

PART III: CONSUMER INFORMATION

GONAL-f[®] Pen (follitropin alfa injection)

This information is part III of a three-part “Product Monograph” published when GONAL-f[®] Pen was approved for sale in Canada and is designed specifically for Consumers. This is only a summary and does not contain all information about GONAL-f[®] Pen. Contact your doctor or pharmacist if you have any questions about the drug.

This leaflet is designed to help you self-administer GONAL-f[®] solution for injection using the prefilled Pen and to answer many of the questions you may have on infertility and GONAL-f[®] therapy.

ABOUT THIS MEDICATION

What is GONAL-f[®]?

GONAL-f[®] is follicle-stimulating hormone (FSH) with no urinary proteins, which stimulates oocyte (egg) development in women. GONAL-f[®] is a highly purified recombinant human form of FSH, manufactured using the latest technology with proven effectiveness and safety in clinical studies.

It is provided in liquid formulation in the prefilled Pen, for easy administration under the skin (subcutaneous injection).

GONAL-f belongs to a group of medicines called “gonadotropins”.

What is GONAL-f[®] used for?

GONAL-f[®] (follitropin alfa for injection) is used to stimulate the maturation of follicles in ovulatory patients undergoing Assisted Reproductive Technologies (ART) such as *in vitro* fertilization (IVF). To complete the maturation of follicles another hormone, hCG (human chorionic gonadotropin) is given.

GONAL-f[®] is also used to stimulate the maturation of follicles in some patients whose menstrual cycle is either irregular or absent. To complete the maturation of follicles another hormone, hCG is given.

When should GONAL-f[®] not be used?

GONAL-f[®] should **not** be used if you:

- Have high levels of FSH indicating primary ovarian failure
- Have uncontrolled thyroid or adrenal dysfunction
- Are allergic (hypersensitive) or have a history of hypersensitivity to FSH or to any of the other ingredients of GONAL-f[®]
- Are pregnant or breastfeeding
- Have ovarian enlargement or a cyst not due to polycystic ovarian disease (PCO)
- Have vaginal bleeding of unknown cause
- Have tumours of the ovary, uterus, breast or brain (hypothalamus or pituitary gland)

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.

The medicinal ingredient in GONAL-f[®]:

Follitropin alfa.

The nonmedicinal ingredients of GONAL-f[®] are:

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.

What dosage forms of GONAL-f[®] are available?

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/0.5 mL (22 µg/0.5 mL)
- 450 IU/0.75 mL (33 µg/0.75 mL)
- 900 IU/1.5 mL (66 µg/1.5 mL)

WARNINGS AND PRECAUTIONS

General

To help avoid side effects and ensure proper use, talk to your doctor or pharmacist before you take GONAL-f[®].

Your fertility should be evaluated before the treatment is started by a doctor experienced in treating fertility disorders.

Porphyria

If you have porphyria or a family history of porphyria, GONAL-f[®] may increase the risk of an acute attack. Tell your doctor immediately if:

- Your skin becomes fragile and easily blistered, especially skin that has been frequently in the sun, and/or
- You have stomach, arm or leg pain.

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

Overstimulation of the Ovary During FSH Therapy

Ovarian Enlargement

Use of FSH therapy to stimulate follicular development may result in the growth of more than one follicle. This may result in mild to moderate uncomplicated ovarian enlargement which may be accompanied by abdominal distention and/or abdominal pain. It is more commonly seen in women with polycystic ovarian syndrome.

Ovarian Hyperstimulation Syndrome (OHSS)

Treatment increases your risk of developing ovarian hyperstimulation syndrome (OHSS). This is when multiple follicles develop and may become large cysts. In rare cases, severe OHSS may be life-threatening. OHSS may cause fluid build-up in your abdominal and chest areas and can cause blood clots to form. Call your doctor right away if you notice severe abdominal swelling, pain in the stomach area (abdomen), feeling sick (nausea), vomiting, sudden weight gain due to fluid build-up, diarrhea, decreased urine output or trouble breathing. However, if you follow your doctor's instructions for the recommended dose and schedule of administration, the occurrence of OHSS is uncommon. GONAL-f[®] treatment seldom causes significant OHSS unless the medicine used to induce final follicular maturation and ovulation (containing human chorionic gonadotropin - hCG) is administered. In cases where OHSS is developing it is recommended to not give hCG, and women should prevent pregnancy at this time by not having sexual intercourse.

Breathing and Blood Clotting

Serious breathing problems (e.g., lung collapse, extreme shortness of breath and worsening of asthma) have been reported with use of gonadotropin therapy.

Treatment with gonadotropin therapy may increase the risk of having a blood clot (thrombosis) which may or may not be associated with Ovarian Hyperstimulation Syndrome. Blood clots can lead to serious medical conditions, such as blockage in the lungs (pulmonary embolus), blood vessel problems (thrombophlebitis), heart attack, stroke, blockage in the arteries in your arms and legs which may result in a loss of your arm or leg. In rare cases, lung complications and/or blood clots have resulted in death.

Reproductive Issues

Since women with infertility undergoing assisted reproduction, particularly IVF, may have tubal abnormalities, the incidence of ectopic pregnancies (pregnancy in the fallopian tubes) might be increased. Early ultrasound to confirm that a pregnancy is in the uterus is important.

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

Reports of multiple births have been associated with fertility treatments. You should discuss the potential risk of multiple births with your doctor before beginning treatment.

The incidence of multiple births with GONAL-f[®] is no different from any other gonadotropin and is dependent upon the protocol

used by the clinic. Your doctor will monitor you closely to help minimize the possibility of a multiple pregnancy. The majority of births (about 80%) are single babies. Of those women who do have multiple births, the majority of these are twins. Only very few women conceive 3 or more babies. Even so, neither single nor multiple births can be guaranteed.

There have been reports of ovarian and other reproductive systems tumours in women who have had infertility treatment. It is not known if treatment with fertility medicines increase the risk of these tumours in infertile women.

INTERACTIONS WITH THIS MEDICATION

GONAL-f[®] is often used with other medicines to stimulate ovulation (e.g, hCG and LH), and may help the maturation of follicles which contains the eggs. If a GnRH agonist or antagonist medicine is also given along with your GONAL-f[®] in your treatment program, you may be told by your doctor to change your dose of GONAL-f[®] over the course of your treatment. No other significant interactions with other medicines have been reported.

PROPER USE OF THIS MEDICATION

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 doctor has instructed you. You should check with your health care provider 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 doctor would have told you how many IUs to inject each day. Give yourself the injection at the same time each day.

Recommended Dose

Every treatment is individualized. Your treatment has been carefully designed for you by your doctor. 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.

Overdosage:

If you have accidentally injected too much GONAL-f[®], do not panic. Simply contact your physician or healthcare professional for further instructions.

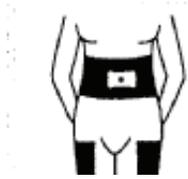
Missed dose

What should I do if I forget to take my GONAL-f®?

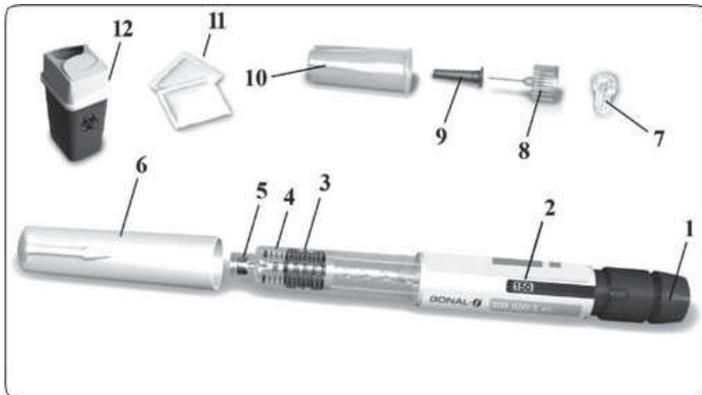
Do not take a double dose to make up for any doses you have missed. Contact your doctor for advice if you forget to take a dose of GONAL-f®.

Where should I 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®.



GONAL-f® Pen, and other materials you may need for injection:



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

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.

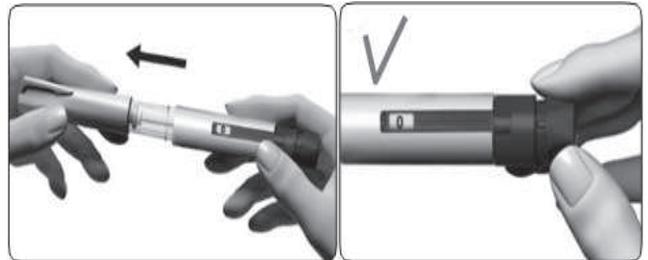
Warning: Do not shake the pen, as this may cause air bubbles to appear in the medication.

- On a clean surface, e.g., clean table or kitchen surface, lay out everything you will need:
 - GONAL-f® Pen
 - One removable injection needle (1/2 inch 29 gauge) [use the single-use disposable needles provided with the GONAL-f® Pen box].
 - Alcohol swabs
 - Sharps disposal container
- 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:

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 GONAL-f[®] 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 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.

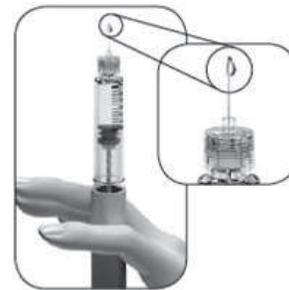


- **Please note: if this is NOT a brand new GONAL-f[®] Pen (you have done previous injections with this pen), then proceed to Section 4: “Setting the dose prescribed by your doctor”.**

- **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 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 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. See section “Where should I 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 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 90° angle into the skin. You might bend the needle if you do not insert it at a 90° 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).
- 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(s) of fluid, proceed to Section 4 “Setting the dose prescribed by your doctor”.
 - 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 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 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.”



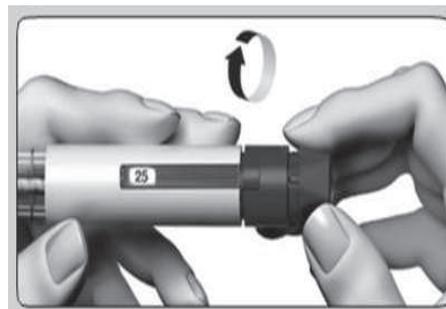
- Grip the outer needle cap and unscrew the needle by turning counter clockwise. Dispose of the used needle safely.



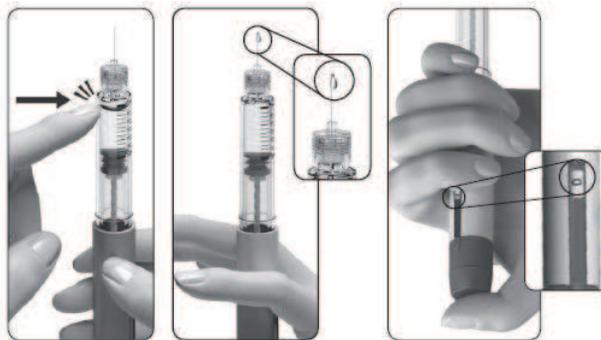
- Never reuse any used needle. Never share needles.
- Please note: your clinic may provide you with a special sharps container designed for GONAL-f®. If you have received the special GONAL-f® sharps container, simply follow the steps to remove the needle that are outlined on the box.
- Recap the pen.

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 doctor”.

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.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Are there any side effects with gonadotropin therapy?

Fertility drugs are safe to take with close monitoring by your doctor. 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 doctor will have is ovarian hyperstimulation syndrome (OHSS). To avoid the development of OHSS, your doctor 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 events were thought to be drug-related. The incidence is not more than that found in the general population.

This is not a complete list of side effects. If you experience any unusual symptoms or side-effects while taking GONAL-f® Pen, you should report them to your doctor or pharmacist immediately. It is also wise to discuss the possibility of side effects with your doctor before you begin treatment.

HOW TO STORE IT

GONAL-f® Pen may be stored by the patient between 2 and 25°C (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°C (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.

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 0701D
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 from:

EMD Serono, A Division of EMD Inc., Canada
2695 North Sheridan Way, Suite 200
Mississauga ON L5K 2N6
A Business of Merck KGaA, Darmstadt, Germany

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