

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

The medicine is dispensed with a doctor's prescription only

## **Cetrotide<sup>®</sup> 0.25 mg**

Powder and solvent for solution for subcutaneous injection

### **Active ingredient:**

cetorelix (as acetate) 0.25 mg

Solvent: water for injection

Inactive ingredients and allergens in this medicine - see section 6.

**Read the entire leaflet carefully before you start using this medicine.** This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

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 to yours.

## **1. WHAT IS THIS MEDICINE INTENDED FOR**

Cetrotide is one of the medicines used during 'assisted reproductive techniques' 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.

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

Cetrotide contains a medicine called 'cetorelix acetate'. 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.

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

## **2. BEFORE USING THIS MEDICINE**

### **Do not use the medicine if:**

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| <ul style="list-style-type: none"><li>• You are sensitive (allergic) to the active ingredient (cetorelix) or to any of the other ingredients the medicine contains (see section 6)</li><li>• You are sensitive (allergic) to medicines similar to Cetrotide (any other peptide hormone)</li><li>• You are pregnant or breastfeeding</li><li>• You have severe kidney disease</li></ul> |
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Do not use Cetrotide if any of the conditions listed above apply to you. If you are uncertain, consult with your doctor before using the medicine.

### **Special warnings about using this medicine**

#### Allergies

Before treatment with Cetrotide, tell your doctor if you have active allergies or have had allergies in the past.

### Ovarian Hyper-Stimulation Syndrome (OHSS)

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 'Side effects'.

### Use of Cetrotide in more than one treatment cycle

Your doctor will examine the benefit against the risk in each case if there is a need of using Cetrotide in more than one treatment cycle. This is due to the little experience with use of Cetrotide in 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.

### **Children and adolescents**

Cetrotide is not indicated for use in children and adolescents.

### **Interactions with other medicines**

**If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.**

### **Pregnancy and breastfeeding**

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

### **Driving and using machines**

This medicine is not expected to affect your ability to drive or operate machines.

## **3. HOW TO USE THE MEDICINE**

Always use the medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose and about how to use the medicine.

### **Using the medicine**

The medicine is intended for subcutaneous injection into your abdomen only. To reduce skin irritation, select a different injection site in the abdomen each day.

- The first injection should be performed under your doctor's supervision. Your doctor or nurse will show you how to prepare and inject the medicine.
- Later on, you can self-inject after receiving an explanation from the doctor regarding symptoms indicative of an allergic reaction, which can be severe or life-threatening and requires immediate treatment (see section 4).
- 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 medicine. Start using Cetrotide a few days afterwards (see the next section 'How much to use').

### **How much to use**

Inject the contents of one Cetrotide vial once a day. It is recommended to use the medicine at the same time every day, with a 24-hour interval between one injection and the next one.

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 medicine until oocyte collection, including 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 medicine until oocyte collection, including the evening before oocyte collection (ovulation induction).

**Do not exceed the recommended dose.**

**If you have accidentally taken a higher dose**

No adverse effects are expected if you accidentally inject more Cetrotide than necessary. The effect of the medicine will last for a longer period. No specific measures are usually required.

**If you forget to take the medicine**

- If you forget a dose, inject it as soon as you remember and inform your doctor.
- Do not inject a double dose to make up for a forgotten dose.

Adhere to the treatment as recommended by your doctor.

**Do not take medicines in the dark! Check the label and dose every time you take medicine.**

**Wear glasses if you need them.**

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

#### **4. SIDE EFFECTS**

As with any medicine, using Cetrotide may cause side effects in some users. Do not be alarmed by this list of side effects; you may not suffer from any of them.

**Discontinue use and contact a doctor immediately if you notice any of the following side effects:**

Allergic reactions

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

**If you notice any of the following side effects, contact your doctor immediately:**

Ovarian Hyper-Stimulation Syndrome (OHSS)

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

- Pain in the lower abdomen along with nausea or vomiting may be symptoms of OHSS. This may indicate that the ovaries over-reacted to the treatment and that large ovarian cysts developed. This side effect is common (may affect up to 1 in 10 patients).
- OHSS may be severe when there is a significant enlargement of the ovaries, reduced urine production, weight gain, breathing difficulties or fluid in the abdomen or chest. This side effect is uncommon (may affect up to 1 in 100 patients).

**Additional side effects**

Common (may affect up to 1 in 10 patients):

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

Uncommon (may affect up to 1 in 100 patients):

- Nausea
- Headache

**If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.**

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 home page ([www.health.gov.il](http://www.health.gov.il)) that directs you to the online form for reporting side effects, or by entering the link: <http://sideeffects.health.gov.il>

## **5. HOW TO STORE THE MEDICINE**

- Avoid poisoning! This medicine, and any other medicine, should 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) which is stated on the package, vial and syringe. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C–8°C). Do not freeze or place next to the freezer compartment or a freezer pack.
- Store in the original package in order to protect from light.
- After dispensing to the patient, the unopened product may be stored in the original package at room temperature (do not store above 30°C) for up to 3 months.
- Use the solution immediately after preparation.
- Do not use the medicine if you notice any change in the appearance of the white powder in the vial. Do not use the medicine if you notice that the prepared solution is not clear and colourless or contains particles.
- Do not throw away any medicine via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

## **6. ADDITIONAL INFORMATION**

**In addition to the active ingredient, the medicine also contains:**

In the powder: mannitol.

In the solvent: water for injection.

**What the medicine looks like and contents of the pack:**

Cetrotide is a powder and solvent for solution for injection. The white powder comes in a glass vial with a rubber stopper. The solvent is a clear and colourless solution in a pre-filled syringe.

The powder vial contains 0.25 mg cetrotide and the pre-filled syringe contains 1 ml solvent.

The medicine is available in packages containing 1 vial and 1 pre-filled syringe or 7 vials and 7 pre-filled syringes. Not all pack sizes may be marketed.

For each vial, the package also contains:

- One needle with yellow marking for injecting the sterile water into the vial and for drawing the medicine that has formed out of the vial.
- One needle with gray marking for injecting the medicine into your abdomen.
- Two alcohol swabs for disinfection.

**Registration holder's name and address:** Merck Serono Ltd., 18 Hakishon St., Yavne 81220.

**Manufacturer's name and address:** Merck Healthcare KGaA, Darmstadt, Germany.

This leaflet was revised in November 2024.

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

## **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 medicine, read these instructions the whole way through.
- This medicine is intended for you – do not let anyone else use it.
- Use each needle, vial and syringe only once.

### **Before you begin**

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

### **2. Wash your hands**

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

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

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

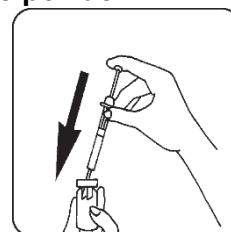
### **Mixing the powder with the water to prepare your medicine**

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

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

#### **2. Adding the sterile water from the pre-filled syringe into the vial with the powder**

- Take the yellow labelled needle out of its wrapping.
- Remove the cap from the syringe pre-filled 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.

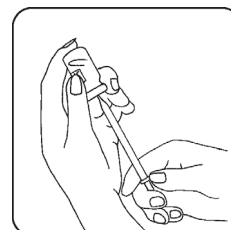


#### **3. Mixing the powder and the water in the vial**

- 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 (restart 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 needle tip is in the rubber stopper. The movement of the needle and 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 solution contents from the vial back into the syringe.

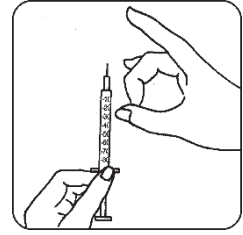


- Put the cap back on the yellow needle. Unscrew the yellow needle from the syringe and place the syringe aside.

## 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 the air bubbles are expelled.
- Do not touch the gray needle and do not let the needle touch anything.

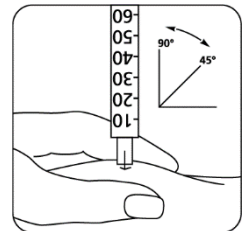


### 2. Disinfecting the injection site

- Choose an injection site in the abdominal area, preferably around the navel. To avoid local skin irritation, 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 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 remove 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

- Take out 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.