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

This medicine can be sold under doctor's prescription only

ORGALUTRAN® 0.25 mg/0.5 ml

Solution for Injection, for Subcutaneous Use

Each pre-filled syringe contains:
0.25 mg ganirelix in 0.5 ml aqueous solution.
For a list of inactive ingredients see section 6. "FURTHER INFORMATION". See also section "Important information about some of the ingredients of **ORGALUTRAN**".

Read the entire leaflet carefully before you start using this medicine.

- This leaflet contains concise information about the medicine. If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their ailment seems similar to yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

1. WHAT THE MEDICINE IS INTENDED FOR?

ORGALUTRAN is intended for the prevention of premature luteinising hormone (LH) surges in women undergoing controlled ovarian hyperstimulation (COH) for assisted reproduction techniques (ART).

Therapeutic group: anti-gonadotrophin-releasing hormones.

ORGALUTRAN belongs to a group of medicines called "anti-gonadotrophin-releasing hormones" which act against the actions of the natural gonadotrophin releasing hormone (GnRH). GnRH regulates the release of gonadotrophins (luteinising hormone (LH) and follicle stimulating hormone (FSH)).
Gonadotrophins play an important role in human fertility and reproduction. In women, FSH is needed for the growth and development of follicles in the ovaries. Follicles are small round sacs that contain the egg cells. LH is needed to release the mature egg cells from the follicles and ovaries (i.e. ovulation). **ORGALUTRAN** inhibits the action of GnRH, resulting in suppression of the release of especially LH.

ORGALUTRAN is used for
In women undergoing assisted reproduction techniques, including in vitro fertilisation (IVF) and other methods, occasionally ovulation may occur too early causing a significant reduction in the chance of getting pregnant. **ORGALUTRAN** is used to prevent the premature LH surge that might cause such a premature release of egg cells.

In clinical studies **ORGALUTRAN** was used with recombinant follicle stimulating hormone (FSH) or corifollitropin alfa, a follicle stimulant with a long duration of action.

2. BEFORE USING THE MEDICINE

2.1 Do not use ORGALUTRAN if:

- you are allergic (hypersensitive) to ganirelix or to any of the other ingredients of **ORGALUTRAN** (for a list of all ingredients, see section 6.1);

- you suffer from hypersensitivity to gonadotrophin releasing hormone (GnRH) or a GnRH analogue;
- you have a moderate or severe kidney or liver disease;
- you are pregnant or breast-feeding.

2.2 Special warnings concerning use of ORGALUTRAN
Before starting treatment with ORGALUTRAN, tell your doctor if:

- Allergic reactions: if you have an active allergic condition, please tell your doctor. Your doctor will decide, depending on the severity, if additional monitoring is required during treatment. Cases of allergic reactions have been reported, as early as with the first dose. Allergic reactions, both generalised and local, including hives (urticaria), swelling of the face, lips tongue, and/or throat that may cause difficulty in breathing and/or swallowing (angioedema and/or anaphylaxis) have been reported. (See also section 4.) If you have an allergic reaction, stop taking Orgalutran and seek immediate medical assistance.
- Latex allergy: The needle cover contains dry natural rubber/latex which comes into contact with the needle and may cause allergic reactions.
- Ovarian hyperstimulation syndrome (OHSS): During or following hormonal stimulation of the ovaries, ovarian hyperstimulation syndrome may develop. This syndrome is related to the stimulation procedure with gonadotrophins. Please refer to the Package Leaflet of the gonadotrophin-containing medicine prescribed for you.
- Multiple births or birth defects: The incidence of congenital malformations after assisted reproduction techniques may be slightly higher than after spontaneous conceptions. This slightly higher incidence is thought to be related to characteristics of the patients undergoing fertility treatment (e.g. age of the woman, sperm characteristics) and to the higher incidence of multiple gestations after assisted reproduction techniques. The incidence of congenital malformations after assisted reproduction techniques using **ORGALUTRAN** is not different from that after using other GnRH analogues in the course of assisted reproduction techniques.
- Pregnancy complications: There is a slightly increased risk of pregnancy outside of the uterus (an ectopic pregnancy) in women with damaged fallopian tubes.
- Women weighing less than 50 kg or more than 90 kg: The efficacy and safety of **ORGALUTRAN** has not been established in women weighing less than 50 kg or more than 90 kg. Ask your doctor for further information.

Children and adolescents
There is no relevant use of **ORGALUTRAN** in children or adolescents.

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

Pregnancy, breast-feeding and fertility
ORGALUTRAN should be used during controlled ovarian stimulation for assisted reproduction techniques (ART). Do not use **ORGALUTRAN** during pregnancy and breast-feeding.
If you are pregnant or breast-feeding, consult the doctor or pharmacist before using any medicine.

Driving and using machines
The effects of **ORGALUTRAN** on ability to drive and use machines have not been studied.

Important information about some of the ingredients of ORGALUTRAN

This medicine contains less than 1 mmol sodium (23 mg) per injection, that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use **ORGALUTRAN** as instructed by the doctor. You should check with the doctor or the pharmacist if you are not sure.
ORGALUTRAN is used as part of the treatment for assisted reproduction techniques (ART) including *in vitro* fertilisation (IVF).

The dosage and method of treatment will be determined by the doctor only.

The usual recommended dosage is:
Ovarian stimulation with follicle stimulating hormone (FSH) or corifollitropin may start at day 2 or 3 of your period. **ORGALUTRAN** (0.25 mg) should be injected just under the skin once daily, starting on day 5 or day 6 of stimulation. Based on your ovarian response, your doctor may decide to start on another day.
ORGALUTRAN and FSH should be administered approximately at the same time. However, the preparations should not be mixed and different injection sites are to be used.

Daily treatment with **ORGALUTRAN** should be continued up to the day that sufficient follicles of adequate size are present. Final maturation of the egg cells in the follicles can be induced by administering human chorionic gonadotrophin (hCG). The time between two **ORGALUTRAN** injections as well as the time between the last **ORGALUTRAN** injection and hCG injection should not exceed 30 hours, as otherwise a premature ovulation (i.e. release of egg cells) may occur. Therefore, when injecting **ORGALUTRAN** in the morning treatment with **ORGALUTRAN** should be continued throughout the gonadotrophin treatment period including the day of triggering ovulation. When injecting **ORGALUTRAN** in the afternoon the last **ORGALUTRAN** injection should be given in the afternoon prior to the day of triggering ovulation.
Do not exceed the recommended dose.

Instructions for use
Injection site
ORGALUTRAN is supplied in pre-filled syringes and should be injected slowly, just under the skin, preferably in the upper leg.
Inspect the solution before use. Do not use if the solution contains particles or is not clear. You may notice air bubble(s) in the pre-filled syringe. This is expected, and removal of the air bubble(s) is not needed. If you administer the injections yourself or have it done by your partner, follow the instructions below carefully. Do not mix **ORGALUTRAN** with any other medicines.

Preparing the injection site
Wash your hands thoroughly with soap and water. Swab the injection site with a disinfectant (for example alcohol) to remove any surface bacteria. Clean about 5 cm (two inches) around the point where the needle will go in and let the disinfectant dry for at least one minute before proceeding.

Inserting the needle
Remove needle cover. Pinch up a large area of skin between finger and thumb. Insert the needle at the base of the pinched-up skin at an angle of 45° to the skin surface. Vary the injection site with each injection.

Checking the correct needle position

Gently draw back the plunger to check if the needle is positioned correctly. Any blood drawn into the syringe means the needle tip has penetrated a blood vessel. If this happens, do not inject **ORGALUTRAN** but remove the syringe, cover the injection site with a swab containing disinfectant and apply pressure; bleeding should stop in a minute or two. Do not use this syringe and dispose of it properly. Start again with a new syringe.

Injecting the solution
Once the needle has been correctly placed, depress the plunger slowly and steadily, so the solution is correctly injected and the skin tissues are not damaged.

Removing the syringe
Pull the syringe out quickly and apply pressure to the site with a swab containing disinfectant.

Use the pre-filled syringe only once.

If you have accidentally taken a higher dose than you should
Contact your doctor.

If you have forgotten to use ORGALUTRAN
If you realize that you forgot a dose, administer it as soon as possible.
Do not inject a double dose to make up for a forgotten dose.
If you are more than 6 hours late (so the time between two injections is longer than 30 hours) administer the dose as soon as possible **and** contact your doctor for further advice.

If you stop using ORGALUTRAN
Do not stop using **ORGALUTRAN** unless advised to by your doctor, as this may affect the outcome of your treatment.

Do not take medicines in the dark! Check the label and the dose each time you take your medicine. Wear glasses if you need them.

If you have any further questions on the use of the medicine, consult with a doctor or a pharmacist.

4. SIDE EFFECTS
As with any medicine, **ORGALUTRAN** may cause side effects in some users.
Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

The chance of having a side effect is described by the following categories:
Very Common side effects: may affect more than 1 in 10 women
- Local skin reactions at the site of injection (predominantly redness, with or without swelling). The local reaction normally disappears within 4 hours of administration.

Uncommon side effects: may affect up to 1 in 100 women
- Headache
- Nausea
- Malaise

Very rare side effects: may affect up to 1 in 10,000 women
- Allergic reactions have been observed, as early as with the first dose.
- Rash
- Facial swelling
- Difficulty breathing (dyspnoea)

- Swelling of face, lips, tongue, and/or throat that may cause difficulty in breathing and/or swallowing (angioedema and/or anaphylaxis)
- Hives (urticaria)
- Worsening of a pre-existing rash (eczema) has been reported in one subject after the first **ORGALUTRAN** dose.

In addition, side effects are reported which are known to occur with controlled ovarian hyperstimulation treatment (e.g. abdominal pain, ovarian hyperstimulation syndrome (OHSS), ectopic pregnancy (when the embryo develops outside the womb) and miscarriage (see the patient information leaflet of the FSH-containing preparation you are treated with).

If a side effect appears, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by using the link "Reporting side effects due to medicinal treatment" at the home page of the Ministry of Health's web site (www.health.gov.il) which refers to the online side effects reporting form, or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Avoid Poisoning! This medicine, as all other medicines, must be stored in a safe place out of the reach of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the packaging. The expiry date refers to the last day of the indicated month.
- **Storage conditions**: 2-30ºC. Do not freeze. Store in the original package, in order to protect from light.
- Inspect the syringe before use. Use only syringes with clear, particle-free solutions and from undamaged containers.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

- In addition to the active ingredient the medicine also contains: mannitol, acetic acid (glacial), water for injections. The pH (a measurement of the acidity) may have been adjusted with sodium hydroxide and/or acetic acid.

- **What ORGALUTRAN looks like and content of the package**
  ORGALUTRAN is a clear and colourless aqueous solution for injection. The solution is ready for use and intended for subcutaneous administration. **The needle cover contains dry natural rubber/latex which comes into contact with the needle.**

ORGALUTRAN is available in packs of 1 pre-filled syringe.

Manufacturer
N.V. Organon, Oss, The Netherlands.

Marketing Authorization Holder
Merck Sharp & Dohme (Israel-1996) Company Ltd., P.O.Box 7121 Petah-Tikva, 49170.

Drug registration no. listed in the official registry of the Ministry of Health
124-95-30448

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