PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Ovitrelle® 250 micrograms

Solution for subcutaneous injection

Pre-filled syringe
Pre-filled pen

The active ingredient and its quantity:
Choriogonadotropin alfa 250 mcg/0.5 ml equivalent to 6500 IU
Inactive ingredients — see section 6.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist. Keep this leaflet at hand; you may need to read it again.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.
If you experience any side effects, speak to your doctor or pharmacist. This includes any possible side effect not listed in this leaflet.

1. WHAT IS THE MEDICINE INTENDED FOR

Ovitrelle contains a medicine called choriogonadotropin alfa, which is produced by recombinant DNA technology. Choriogonadotropin alfa is similar to a hormone naturally found in the body called chorionic gonadotropin, which is associated with the reproductive system and fertility.
Ovitrelle is used together with other medicines:

- To help develop and ripen several follicles in women undergoing fertility treatment such as in vitro fertilization (IVF). Other medicines will be given first to bring about the development of several follicles.
- To help release an egg from the ovary in women who do not ovulate, or women who ovulate infrequently. Other medicines will be given first to develop and ripen the follicles.

Therapeutic group: Gonadotropin hormones.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient choriogonadotropin alfa, or to any of the ingredients of the medicine (see section 6).
- you have a tumor in the hypothalamus or pituitary gland (both are parts of the brain).
- you have enlarged ovaries or sacs of fluid within the ovaries (ovarian cysts) of unknown origin.
- you have vaginal bleeding of an unknown origin.
- you have cancer of the ovaries, womb or breast.
- you have severe inflammation of the veins or a blood clot in the veins (active thromboembolic disorders).
- you have a condition that makes a normal pregnancy impossible, such as menopause, early menopause (ovarian failure) or malformation of sexual organs.

Do not use Ovitrelle if any of the conditions listed above apply to you. If you are uncertain, consult your doctor before using the medicine.

Special warnings regarding use of the medicine

- Before the treatment is started, you and your fertility treatment partner must be evaluated by a doctor experienced in the treatment of fertility problems.
- Ovarian hyperstimulation syndrome (OHSS)
  Treatment with Ovitrelle may increase the risk of developing OHSS, a condition in which the follicles develop too much and become large cysts.
  If you suffer from lower abdominal pain, gain weight rapidly, suffer from vomiting or nausea, or if you have difficulty in breathing, **do not** give yourself an injection of the medicine and refer to a doctor immediately (see section 4 “Side effects”). If you develop OHSS, the doctor may tell you to abstain from having sex or to use a barrier contraceptive method (e.g. condom, diaphragm) for at least 4 days.
  The risk of OHSS is reduced if the usual dose of Ovitrelle is used, and if you are monitored closely throughout the entire treatment cycle (e.g. blood tests for estradiol levels and ultrasound).
- Multiple pregnancy and/or birth defects
  When using Ovitrelle, there is a higher risk of a pregnancy with more than one fetus (multiple pregnancy, usually twins) compared to a pregnancy resulting from natural conception. Multiple pregnancy may lead to medical complications for you and your babies. When undergoing fertility treatments, the risk of having a multiple pregnancy is related to your age, the quality and the number of fertilized eggs or embryos inserted. Multiple pregnancies and specific characteristics of couples with fertility problems (e.g. age) may also be associated with an increased risk of birth defects.
  The risk of multiple pregnancy is reduced if you are monitored closely throughout the entire treatment cycle (e.g. blood tests for estradiol levels and ultrasound).
- Ectopic pregnancy
  Extrauterine pregnancy (an ectopic pregnancy) may occur in women with damaged fallopian tubes (the tube which carries the egg from the ovary to the womb). Therefore, your doctor should perform an early ultrasound examination to rule out the possibility of pregnancy outside the womb.
- Miscarriage
  Women undergoing fertility treatment or ovarian stimulation to produce eggs, are more likely to have a miscarriage, in comparison to the average woman.
- Blood clotting problems (thromboembolic event)
  Talk to your doctor before using Ovitrelle if you or a member of your family had blood clots in the legs or in the lungs, or a heart attack or stroke. You might have a higher risk of serious blood clots or existing blood clots might become worse with Ovitrelle treatment.
- Tumors of sexual organs
  There have been reports of tumors in the ovaries and other sex organs, both benign and malignant, in women who have undergone multiple regimens for infertility treatment.
- Pregnancy test
  If you do a pregnancy test (blood or urine) after use of Ovitrelle, and up to 10 days afterwards, you may get a false positive test result. If you are not sure, refer to the doctor.

Children and adolescent girls

Ovitrelle is not intended for use in children or adolescent girls.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Pregnancy and breastfeeding
Do not use Ovitrelle if you are pregnant or breastfeeding.
If you are pregnant or breastfeeding, consult the doctor before taking this medicine.

Driving and using machines
It is not expected that Ovitrelle will affect your ability to drive or operate machines.

Important information regarding some of the ingredients of the medicine
This medicine contains less than 23 mg sodium per dose and is therefore considered "sodium-free".

3. HOW SHOULD YOU USE THE MEDICINE

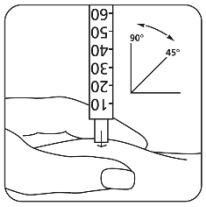
Always use in accordance with the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to take the medicine.

The dosage and manner of use will be determined by the doctor only.
The usual dosage is generally:
One pre-filled syringe/pen (250 microgram/0.5 ml), administered as a single injection.
The doctor will explain to you exactly when to inject the medicine.

Do not exceed the recommended dose.

<u>Pre-filled syringe</u>:
- Ovitrelle is intended for subcutaneous use, meaning, is given by injection under the skin.
- Each pre-filled syringe is for single-use only. Only clear solution without particles should be used.
- The doctor or nurse will explain to you how to use the Ovitrelle pre-filled syringe.
- Inject the medicine in accordance with the doctor's or nurse's instructions.
- After the injection, dispose of the used syringe safely.

Instructions for use – injection instructions:
If you are injecting Ovitrelle by yourself, please carefully read the following instructions:
1. Wash your hands. It is important that your hands and the items you use be as clean as possible.
2. Assemble all the items you will need. Please note that alcohol swabs are not contained in the package. Find a clean area and lay out all the items:
   - 2 alcohol swabs
   - one pre-filled syringe containing the medicine
3. The injection:
   Immediately inject the solution: The doctor or nurse will have already advised you on where to inject (e.g. tummy or front of the thigh). Wipe the area selected for injection with an alcohol swab.
   Pinch the skin between two fingers and insert the needle for injection at a 45°-90° angle using a rapid insertion motion. Inject under the skin, as you were instructed. Do not inject directly into a vein. Inject the solution by gently pushing the plunger.
   Slowly inject all the solution and then immediately withdraw the needle from the skin and clean the skin with an alcohol swab using a circular motion.



4. Dispose of all used items:
   As soon as you have finished injecting, immediately discard the empty syringe into a sharps container. If any unused solution remains, discard it.

<u>Pre-filled pen</u>:
- If you administer Ovitrelle to yourself, carefully read and follow the "Instructions for use" provided in the carton package of the product.
- Ovitrelle is intended for subcutaneous use, meaning, is given by injection under the skin.
- Each pre-filled pen is for single-use only.
- The doctor or nurse will explain to you how to use the Ovitrelle pre-filled pen.
- Inject the medicine according to the doctor's or nurse's instructions.
- After injecting, dispose of the used needle safely and throw out the pen.

If you accidentally took a higher dosage, the effects of an overdose of Ovitrelle are unknown, nevertheless, there is a possibility that ovarian hyperstimulation syndrome (OHSS) may occur. See the explanation in section 4. If you took an overdose or if a child accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine, talk to the doctor as soon as you remember.

Adhere to the treatment regimen recommended by the doctor.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Ovitrelle may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Discontinue use and refer to the doctor immediately if you notice any of the following serious side effects – you may need urgent medical treatment:
- Allergic reactions such as rash, fast or uneven pulse, swelling of the tongue and throat, sneezing, wheezing or serious breathing difficulty are very rare effects (may occur in up to 1 in 10,000 users).
- Lower abdominal pain, abdominal distension or abdominal discomfort together with nausea or vomiting may be the symptoms of ovarian hyperstimulation syndrome (OHSS). This may indicate that the ovaries overreacted to the treatment and that large ovarian cysts developed (also see section 2 "Ovarian hyperstimulation syndrome"). This effect is common (may occur in up to 1 in 10 users).
- OHSS may become severe with clearly enlarged ovaries, decreased urine production, weight gain, difficulty in breathing and possible fluid accumulation in the stomach or chest. This effect is not common (may occur in up to 1 in 100 users).

- Serious complications of blood clots (thromboembolic events) sometimes independent of OHSS may occur very rarely. This could cause chest pain, breathlessness, stroke or heart attack (also see section 2 “Blood clotting problems”).

Additional side effects

Common side effects (may occur in up to 1 in 10 users):
- Headache
- Local reactions at the injection site, such as pain, redness or swelling

Uncommon side effects (may occur in up to 1 in 100 users):
- Diarrhea

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to an online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

If a side effect occurs, if a side effect worsens or if you are suffering from a side effect not mentioned in this leaflet, consult the doctor.

5. HOW SHOULD THE MEDICINE BE STORED

- Avoid poisoning! This medicine, and any other medicine, must be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- **Pre-filled syringe:** Store in a refrigerator, at a temperature of 2°C-8°C. Store in the original package. Ovitrelle can be stored at room temperature below 25°C for up to 30 days, but do not refrigerate again during this period. If you did not use the medicine during this 30-day period, discard it in the waste bin.
  Ovitrelle is for single-use; any unused solution should be discarded.
- **Pre-filled pen:** Store in the refrigerator at a temperature of 2°C-8°C. Do not freeze.
  Do not use the product if you notice signs of deterioration, if the liquid contains particles or is not clear.
- Do not discard medicines in the wastewater or household waste bin. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

- **In addition to the active ingredient, the medicine also contains:**
  Pre-filled syringe:
  Mannitol, L-methionine, poloxamer 188, diluted phosphoric acid, sodium hydroxide, water for injection
  Pre-filled pen:
  Mannitol, L-methionine, poloxamer 188, disodium hydrogen phosphate dihydrate, sodium dihydrogen phosphate monohydrate, diluted phosphoric acid, sodium hydroxide, water for injection

- **What the medicine looks like and the contents of the package**
  <u>Pre-filled syringe</u>:
  Ovitrelle is a solution for injection, provided in a package of one pre-filled syringe.

  <u>Pre-filled pen</u>:
  Ovitrelle is a clear, colorless to yellowish solution for injection in a pre-filled pen for injection. Each pen contains 0.5 ml solution and comes in a package of one pre-filled pen and two needles for injection (one spare).

- **License holder and address:** Merck Serono Ltd., 18 Hakishon St., Yavne 81220

- **Manufacturer and address:** Merck Serono S.p.A., Modugno (Bari), Italy

- **Registration number of the medicine in the National Drug Registry of the Ministry of Health:** 132 74 31099

Revised in December 2021 according to MOH guidelines.