

**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.

Pre-filled syringe:

- 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:

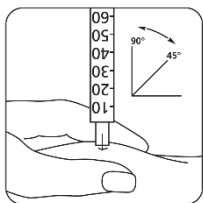
If you are injecting Ovitrelle by yourself, please carefully read the following instructions:

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.

Pre-filled pen:

- 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 each time 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**

Pre-filled syringe:

Ovitrelle is a solution for injection, provided in a package of one pre-filled syringe.

Pre-filled pen:

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.

Instructions for use

 **VITRELLE[®]**
250 micrograms
pre-filled pen

Choriogonadotropin Alfa

تعليمات الاستعمال

أوفيتريل[®]
250 ميكروغرام
قلم جاهز للحقن

הוראות שימוש

אוביטרל[®]
250 מיקרוגרם
עט מוכן להזרקה



MERCK

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Important information about the Ovitrelle pre-filled pen

- Read the Instructions for use and the Patient leaflet before using Ovitrelle.
- Always follow these instructions for use and training provided by your healthcare provider, as they may differ from your past experience. This information will allow to prevent incorrect treatment or infection due to needle stick or broken glass injury.
- The Ovitrelle pen is intended for subcutaneous injection only.
- The Ovitrelle pen is intended for single use only.
- Each Ovitrelle pack contains one injection needle and one spare needle.
- Only use the Ovitrelle pen if your healthcare provider has trained you on how to use it correctly.
- Store in a refrigerator.

Do not freeze.

Do not share the pen and/or needle with another person.

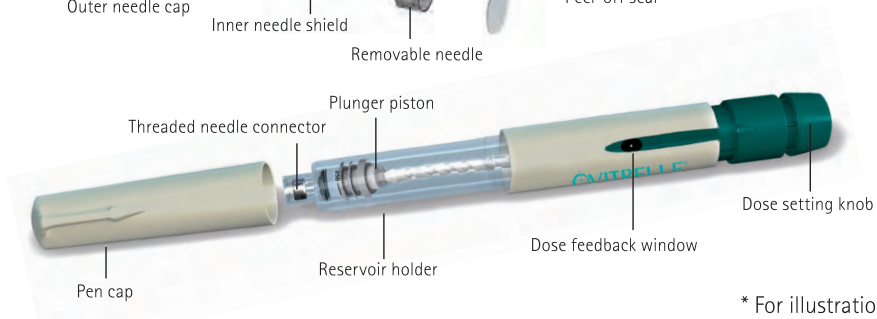
Do not use the Ovitrelle pen if it has been dropped, cracked or damaged, as this may cause injury.

Get familiar with the Ovitrelle pre-filled pen

The needle*:



The pen:



* For illustration only

Step 1 Prepare the supplies

- 1.1. Prepare a clean and flat surface, such as a table or countertop, in a well-lit area.
- 1.2. You will also need (not included in the pack):
 - Alcohol swabs and a sharps container (Figure 1).
- 1.3. Wash your hands with soap and water and dry them well (Figure 2).
- 1.4. Use your hand to remove the Ovitrelle pen from the pack.

Do not use any tools, using tools might damage the pen.

- 1.5. Check the name on the pen: "Ovitrelle 250 micrograms".
- 1.6. Check the expiration date on the pen label (Figure 3).

Do not use the Ovitrelle pen if the expiration date has passed or if "Ovitrelle 250 micrograms" is not written on it.



Figure 1



Figure 2



Figure 3

Step 2 Get ready for injection

- 2.1. Pull-off the pen cap (Figure 4).
- 2.2. Check that the medicine is clear, colourless to slightly yellow and does not contain particles.

Do not use the pen if the medicine is discoloured or cloudy, as this may cause infection.

Choose your injection site:

- 2.3. Your healthcare provider should show you the injection sites to use around the abdominal area (Figure 5).
- 2.4. Clean the skin at the injection site by wiping with an alcohol swab.

Do not touch or cover the cleaned skin.

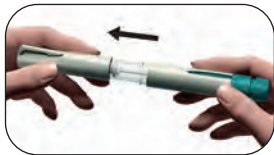


Figure 4

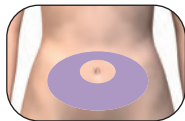


Figure 5

Step 3 Attach the needle

- 3.1. Get a new needle. Only use the "single-use" needles supplied.
- 3.2. Check that the outer needle cap is not damaged.
- 3.3. Hold the outer needle cap firmly.
- 3.4. Check that the peel-off seal on the outer needle cap is not damaged or loose, and that the expiration date has not passed (Figure 6).
- 3.5. Remove the seal (Figure 7).

Do not use the needle if it is damaged, expired or if the outer needle cap or the seal is damaged or loose. Using an expired needle or needles with damaged seal or outer cap may lead to infection. Throw it away in a sharps container and use the other needle provided in the pack.

Contact your healthcare provider if you have questions.



Figure 6



Figure 7

3.6. Screw the outer needle cap onto the threaded tip of the Ovitrelle pen until you feel a light resistance (Figure 8).

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

3.7. Remove the outer needle cap by pulling it gently (Figure 9).

3.8. Put it aside for later use (Figure 10).

Do not discard the outer needle cap, as it will prevent needle stick injury and infection when detaching the needle from the pen.

3.9. Hold the Ovitrelle pen with the needle pointing upward (Figure 11).

3.10. Carefully remove and discard the green inner needle shield (Figure 12).

Do not recap the needle with the green inner needle shield, as this may lead to needle stick injury and infection.



Figure 8



Figure 9



Figure 10



Figure 11



Figure 12

3.11. Look closely at the tip of the needle for tiny droplets of liquid.

If	Then
You see a tiny droplet of liquid	Proceed to Step 4 Set your dose to 250.
If you do not see a tiny droplet at or near the needle tip	You must perform the steps on the next page to remove air from the system.

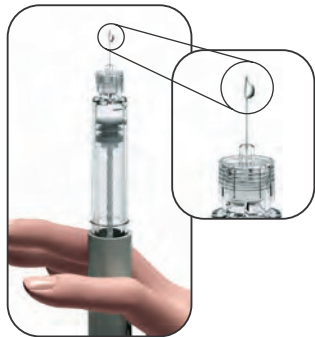


Figure 13

If you do not see a tiny droplet(s) of liquid at or near the needle tip when you use a new pen:

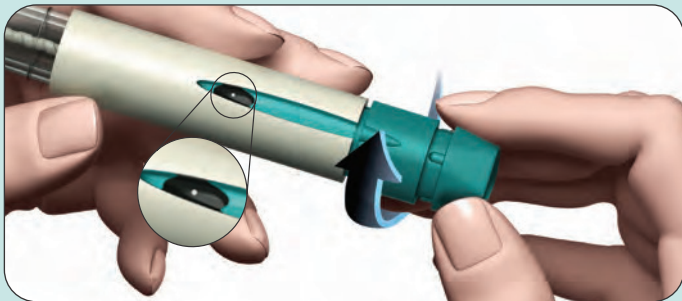


Figure 14

1. Gently turn the dose setting knob forward until the **Dose feedback window** shows a dot (●) (Figure 14).
 - You can turn the dose setting knob backward if you turn it past the dot (●).



Figure 15

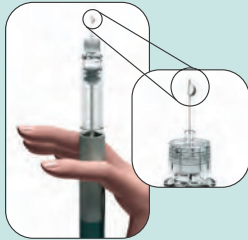


Figure 16

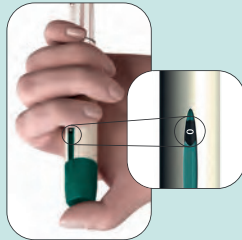


Figure 17

2. Hold the pen with the needle pointing upward.
 3. Tap the reservoir holder gently (Figure 15).
 4. Press the dose setting knob **as far as it will go**. A tiny droplet of liquid will appear at the tip of the needle (Figure 16)*.
 5. Check that the **Dose feedback window** shows "0" (Figure 17).
- * **Note:** If you do not see any liquid, restart at step 1 (in this section) one more time only. If a tiny droplet of liquid does not appear the second time either, contact your healthcare provider.

Step 4 Set your dose to 250

- 4.1. Gently turn the dose setting knob **forward** until **"250"** shows in the Dose feedback window.
- The Dose feedback window will show a straight line while turning until you can read the number **"250"** (Figure 18).

Do not push or pull the dose setting knob while you turn it.

- 4.2. Check that the **Dose feedback window** displays **"250"** (Figure 19) before you move on to Step 5 below.

Contact your healthcare provider if you need help.



Figure 18

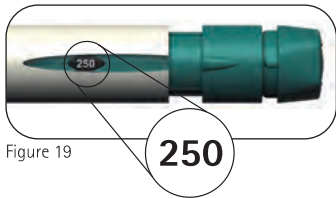


Figure 19

Step 5 Inject your dose

Important: Inject the dose as you were trained to do by your healthcare provider.

5.1. Slowly insert the needle into the skin entirely (Figure 20).

5.2. Place your thumb in the middle of the dose setting knob. **Slowly press the dose setting knob down as far as it will go** and hold it to complete the full injection (Figure 21).



Figure 20

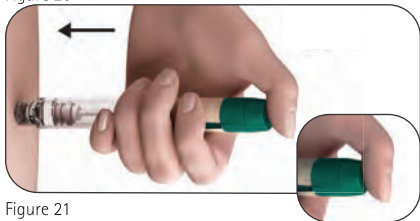


Figure 21

5.3. Hold the dose setting knob pressed down for at least 5 seconds (5s) before you remove the needle from the skin (Figure 22).

- The dose number shown in the **Dose feedback window** will turn back to "0".
- After a minimum of 5 seconds, pull the needle out of the skin **while keeping the dose setting knob pressed down** (Figure 23).
- When the needle is out of the skin, release the dose setting knob.

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



Figure 22

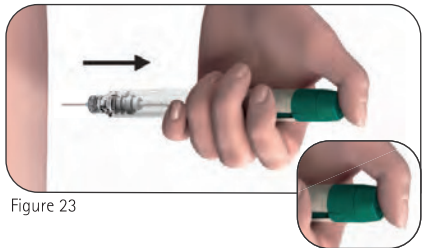


Figure 23

Step 6 Remove the needle after the injection

- 6.1. Place the outer needle cap on a flat surface.
- 6.2. Hold the Ovitrelle pen firmly with one hand and slip the needle into the outer needle cap (Figure 24).
- 6.3. Continue by pushing the capped needle against a firm surface until you hear a "click" (Figure 25).
- 6.4. Grip the outer needle cap and unscrew the needle by turning it in the opposite direction (Figure 26).
- 6.5. Dispose of the used needle safely in a sharps container (Figure 27). Handle the needle with care to avoid getting injured by the needle.

Do not reuse or share any used needle with another person.



Figure 24



Figure 25



Figure 26



Figure 27

Step 7 After the injection

7.1. Check that you have received a complete injection:

- Check that the **Dose feedback window** shows "0" (Figure 28).

If the Dose feedback window shows "**0**", you have completed your dose.

If the Dose feedback window does **not** show "**0**", contact your healthcare provider.

Do not attempt to inject a second time.

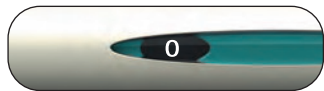


Figure 28

Step 8 Dispose of the Ovitrelle pre-filled pen

Important: The Ovitrelle pen and needles supplied are for single use only.

- 8.1. Put the pen cap back onto the pen (Figure 29).
- 8.2. Ask your healthcare provider how to dispose of the empty Ovitrelle pen.

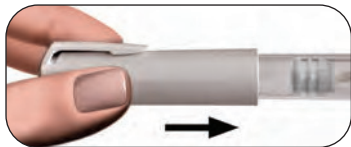


Figure 29

Contact your healthcare provider if you have questions.

The Instructions for use were revised in February 2023 according to MOH guidelines.



Solution for injection in pre-filled pen
 תמיסה להזרקה בעט מוכן להזרקה
 מכלול לחיפה בנזאליה

VITRELLE®
 250 micrograms
 pre-filled pen

אופטיריל®
 250 מיקרוגרם
 קלם זאחז לחיפה

אוביטלר®
 250 מיקרוגרם
 עט מוכן להזרקה

N54G1603D

