSS). 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 healthcare professional.

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 healthcare professional.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Interaction with PERGOVERIS:

- PERGOVERIS should not be administered as a mixture with other medicinal products in the same injection, except for follitropin alfa, if prescribed by your healthcare professional. PERGOVERIS may be mixed in the same syringe with follitropin alfa and given in one injection.

Usual dose:

The usual dose is one vial of PERGOVERIS taken every day for up to three weeks. According to your response, your healthcare professional may increase your dose of follitropin alfa usually by 37.5-75 IU at 7 to 14-day intervals.

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

How to take PERGOVERIS:

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

See the detailed "Instructions for Use" that comes with PERGOVERIS for information on how to prepare and inject PERGOVERIS.

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 healthcare professional, 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 healthcare professional.

What are possible side effects from using PERGOVERIS?

These are not all the possible side effects you may have when taking PERGOVERIS. If you experience any side effects not listed here, tell your healthcare professional.

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 healthcare professional 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 healthcare professional 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 healthcare professional.

This is not a complete list of side effects. For any unexpected effects while taking PERGOVERIS, contact your healthcare professional.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Do not store above 25°C. Avoid freezing. Store in the original package in order to protect from light.

Do not use PERGOVERIS after the expiry date which is stated on the vial 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.

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

The medicine must be administered immediately after reconstitution.

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.

Keep out of reach and sight of children.

If you want more information about PERGOVERIS:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website:
<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>; <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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INSTRUCTIONS FOR USE (Powder and diluent for solution for injection)

follitropin alfa 150 IU/lutropin alfa 75 IU

How to take PERGOVERIS

PERGOVERIS is for subcutaneous use that means given by injection just under the skin. Each vial is intended for a single use only.

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

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

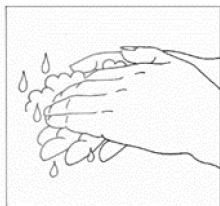
When the desired response has been obtained, a single injection of hCG is given 24-48 hours after the last injection of PERGOVERIS. It is recommended that you have sexual intercourse on the day of, and the day following administration of the hCG. Alternatively, intrauterine insemination (IUI) or *in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

If an excessive response occurs, treatment should be stopped and hCG withheld. For the following cycle, your healthcare professional 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 healthcare professional according to your own specific needs. It is very important that you keep your appointments and follow your healthcare professional's instructions, particularly with regard to the amount and frequency of the medication you are taking.

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

- 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) (or as instructed by your healthcare professional)
 - one vial of diluent (liquid)
 - three alcohol swabs
 - one syringe
 - one needle for mixing (long)

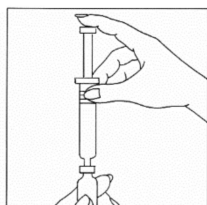
- one fine bore needle for subcutaneous injection (short)
- sharps container (which may be provided by your clinic or pharmacist)

DRAWING UP THE DILUENT FROM THE VIAL

Remove the protective cap from the vial containing the diluent. Use an alcohol swab to clean the rubber stopper and metal ring. Discard the alcohol swab.

Remove the syringe from its package and carefully remove the cap off of the long mixing needle, taking care not to let the needle touch any surface. Pull the plunger back until it is at the line next to the number showing the amount of diluent that you need to draw up as advised by your healthcare provider (for example: 1 cc).

Place the vial of diluent on a clean, flat surface. Push the needle through the center of the rubber stopper on the vial. Then, push the plunger all the way in.



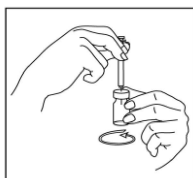
Keeping the needle in the vial, lift the vial and turn it upside down. Check to see that the needle tip is in the liquid. Be sure you completely cover the needle tip with liquid before pulling back on the plunger. Slowly pull the plunger back until you see the required amount of diluent in the syringe. Discard the vial containing any unused diluent into a sharps container. Carefully replace the cap on the needle and place the syringe on a clean surface.

MIXING THE MEDICATION FOR INJECTION

Remove the protective cap from the PERGOVERIS powder vial. Use an alcohol swab to clean the rubber stopper and metal ring. Discard the alcohol swab.

Pick up the syringe containing the diluent and carefully remove the cap. Push the needle through the center of the rubber stopper on the PERGOVERIS powder vial. Slowly inject the diluent into the powder vial by pushing down on the plunger.

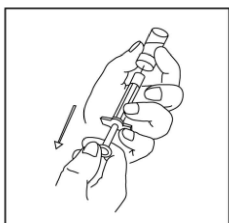
Leaving the needle in the vial, gently rotate the vial between your fingers until all of the powder is dissolved. Do not shake. Check that the solution is clear and colourless. Do not use if the solution is cloudy, discoloured, or contains particles.



DRAW UP THE MEDICATION

After the powder has dissolved, turn the vial upside down, and gently draw up the entire contents of the vial into the syringe, being careful not to pull the plunger out of the syringe. It may help to slowly tip the vial.

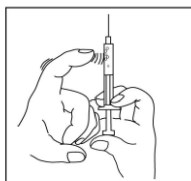
Be sure you completely cover the needle tip with liquid before you pull back the plunger.



CHANGE THE NEEDLE

Hold the syringe with the needle pointing upwards. Create a small airspace at the top of the barrel by gently pulling the plunger back. Carefully recap the needle, then twist and remove the mixing needle. Replace the long mixing needle with the fine-bore, short needle for injection. Twist to attach, and pull to remove the cap.

Hold the syringe with the needle pointing upwards and gently flick the syringe so that, if there are any large air bubbles, they will rise to the top.



If large air bubbles are present, gently push the plunger upwards until a small droplet of liquid appears at the tip of the needle. Replace the cap on the needle. Place the syringe on a clean surface.

Do not worry if you are unable to remove very tiny bubbles; they will do you no harm.

PREPARE THE INJECTION SITE

Select the site of injection (e.g. top of thigh, tummy). Choose a different site each day. Wipe the chosen area with an alcohol swab, cleansing an area of approximately 5 cm x 5 cm (an area about the size of a tea bag). Lay the used side of the swab next to your working surface or on the alcohol swab wrapper.

INJECTING THE MEDICATION

Pick up the syringe and remove the cap from the needle. Using the hand with which you write, hold the syringe like a pencil or as if “throwing a dart”. With your other hand, gently squeeze the skin together to make a little elevation at the injection site. Using a “dart like motion”, insert the needle at a 90° angle. (You need very little force but quick action).

Inject the solution by gently pushing on the plunger with your index finger. Take as much time as you need to inject all the solution. As you release the skin from your grip, withdraw the needle by pulling it

straight out. Clean the skin with the clean side of the alcohol swab using a circular motion. If there is minor oozing you may need to apply a small amount of pressure.

INSTRUCTIONS FOR USE (Solution for Injection in a Pre-filled Pen)

(300 IU/150 IU in 0.48 mL; 450 IU/225 IU in 0.72 mL; 900 IU/450 IU in 1.44 mL)

How to take PERGOVERIS:

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

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 healthcare professional may increase your dose of follitropin alfa usually by 37.5-75 IU at 7 to 14-day intervals.

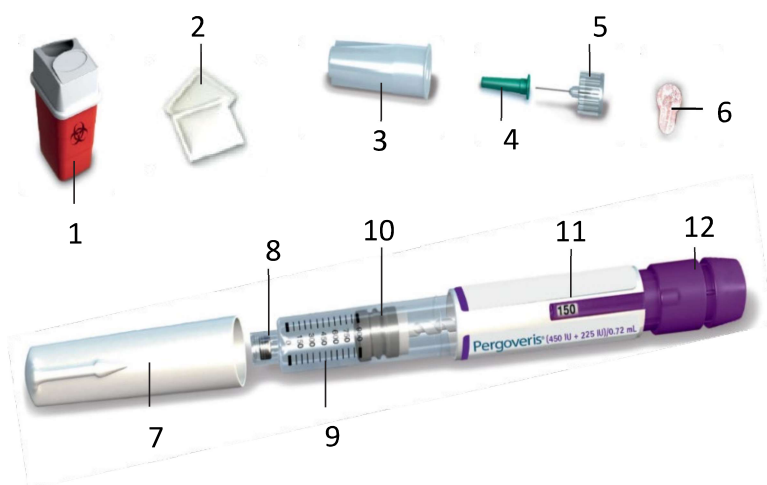
When the desired response has been obtained, a single injection of hCG is given 24-48 hours after the last injection of PERGOVERIS. It is recommended that you have sexual intercourse on the day of, and the day following administration of the hCG. Alternatively, intrauterine insemination (IUI) or *in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

If an excessive response occurs, treatment should be stopped and hCG withheld. For the following cycle, your healthcare professional 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 healthcare professional according to your own specific needs. It is very important that you keep your appointments and follow your healthcare professional's instructions, particularly with regard to the amount and frequency of the medication you are taking.

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:

- Let the pre-filled pen sit at room temperature for at least 30 minutes before use to allow the medicine to reach room temperature.

Do not use a microwave or other heating element to warm up the pen.

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



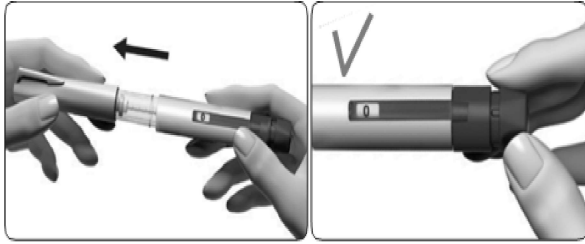
- On a clean surface, e.g., clean table or kitchen surface, lay out everything you will need:
 - PERGOVERIS pre-filled pen
 - One removable injection needle
 - Alcohol swabs
 - Sharps disposal container
- Verify the **expiration date** on the label. Do not use expired medication.



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 healthcare professional will tell you how many IUs of follitropin alfa to inject each day.



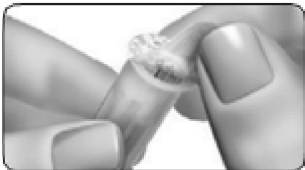
- Prepare your needle for injection:
 - Get a new needle – only use the “single-use” needles supplied
 - Hold the outer needle cap firmly
 - Check that the peel-off seal on the outer needle cap is not damaged or loose:

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.

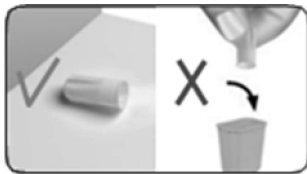


- Important Note: Do not attach the needle too tightly; the needle could be difficult to remove after the injection.

- 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.

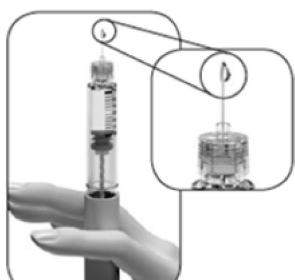


- Carefully remove the green inner shield by pulling it straight off and discard it.
 - Warning: Do not recap the needle with the green inner shield as this can lead to needle stick.



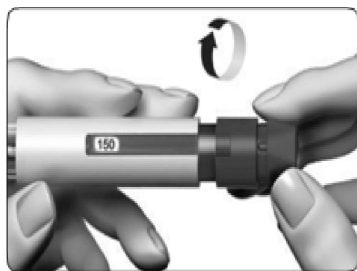
- **Please note: if this is NOT a brand new PERGOVERIS pen (you have done previous injections with this pen), then proceed to Section 4: “Setting the dose prescribed by your healthcare professional”.**

- **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 healthcare professional

- 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.

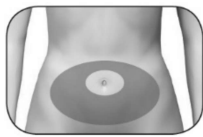


- Important Note: Check that the Dose Display shows your prescribed dose before you move on to the next step.

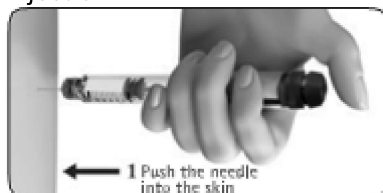


5. Injecting the dose

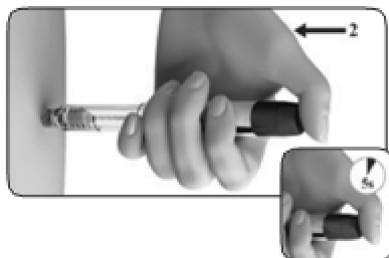
- Choose an injection site in the area your healthcare professional or nurse has told you to give the injection.
 - Note: To minimize skin irritation, select a different injection site each day.



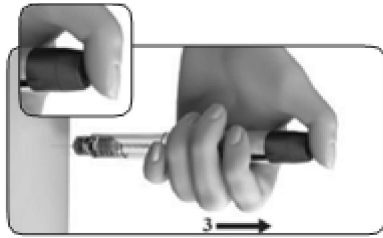
- Clean the skin by wiping the area with an alcohol swab. Allow the site to dry.
- Set the alcohol wipe to the side.
- Verify once more that the Dose Display is showing the correct dose. If it is not the correct dose, you must adjust it by turning the dose setting knob either clockwise or counter-clockwise (see Step 4 “Setting your dose prescribed by your healthcare professional”).
- Inject the dose as you were trained to do by your healthcare professional 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 90° angle into the skin. You might bend the needle if you do not insert it at a 90° angle.
 - Place your thumb in the middle of the dose setting knob.
 - Slowly 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.



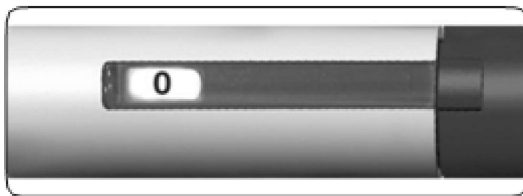
- Do not release the dose setting knob until you remove the needle from your skin.



- 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.



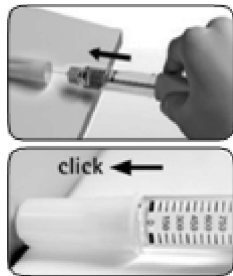
- Repeat Section 1 “Before you start using PERGOVERIS” through Section 2 “Getting your PERGOVERIS pen ready for injection” with a second pen.
- **For a brand new pen that you are using for the first time**, look closely at the tip of the needle for a tiny drop of fluid.

- If you see a tiny drop(s) of fluid, proceed to Section 4 “Setting the dose prescribed by your healthcare professional”.
- 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.”



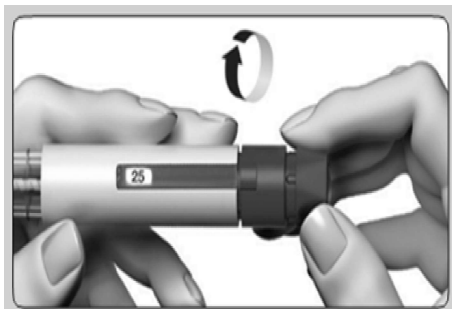
- Grip the outer needle cap and unscrew the needle by turning counter clockwise. Dispose of the used needle safely.



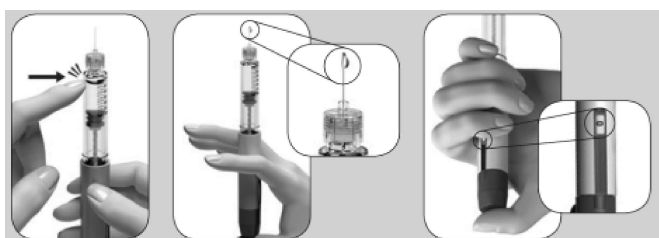
- Never reuse any used needle. Never share needles.
- Recap the pen.

7. Preparing your new PERGOVERIS pen for first time use

- 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 healthcare professional”.

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.