PART III: CONSUMER INFORMATION

LUVERIS® (Lutropin alfa for injection)
lyophilized powder for reconstitution

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

ABOUT THIS MEDICATION

What the medication is used for:

- Biologic medication used to treat hypogonadotropic hypogonadism in women
- Purified hormone that should be taken under close supervision of the doctor who prescribed it

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.

LUVERIS provides you with LH that may be necessary to be given along with GONAL-F® (follitropin alfa for injection) that provides you with FSH. FSH is necessary for the recruitment, growth, and maturation of the ovarian follicles which contain eggs known as ova or oocytes. The addition of LUVERIS to GONAL-F may enhance this process. This occurs during the first half of the female reproductive cycle. After LUVERIS and GONAL-F are given to help develop ovarian follicles, another hormone, hCG (human chorionic gonadotropin), may be given mid-cycle to mature the eggs and cause ovulation.

When it should not be used:

- If you are allergic (hypersensitive) to gonadotropins (such as luteinizing hormone, follicle stimulating hormone or human chorionic gonadotropin), or any of the other ingredients of LUVERIS.
- If you have been diagnosed as having ovarian, uterine or breast cancer.
- If you have had a brain tumour diagnosed.
- If you have ovarian enlargement or ovarian cyst unrelated to polycystic ovarian disease and of unknown origin.
- If you have unexplained vaginal bleeding.

The medicine must not be used when a condition exists which would make a normal pregnancy impossible, such as:

- Premature menopause
- Malformation of sexual organs
- Specific tumours of the womb

What the medicinal ingredient is:
It is called lutropin alfa, and is a protein naturally found in the body. Through recombinant DNA (rDNA) technology the products manufactured are composed of highly purified hormones that offer a consistent dosage and do not contain urinary proteins.

What the important nonmedicinal ingredients are:
Sucrose, L-methionine, disodium phosphate dihydrate, sodium dihydrogen phosphate monohydrate, and Polysorbate 20.

What dosage forms it comes in:
Dry powder for reconstitution. A solution is prepared (75 IU LUVERIS with 1 mL Sterile Water for Injection) and then injected subcutaneously.

WARNINGS AND PRECAUTIONS

BEFORE you use LUVERIS talk to your doctor or pharmacist if:

- You have sex hormone-dependent tumours of the reproductive tract and accessory organs
- You have active, untreated tumours of the hypothalamus or pituitary gland
- You are pregnant or are breast-feeding your baby
- You have ovarian failure
- You have abnormal uterine bleeding of unknown origin
- You have hypersensitivity to gonadotropins or to any of the non-medicinal ingredients

Compared with natural conception, the incidence of multiple pregnancies (mainly twins) and births is increased in patients undergoing this type of treatment. However, this can be minimized by using the recommended dose and schedule of administration.

Miscarriages are higher than in the normal population, but comparable with the rates found 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.

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 ask your doctor.

Birth defects after ART (Assisted Reproduction Techniques) may be slightly higher than after spontaneous conceptions, although this is not confirmed. This could be due to differences

in parental factors like maternal age, genetics, as well as the ART procedures and multiple pregnancies.

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.

LUVERIS has not been shown to affect the activity of co-administered GONAL-F.

PROPER USE OF THIS MEDICATION

Usual dose:
LUVERIS is usually taken every day for up to three weeks simultaneously with injections of FSH. The usual dose starts with 75 IU of LUVERIS together with 75 IU or 150 IU of FSH. According to your response, your doctor may increase your dose of FSH by preferably 37.5-75 IU at 7-14 day intervals. Your physician may decide to extend your treatment up to 5 weeks.

Overdose:
The effects of an overdose of LUVERIS are unknown, nevertheless there is a possibility that ovarian hyperstimulation syndrome may occur. If you inject more medication at one time that you were prescribed, you should contact your doctor.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:
If you forget to take LUVERIS, do not take a double dose. In the case of a forgotten dose, please contact your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

As with any drug, you may experience side effects when taking LUVERIS. In clinical trials, the most common side effects (experienced by more than 2% of patients) were headache, pelvic and abdominal pain, nausea, OHSS, breast pain, ovarian cysts, flatulence, injection site reactions, general pain, constipation, fatigue, painful menstruation, ovarian disorder, diarrhea and upper respiratory tract infections.

When taking LUVERIS, 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.

It is important to regularly tell your health care professional how you are feeling and if you have developed any new symptoms while taking LUVERIS.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

The most serious side effect associated with LUVERIS is ovarian hyperstimulation syndrome (OHSS). If you experience the early warning signs of OHSS, including severe abdominal pain, nausea, vomiting and weight gain, contact your doctor as soon as possible.

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

HOW TO STORE IT

Lyophilized vials are stable when stored at 2-25°C and protected from light. Do not expose to extreme heat or cold. Do not use the product after the expiry date indicated on the label.

Do not use LUVERIS if you notice any signs of deterioration or damage to the container. The solution should not be administered if it contains particles or is not clear.

How to prepare and inject a dose of LUVERIS
Before you start, clean your work surface. Wash your hands well with soap and water.

It is important that your hands and the items you use be as clean as possible. Needles should not touch any surface except inside the LUVERIS vial and your skin that has been cleaned with alcohol. Keep needles capped prior to use. Make sure you use a new needle each time you inject to avoid contamination. Dispose of all used needles and glass in the disposal container provided.

Assemble everything you need:

- Two alcohol swabs
- One vial of diluent
- One vial of LUVERIS
- One syringe
- One needle for mixing (long)
- One fine-bore needle for subcutaneous injection (short)

If you use your kitchen to prepare the injection, ensure that all medicines and needles are kept well away from food. As for the injection itself, it can be given in any room where you feel comfortable.

Opening and drawing up the diluent
Opening the vial(s) of diluent:
You should have one vial containing diluent (clear liquid) and one vial containing LUVERIS (white powder) as prescribed by your doctor.

- Remove the protective cap from the vial containing the diluent.

- Use an alcohol swab to cleanse the metal ring and rubber stopper.
- Discard the alcohol swab.

Drawing up the diluent from the vial:

- Remove the syringe from its package and carefully uncover the 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 (example 1 cc).
- Place the vial on a clean, flat surface. Push the needle through the centre 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 the disposal container.
- Carefully replace the cap on the needle and place the syringe on a clean surface.

Preparing the injection solution

- Remove the protective cap from the LUVERIS powder vial. Use an alcohol swab to cleanse the metal ring and rubber stopper. Discard the alcohol swab.
- Pick up the syringe containing the diluent and carefully remove the cap.
- Slowly inject the required amount of diluent into the powder vial.
- 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 colorless. Do not use if the solution is cloudy, discolored, or contains particles.

Drawing up the solution

- 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.
- You may also mix LUVERIS and GONAL-F together as an alternative to injecting each product separately. Add the GONAL-F solution into the vial of LUVERIS.

Changing the needle

- Hold the syringe with the needle pointing upwards. Create an airspace at the top of the barrel by gently pulling the plunger back. Carefully recap the needle, then twist and remove it.
- Replace the long mixing needle with the fine-bore short needle for injection. Hold the syringe with the needle pointing upwards and gently flick the syringe if there are any visible air bubbles. Gently push the plunger until all the air bubbles are gone.
- Do not worry if you are unable to remove very tiny bubbles. Gently push the plunger upwards until a small droplet of liquid appears at the tip of the needle.
- Replace the cap on the needle and place the syringe on a clean surface.

Preparing the injection site

- Select the site of injection (e.g. top of thigh, tummy). Refer to the injection site diagram provided to you by your physician in the "Patient Instructions for LUVERIS". 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 square tea bag).
- Lay the used side of the swab next to your working surface or on the alcohol swab wrapper.

Injecting the solution

- Pick up the syringe and remove the cap from the needle. Invert the needle and 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.

Disposal

Once you have finished your injection, immediately discard the needles and syringe (without recapping the needle) into the disposal container.

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 Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to: Canada Vigilance Program**
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site 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 professionals can be found at: http://www.emdserono.ca or by contacting the sponsor, EMD Serono, A Division of EMD Inc, Canada at: 1-888-737-6668.

EMD Serono is a business of Merck KGaA, Darmstadt, Germany

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