PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

GONAL-f® Pen

(follitropin alfa injection)

Read this carefully before you start taking **GONAL-f®** 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 **GONAL-f®**.

What is GONAL-f® used for?

- GONAL-f® (follitropin alfa injection) is used to help eggs develop in women as part of Assisted Reproductive Technologies (ART), which are procedures that may help you become pregnant, such as IVF (In Vitro Fertilization). To help eggs develop fully, another hormone called hCG (human chorionic gonadotropin), is given.
- GONAL-f® is also used to help eggs develop in some patients with irregular or absent menstrual cycles. To complete the development of eggs, another hormone, hCG, is given.

How does GONAL-f® work?

GONAL-f® is a hormone called FSH (follicle stimulating hormone), which belongs to a group of medicines called "gonadotropins". Gonadotropins are involved in reproduction and fertility.

GONAL-f® is a purified form of FSH that causes eggs to develop in women. GONAL-f® is a highly purified form of FSH that is manufactured using the latest technology with proven effectiveness and safety in clinical studies.

What are the ingredients in GONAL-f®?

Medicinal ingredients: Follitropin alfa

Non-medicinal ingredients: Poloxamer 188, sucrose, L-methionine, sodium dihydrogen phosphate monohydrate, disodium phosphate dihydrate, m-cresol, phosphoric acid, sodium hydroxide and water for injection.

This product does not contain latex.

GONAL-f® comes in the following dosage forms:

GONAL-f® Pens are available as a solution in a cartridge pre-assembled in a multi-use disposable prefilled pen, ready to use.

GONAL-f® Pens are available in the following dosage forms:

- 300 IU/0.48 mL
- 450 IU/0.72 mL
- 900 IU/1.44 mL

Do not use GONAL-f® if:

- You have a high level of FSH in your blood that show your ovaries do not work at all.
- Your thyroid or adrenal function is not under control.
- You are allergic to recombinant human FSH or any of the ingredients in GONAL-f®.
- You are currently pregnant or breastfeeding
- You have large ovaries or sacs of fluid within your ovaries (ovarian cysts) not due to polycystic ovarian disease (PCOS)
- You have abnormal bleeding from your uterus or vagina from an unknown cause.
- You have tumours of the ovary, uterus, breast or brain (hypothalamus or pituitary gland)

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

Porphyria

If you have porphyria or someone in your family has porphyria, GONAL-f® may increase the risk of a sudden attack. Tell your healthcare professional immediately if:

- Your skin becomes fragile and easily blistered, especially skin that is in the sun a lot, and/or
- You have stomach, arm or leg pain

In case of the above events your healthcare professional may recommend that you stop treatment.

Overstimulation of the Ovary During FSH Therapy

Ovarian Enlargement

Using FSH therapy to help eggs develop can lead to the growth of more than one egg. This may cause your ovaries to be abnormally large. Symptoms of large ovaries include bloating or pain in your lower stomach (pelvic) area. This is more likely to happen in women with polycystic ovarian syndrome (PCOS).

Ovarian Hyperstimulation Syndrome (OHSS)

This treatment increases the chance of a condition called ovarian hyperstimulation syndrome (OHSS). OHSS is a serious medical condition that can happen when your ovaries produce too many eggs (overstimulated). OHSS can cause fluid to suddenly build up in the area of your stomach and chest and can cause blood clots to form. In rare cases, severe OHSS can cause death. OHSS may also happen after you stop using GONAL-F®. Stop using GONAL-F® and call your healthcare professional right away if you have symptoms of OHSS, including: severe swelling of the stomach area, trouble breathing, diarrhea, severe lower stomach (pelvic) area pain, feeling sick (nausea), vomiting, decreased urine output, and weight gain.

However, if you are not ovulating, and if the recommended dose and schedule of administration are adhered to, the occurrence of OHSS is less likely. GONAL-f® treatment will hardly ever cause a severe case of OHSS unless another medicine called hCG is given to help the final egg development. If the risk of OHSS exists or OHSS is starting, its best not to get hCG, and women should avoid getting pregnant by not having sex.

Breathing and Blood Clotting

Using gonadotropin can lead to serious breathing problems like collapsing of the lungs, extreme shortness of breath and worsening of asthma.

It may also raise the chance of getting a blood clot, which can cause major health issues like blockage in the lungs, blood vessel problems, heart attack, stroke, or blockage in the arteries in your arms and legs. In rare cases, these problems have led to death.

Reproductive Issues

GONAL-F® may increase your chance of having a pregnancy that is abnormally outside of your womb (ectopic pregnancy). Your chance of having a pregnancy outside of your womb is increased if you also have fallopian tube problems. Call your healthcare provider right away if you have symptoms of an ectopic pregnancy including: stomach or pelvic pain especially on one side, neck pain, nausea and vomiting, shoulder pain, and rectal pain.

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

When using GONAL-f®, 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. The chance of this occurring depends on the schedule of your medication and is similar between GONAL-f® and other drugs like GONAL-f® (gonadotropins). Your healthcare professional will monitor you closely to help minimize the possibility of multiple pregnancy.
In women receiving fertility treatment, tumours (in the ovary) have been reported. It is not known if treatment with fertility medicines increase the chance of a tumour developing in these women.

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

The following may interact with GONAL-f®:

GONAL-f® is often used with other medicines to help eggs develop. If you're also taking GONAL-f® at the same time as a "gonadotropin-releasing hormone" (GnRH) agonist or antagonist (these medicines reduce your sex hormone levels and stop you ovulating, your healthcare provider may adjust your GONAL-f® dose. Major interactions with other medicines have not been reported.

How to take GONAL-f®:

How is GONAL-f® administered?
Due to its high level of purity, GONAL-f® is approved for subcutaneous injection (just under the skin), which is easier and less painful than intramuscular injections (in the muscle). In fact, with professional guidance, you can learn to do your own injections in the comfort and privacy of your own home.

Why is GONAL-f® provided in the prefilled Pen?

GONAL-f® is provided in the prefilled pen to help you easily self-administer accurate and consistent GONAL-f®. It is designed so that it is easy to read and set the dosage dial confirmation before injecting the medication. The pen reservoir is clear so that the amount of medication available in the Pen can be seen at all times.

How to use GONAL-f®:

Understandably, you may be a little anxious at first about giving yourself an injection. That is why this information has been produced. Refer to it as necessary and follow each instruction step by step.

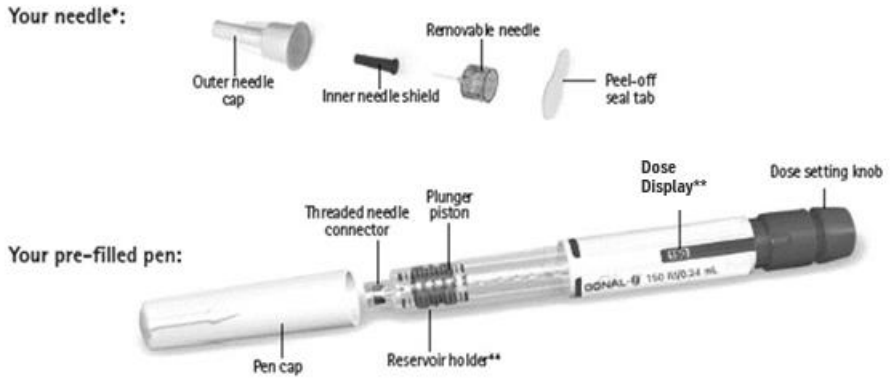
Always take GONAL-f® exactly as your healthcare professional has instructed you. You should check with your healthcare professional if you are unsure.

Before starting to use your pen, please read these instructions the whole way through first. This pen has been prescribed for you – do not let anyone else use it. The numbers on the Dose Display are measured in International Units or IU. Your healthcare professional would have told you how many IUs to inject each day. Give yourself the injection at the same time each day.

How to inject GONAL-f®:

The most easily accessible areas for subcutaneous injection are the abdomen and thighs. The absorption of GONAL-f® is the same regardless of the injection site selected. You may find the injection is more comfortable if you vary the site each time you inject GONAL-f®.

Get familiar with your GONAL-f® Pen:



*For illustration purposes only. The needles supplied may look slightly different.

**The numbers in the Dose Display and reservoir holder represent the number of International Units (IU) of medicine.

1. Before you start using your GONAL-f® Pen

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

- Take the carton out of the refrigerator for at least 30 minutes before use to let it warm to room temperature. Do not use a microwave or other heating element to warm up the pen.

Warning: Do not shake the pen, as this may cause air bubbles to appear in the medication.

- On a clean surface, e.g., clean table or kitchen surface, lay out everything you will need:

- GONAL-f® Pen
- One removable injection needle (8 mm 31 gauge) [use the “single-use” disposable needles provided with the GONAL-f® Pen box]
- Alcohol swabs and a sharps container (not included in the pack)

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

2. Getting your GONAL-f® Pen ready for injection

- Take off the pen cap.
- Wipe the end of the threaded tip (containing the rubber center) using an alcohol swab.
- Look carefully at the reservoir holder. Check that the reservoir holder is not cracked and that the solution is clear and does not contain particles. If the reservoir holder is cracked or if the solution is discoloured or cloudy, obtain a new pen.
- Verify that the Dose Display is set to “0”.

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:

- Remove the peel-off seal.

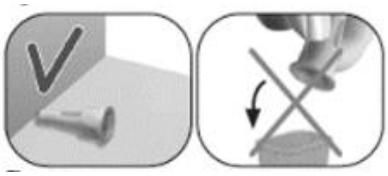
<u>CAUTION:</u> If the peel-off seal is damaged or loose, do not use the needle. Throw it away in a sharps disposal container. Get a new needle.

3. Attach the needle

- Screw the threaded tip of the GONAL-f® Pen into the outer needle cap until you feel a light resistance.

  - <u>Important Note:</u> 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 straight off.

- 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 GONAL-f® Pen with the needle pointing upwards.

- Carefully remove the green inner shield by pulling it straight off and discard it.

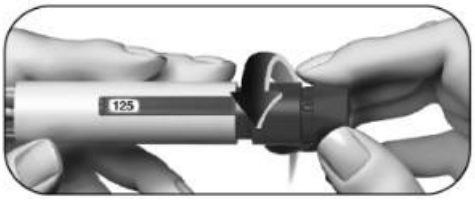
  - Warning: Do not recap the needle with the green inner shield as this can lead to needle stick injury
- Please note: if this is NOT a brand new GONAL-f® Pen (you have done previous injections with this pen), then proceed to Section 4: “Setting the dose prescribed by your healthcare professional”.

- **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 yourhealthcare professional”.
    - If you do not see a tiny drop(s), please refer to Section 7 “Preparing your new GONAL-f® 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.



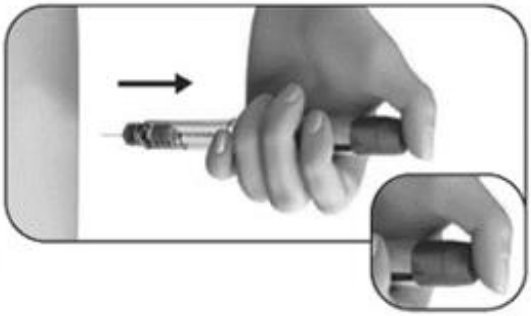
- Important Note: Check that the Dose Display shows your prescribed dose before you move on to the next step.

5. Injecting the dose

- Choose an injection site in the area your healthcare professional has told you to give the injection.
    - Note: To minimize skin irritation, select a different injection site each day. See section "How to inject GONAL-f®?" for more details.
- 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.
    - 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 then 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).
- Use the clean side of your alcohol swab to gently clean the injection site. If there is minor oozing you may need to apply a small amount of pressure for a few seconds.

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 GONAL-f® 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 your GONAL-f® Pen” through Section 2 “Getting your GONAL-f® 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 of fluid, proceed to Section 4 “Setting the dose prescribed by your healthcare professional”.
    - If you do not see a tiny drop(s), please refer to Section 7 “Preparing your new GONAL-f® 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 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:

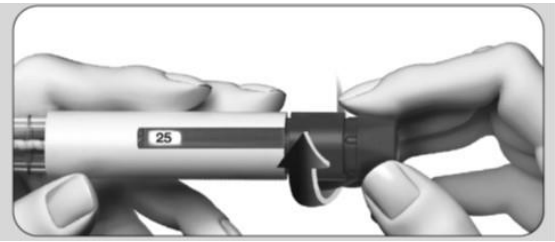
- Place the outer needle cap on a flat surface.
- Hold the GONAL-f® Pen firmly with one hand, and slip the needle into the outer needle cap. Be careful not to prick yourself with the needle.
- Continue by pushing the capped needle against a firm surface until you hear a “click.”

Grip the outer needle cap and unscrew the needle by turning counterclockwise. Dispose of the used needle safely.

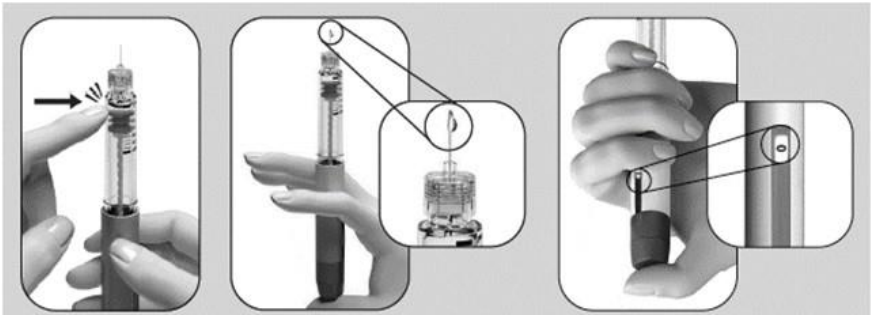
- Never reuse any used needle. Never share needles.
- Please note: your clinic may provide you with a special sharps container designed for GONAL-f®. If you have received the special GONAL-f® sharps container, simply follow the steps to remove the needle that are outlined on the box.
- Recap the pen.

7. Preparing your new GONAL-f® 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”.

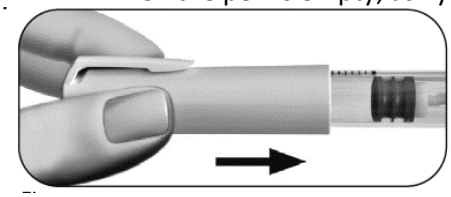


- You may need to repeat this step if you do not see a tiny drop of liquid appearing at the tip of the needle.
- Proceed to Section 4 “Setting the dose prescribed by your healthcare professional”.

Storing the GONAL-f® Pen:

CAUTION: Never store the pen with the needle attached. Always remove the needle from the GONAL-f 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.

Usual dose:

Every treatment is individualized. Your treatment has been carefully designed for you by your healthcare professional. Over the course of your treatment, doses may range between 75 to 450 IU depending on your specific medical condition and your response to the medicine.

The GONAL-f® Pens have been designed to allow simple and flexible dosing that covers most treatment protocols or dosing regimens.

Overdose:

If you think you, or a person you are caring for, have taken too much GONAL-f®, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

Do not take a double dose to make up for any doses you have missed. Contact your healthcare professional for advice if you forget to take a dose of GONAL-f®.

What are possible side effects from using GONAL-f®?

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

Fertility drugs are safe to take with close monitoring by your healthcare professional. As with all medication, there is a potential for side effects.

The following side effects have been reported with the use of GONAL-f® during clinical trials and post-market use:

Common and Very Common: may affect 1 to 10 users in 100

- Ovarian cysts
- Mild to moderate ovarian enlargement
- Breast tenderness
- Mild to moderate OHSS
- Mild to severe injection site reaction (such as pain, redness, bruising, swelling and/or irritation)
- Headache
- Stomach pain or bloating
- Feeling sick (nausea), vomiting, diarrhea

Uncommon, Rare and Very Rare: may affect less than 1 to 10 users in 1,000

- Severe OHSS
- Blood clots (thrombosis)
- Difficulty breathing (acute pulmonary distress)
- Worsening of asthma
- Mild to severe allergic reactions (hypersensitivity) such as rash, red skin, hives, swelling of your face with difficulty breathing may occur. These reactions can sometimes be serious.

The greatest concern your healthcare professional will have is ovarian hyperstimulation syndrome (OHSS). To avoid the development of OHSS, your healthcare professional will carefully monitor your response to GONAL-f®. Ovarian enlargement, sometimes accompanied by abdominal bloating and pain, may occur in about 20% of women taking gonadotropins. This is generally reversed with cessation of treatment and severe life-threatening cases are rare.

A causal relationship between treatment with fertility drugs and ovarian cancer has not been established.

The following medical events have been reported subsequent to pregnancies resulting from gonadotropin therapy in controlled clinical trials: spontaneous abortion, tubal pregnancy, premature labour, postpartum fever and congenital abnormalities.

None of these events were thought to be drug-related. The incidence is not more than that found in the general population.

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:

GONAL-f® Pen may be stored by the patient between 2 and 25 ºC (in the refrigerator or at room temperature) for a single period of not more than 3 months. After first use, the pen may be stored at 25 ºC (room temperature) for a maximum of 28 days.

Do not use the GONAL-f® Pen if the solution contains particles or is not clear.

Do not freeze. Protect from light.

Keep in a safe place out of the reach of children.

Do not use after the expiry date.

If you want more information about GONAL-f®:

- 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 1-800-387-8479.

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

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