

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

The medicine is dispensed with a  
doctor's prescription only

Cetrotide® 0.25 mg

Powder and solvent for solution for injection

A vial containing powder  
A syringe containing a solvent  
**For subcutaneous injection**

**The active ingredient:**  
Cetorelix (as acetate) 0.25 mg

Solvent: water for injection  
Inactive ingredients: see section 6

**Read the leaflet carefully in its entirety before using the medicine:**

- Keep this leaflet; you may need to read it again.
- This leaflet contains concise information about the medicine. If you have further questions, refer to your doctor or pharmacist.
- This medicine has been prescribed to treat your medical condition. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar to yours.
- If a side effect occurs, if any of the side effects worsen or if you notice a side effect not mentioned in this leaflet, refer to your doctor or pharmacist.

1. WHAT IS THE PREPARATION CETROTIDE AND WHAT IS IT INTENDED FOR

**What is the preparation Cetrotide**

Cetrotide contains a medicine called 'Cetorelix acetate'. This medicine stops your body from releasing an oocyte from the ovary (ovulation) during your menstrual cycle. Cetrotide belongs to a group of preparations called 'anti-gonadotropin-releasing hormones'.

**What is the preparation Cetrotide intended for**

Cetrotide is one of the preparations used in 'assisted reproductive technologies' to help you become pregnant. It stops the immediate release of oocytes, because if the oocytes are released too early (premature ovulation), your doctor may not be able to collect them.

**How Cetrotide works**

Cetrotide inhibits the activity of the natural hormone called luteinizing hormone-releasing hormone (LHRH).

- LHRH – a hormone which regulates another hormone called luteinizing hormone (LH).
- LH – luteinizing hormone which stimulates ovulation during the menstrual cycle.

Essentially, Cetrotide stops the chain of events that leads to release of an oocyte from your ovary. When your oocytes are ready for collection, you will be given another preparation that will cause them to be released (ovulation induction).

**Therapeutic group:** Anti-gonadotropin-releasing hormones.

2. BEFORE USING THE PREPARATION CETROTIDE

**Do not use Cetrotide**

- If you are hypersensitive (allergic) to cetorelix acetate or to any of the additional ingredients contained in the medicine (see section 6).
- If you are hypersensitive (allergic) to medicines similar to Cetrotide (any other peptide hormone).
- If you are pregnant or breastfeeding.
- If you have severe kidney disease.

Do not use Cetrotide if any of the conditions mentioned above apply to you. If you are uncertain, consult with your doctor or pharmacist before commencing treatment.

**Special warnings regarding use of Cetrotide:**  
**Allergies**

Before treatment with Cetrotide, report to the doctor about any existing or past allergic effects.

**OHSS – Ovarian Hyper-Stimulation Syndrome**

Use of Cetrotide combines treatment with other medicines that cause stimulation of your ovaries, in order to develop more oocytes ready to be released. During or after receiving these medicines, you may develop OHSS. This is a situation in which the follicles develop too much and become large cysts. For possible signs that require follow-up and what to do in such a case, please see section 4 'Possible Side Effects'.

**Use of Cetrotide for more than one treatment cycle**

Your doctor will weigh the benefit against the risk in each case, to decide whether Cetrotide should be used for more than one treatment cycle. This is due to the little experience with use of Cetrotide for more than one treatment cycle.

**Liver disease**

Tell your doctor before using Cetrotide if you have a liver disease. Cetrotide has not been investigated in patients with hepatic disease.

**Kidney disease**

Tell your doctor before using Cetrotide if you have a kidney disease. Cetrotide has not been investigated in patients with kidney disease.

**Young girls and adolescents**

Cetrotide is not indicated for use in young girls and adolescents.

**Use of other medicines with Cetrotide**

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

**Pregnancy and breastfeeding**

Do not use Cetrotide if you are pregnant, if you think you may be pregnant or if you are breastfeeding.

If you are pregnant or breastfeeding, consult the doctor or pharmacist before using medicines.

**Driving and use of machinery**

Use of Cetrotide is not expected to affect your ability to drive a vehicle or operate machinery.

3. HOW SHOULD YOU USE THE PREPARATION CETROTIDE

Always use Cetrotide according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain. The dosage and treatment regimen will be determined by the doctor only.

**Do not exceed the recommended dose.**

**Using the preparation Cetrotide**

The preparation is intended for subcutaneous injection into your abdomen only. To reduce irritation to the skin, choose a new injection site in the abdomen each day.

- The first injection of Cetrotide should be performed under your doctor's supervision: your doctor or nurse will show you how to prepare and inject the preparation.
- Later on, you can self-inject after receiving an explanation from the doctor regarding symptoms indicative of an allergic reaction, and the severe and life-threatening implications of such a reaction and the immediate treatment necessary in such a case (please see section 4 'Possible Side Effects').
- Carefully read and follow the instructions in the last part of this leaflet called 'Instructions for dissolving and injecting Cetrotide'.
- On the first day of the treatment cycle, you will start using a different preparation. Start using Cetrotide a few days afterwards (see the next section 'How much should be used').

**How much should be used**

Inject the contents of one vial (Cetrotide 0.25 mg) once a day. It is advisable to use the preparation at the same time every day, with a 24-hour interval between one injection and the next.

- You can choose to inject every morning or every evening.
- If you inject every morning: Start the injections on day 5 or 6 of the treatment cycle.

Your doctor will tell you the exact day and time. Continue using the preparation until oocyte collection, including on the morning of oocyte collection (ovulation induction).

OR

- If you inject every evening: Start the injections on day 5 of the treatment cycle.

Your doctor will tell you the exact day and time. Continue using the preparation until oocyte collection, including the evening before oocyte collection (ovulation induction).

**If you used more Cetrotide than you need**

No adverse effects are expected if you accidentally injected more Cetrotide than necessary. The effect of the preparation will last for a longer period of time. There is usually no need to take any measures.

**If you forgot to inject Cetrotide**

- If you forgot a dose, inject it as soon as you remember and report to your doctor.
- Do not inject a double dose to compensate for a forgotten dose.

Adhere to the treatment regimen recommended by the doctor.

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

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

4. POSSIBLE SIDE EFFECTS

As with any medicine, use of Cetrotide 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 a doctor immediately if you notice any of the following side effects:**

**Allergic reactions (hypersensitivity)**

- Warm feeling, skin redness, itching (often in the groin or armpit area), red, itching, raised areas (hives), runny nose, fast or uneven pulse, swelling of the tongue or throat, sneezing, wheezing or serious breathing difficulties or dizziness. You may be having an allergic reaction to this medicine that may be serious and life-threatening. These effects are uncommon (may affect up to 1 in 100 women).

**If you notice any of the following side effects, refer to a doctor immediately:**

**Ovarian Hyper-Stimulation Syndrome (OHSS)**

This effect may occur because you are using other medicines for stimulation of the ovaries.

- The symptoms of OHSS are pain in the lower abdomen with nausea or vomiting, which can indicate hyper-reactivity of the ovary to treatment and that large cysts have formed. This side effect is common (may affect up to 1 in 10 women).
- OHSS becomes severe when there is a significant enlargement of the ovaries, reduced urine production, weight gain, breathing difficulties or fluid accumulation in the abdomen or chest. This side effect is uncommon (may affect up to 1 in 100 women).

**Additional side effects:**

Common side effects (may affect up to 1 in 10 women):

- Mild and short-lasting irritation of the skin at the injection site, such as: redness, itching or swelling.

Uncommon side effects (may affect up to 1 in 100 women):

- Nausea
- Headache

If a side effect occurs, if any of the side effects worsen, or if you suffer from a side effect not listed in this leaflet, consult with your doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting Side Effects of Drug Treatment" found on the Ministry of Health homepage ([www.health.gov.il](http://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>

5. HOW SHOULD THE PREPARATION CETROTIDE BE STORED

Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach of children and/or infants to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor!

Do not use Cetrotide after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

The Cetrotide powder in the vial and the sterile water (solvent) in the prefilled syringe have the same expiry date. The date is printed on the label and package.

Store in a refrigerator (at temperature of 2°C–8°C). After dispensing to the patient, an unopened product may be stored in its original packaging at room temperature (do not store above 30°C) for up to 3 months.

Do not freeze or place next to the freezer compartment or a freezer pack.

Store the vial in its original package to protect it from light. Use the solution immediately after preparation.

Do not use Cetrotide if you notice any change in the appearance of the white powder in the vial.

Do not use Cetrotide if you notice that the prepared solution is not clear and colorless or if it has particles.

Do not throw medicines into the sewage system or the 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

**What does Cetrotide contain**

- The active ingredient is cetorelix acetate. Each vial contains 0.25 mg cetorelix acetate.
- In addition to the active ingredient, the medicine also contains mannitol.
- The solvent is water for injection.

**What the preparation Cetrotide looks like and the contents of the package**

Cetrotide is a white powder in a glass vial with a rubber stopper, intended for preparation of a solution for injection.

The preparation is available in packages that contain 1 or 7 vials (not all the package sizes are marketed).

For each vial, the package also contains:

- A syringe prefilled with sterile water for injection (solvent) to dissolve the powder in the vial.
- Needle with yellow marking for injecting the sterile water into the vial and for drawing the medicine that has formed out of the vial.
- Needle with gray marking for injecting the medicine into your abdomen.
- 2 alcohol swabs for disinfection.

**License holder and importer:** Merck Serono Ltd., 18 Hakishon St., Yavneh 81220.

**Name of the manufacturer:** Merck Healthcare KGaA, Darmstadt, Germany.

**Registration number of the medicine in the National Drug Registry of the Ministry of Health:** 117-19-29780

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved by it in April 2016 and was updated according to the guidelines of the Ministry of Health in December 2018.

**Instructions for dissolving and injecting Cetrotide:**

- This section explains to you how to mix the powder and sterile water (the solvent) together and then how to inject the medicine.
- Before starting to use this preparation, read these instructions the first time in their entirety.
- This preparation is intended for you – do not allow anyone else to use it.
- Use each needle, vial and syringe only once.

**Before you begin**

**1. This product must be at room temperature prior to injection. Remove it from the refrigerator approximately 30 minutes before using it.**

**2. Wash your hands**

- It is important that the palms of your hands and the items you will use are as clean as possible.

**3. Choose a clean surface and place everything you need on it**

- One vial of powder.
- One syringe prefilled with sterile water (solvent).
- Needle with yellow marking – for injecting the sterile water into the vial and for drawing the medicine that has formed out of the vial.
- Needle with gray marking – for injecting the medicine into your abdomen.
- Two alcohol swabs.

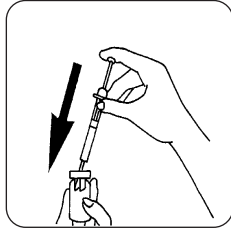
**Mixing the powder with the water to prepare your medicine**

**1. Remove the plastic cover of the vial.**

- You will find a rubber stopper underneath – leave it on the vial.
- Clean the aluminum ring and the rubber stopper with an alcohol swab.

**2. Adding the sterile water from the prefilled syringe into the vial with the powder**

- Take the yellow labelled needle out of its wrapping.
- Remove the cap from the syringe prefilled with solvent. Attach the yellow needle to the syringe and remove the cap from the needle.
- Hold the syringe and push the needle through the center of the rubber stopper into the vial.
- Inject the water in the syringe into the vial by slowly pushing the plunger of the syringe. Do not use any other source of water for this purpose.
- Leave the syringe stuck in the rubber stopper of the vial.

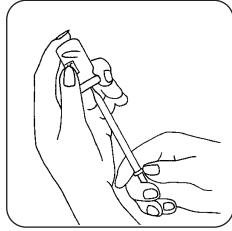


**3. Mixing the powder and the water in the vial**

- Carefully hold the syringe and vial and gently mix the powder and water in the vial until you obtain a clear solution without particles.
- Avoid shaking that will cause formation of bubbles.

**4. Refilling the syringe with the medicine content from the vial**

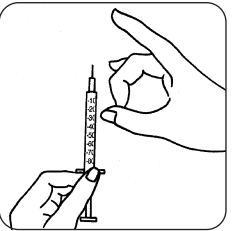
- Turn the vial upside down so that the rubber stopper is facing downward.
- Then, gently pull the syringe plunger back, in order to draw the medicine from the vial into the syringe. Be sure not to pull the plunger completely out of the syringe. If you accidentally pulled the plunger out of the syringe, this dose is no longer sterile. Make sure to discard it and prepare a new dose (beginning from step 1).
- If the solution was only partially drawn out and some of the solution remains in the vial, gently pull the needle out until the end of the tip of the needle is in the rubber stopper. The movement of the needle and of the fluid can be followed by looking from the side, through the gap in the rubber stopper.
- It is important to draw out all of the contents of the solution from the vial back into the syringe.
- Put the cap back on the yellow needle. Unscrew the yellow needle from the syringe and place the syringe on the side.



**Preparing the injection site and injecting the medicine**

**1. Expelling air bubbles**

- Remove the injection needle with the gray mark from its wrapping and screw it on to the syringe. Remove the cap of the needle.
- Hold the syringe with the gray needle so that the needle points upward and check if there are air bubbles.
- To expel the air bubbles, gently tap on the syringe with your finger until all the air accumulates at the top of the syringe – then, gently push the plunger of the syringe until all air bubbles are expelled.
- Do not touch the gray needle and do not let the needle touch anything.

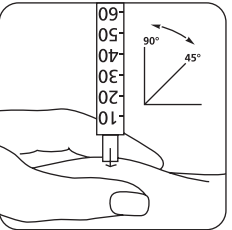


**2. Disinfecting the injection site**

- Choose an injection site in the abdominal area, preferably around the navel. To avoid local irritation of the skin, choose a different injection site in the abdomen every day.
- Clean the selected injection site with the second alcohol swab – using a circular motion.

**3. Insertion into the skin**

- Hold the syringe in one hand – as you would hold a pencil.
- With the other hand, gently pinch up the skin surrounding the injection site to form a fold.
- Gently insert the gray needle completely at the injection site into the skin fold, formed by pinching the skin, at an angle of 45-90 degrees. Then let go of the pinched skin.



**4. Injecting the medicine**

- Gently pull the plunger of the syringe slightly backwards. If blood appears in the syringe, stop and continue as described in step 5.
- If no blood appears in the syringe, inject the solution slowly by pushing the plunger of the syringe until the end.
- After the entire contents of the syringe are injected and the syringe is empty, slowly withdraw the needle from the skin, at the same angle as it was inserted.
- Press gently on the injection site with the second alcohol swab.

**5. In case of appearance of blood**

- Withdraw the needle slowly at the same angle as it was inserted.
- Press gently on the injection site with the second alcohol swab.
- Empty the contents of the syringe into the sink and follow the instructions in step 6 below.
- Wash your hands and start again from step 1 with a new vial and syringe filled with solvent.

**6. Discarding the medicine**

- The vial, syringe and needles are for single use only.
- After use, put the caps back on the needles so they can be discarded safely.
- Ask the pharmacist how to properly dispose of the used vial, syringe and needles.