

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

CRINONE® 8%

Progesterone Vaginal Gel

Prolonged release

The active ingredient: Progesterone 8% w/w

Each applicator contains a dose of 90 mg progesterone as gel.

- Inactive and allergenic ingredients in the preparation – see section 2 "Important information about some of the ingredients in the medicine" and 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 the leaflet at hand; you may need to read it again.

This medicine has been prescribed to treat 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 side effects of any sort, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

1. WHAT IS THE MEDICINE INTENDED FOR

For the treatment of infertility due to inadequate levels of the female hormone progesterone during the menstrual cycle.

For use during *in vitro* fertilization, including in cases of unexplained infertility, problems associated with the fallopian tubes or the womb.

Therapeutic group: Progesterone – belongs to the group of female sex hormones (progestogens).

2. BEFORE USING THE MEDICINE

Do not use the medicine:

- If you are sensitive (allergic) to the active ingredient, progesterone, or any of the additional ingredients contained in the medicine (see section 6).
- If you have vaginal bleeding of an unknown cause.
- In case of porphyria (inability to break down certain substances [porphyrins] in the blood, which is hereditary).
- In case of suspicion or diagnosis of cancer of the breast or genital organs.
- If you have had in the past a blood clot caused by swelling of the veins (thrombophlebitis), blocked blood vessels (thromboembolic disorder) or a stroke.
- If you are pregnant and the fetus has died in the womb (missed abortion).

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

Special warnings regarding use of the medicine

Before treatment with the medicine, tell the doctor if any of the following apply to you. The doctor may want to monitor you more often during the course of treatment:

- You have liver or kidney problems
- You have heart problems or diabetes
- You have asthma
- You have epilepsy or often have migraines
- You have ever had depression

Inform the doctor in case of any unexpected bleeding so that the doctor can check the cause of this.

Children and adolescents

Crinone is not intended for use in young girls and female adolescents.

Tests and follow-up

The doctor will refer you for tests before commencing treatment with the medicine as well as during the course of treatment. Especially:

- Before using the medicine, the doctor will have to perform a smear test and examine your breasts and pelvic area.
- During treatment, the doctor will check if you have any problems in the uterus, such as: thickening of the lining (endometrial hyperplasia). In addition, signs of blood clots in the blood vessels will be checked.

Drug interactions:

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

Do not use this medicine concomitantly with any other medicines inserted into the vagina.

Pregnancy and breastfeeding

- Crinone is not usually used during pregnancy. However, if you used Crinone in order to become pregnant, it may be necessary to continue treatment to support the pregnancy.
- Do not use when breastfeeding.

Driving and operating machinery

Crinone has no influence on the ability to drive or use machines.

Important information about some of the ingredients in the medicine

Crinone contains sorbic acid, which may cause local skin reactions such as contact dermatitis. When using the preparation, these skin reactions may also occur on your partner's penis during intercourse. This can be prevented by using a condom.

3. HOW SHOULD YOU USE THE MEDICINE

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine.

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

The recommended dosage is usually:

1. For treatment of infertility – insert the contents of one Crinone 8% applicator into the vagina each day, starting from the day the doctor has told you that you are ovulating, or, arbitrarily, from the 18th to 21st day of your menstrual cycle (the first day of your period is considered the first day of the menstrual cycle).
2. In cases of *in vitro* fertilization – starting from the day of the embryo transfer, insert one Crinone 8% applicator into the vagina, once a day, preferably in the morning hours. Once pregnancy is confirmed, the doctor may tell you to continue using Crinone for 30 days, to support the new pregnancy.

The applicator is designed in such a way that it supplies the exact amount of gel (1.125 g, which contains 90 mg progesterone). A small amount of gel is expected to remain in the applicator. The applicator can be discarded after use, since you have received all the required dose.

Do not exceed the recommended dose.

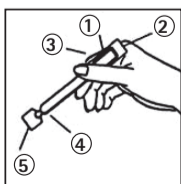
Do not swallow. The medicine is intended for vaginal use.

Instructions for use:

This medicine is intended for vaginal use only, by using the pre-filled applicator provided in the pack.

Before using the applicator, read all the instructions below:

What the applicator looks like

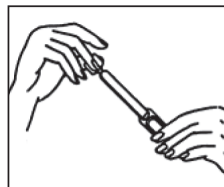


1. Air tank
2. Flat part of the thick end
3. Thick end
4. Thin end
5. Cap

Getting the applicator ready for use

Hold the applicator so that the thick end is between your thumb and index finger. Direct the thin end of the applicator downward and shake the applicator down to move all of its content to the thin end.

Opening the applicator



Hold the applicator by the flat part of the thick end. Twist off and remove the cap from the opposite thin end. To avoid leakage of the gel before use, do not press on the air tank at the thick end at this stage.

Inserting the applicator



Lean back or lie down with your knees bent and spread apart. Gently insert the applicator well into the vagina, until your hand touches your body.

Press on the air tank at the thick end of the applicator firmly to release the gel from the applicator into the vagina.

Special instructions for using the preparation above approximately 760 meters above sea level:

Using a sharp instrument, make a single puncture in the flat part of the thick end (that looks like a bubble) of the applicator. This will release the air pressure that builds up between the inner and outer parts of the applicator caused by the high altitude.

This will not affect the amount of gel provided!

Continue using according to the instructions above.

In this case, place your finger on the puncture you made in the applicator. Press the thick end of the applicator to release the gel into the vagina. Some gel may remain in the applicator, but do not worry, you will still receive the desired dose.

After using the applicator

Dispose of the applicator, including the small amount of gel left in the applicator. The applicator is intended for single use.

Wash your hands with soap and hot water.

Crinone Gel can stay in the vagina for several days. You may have discharge that looks like beige-brown clumps or cloudy white discharge during this time. Do not worry about it.

If you accidentally took a higher dosage

It is unlikely that you will take a higher dosage, since the applicator contains the exact dose of gel.

If you took an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine

Do not take a double dose to compensate for a forgotten dose. If you forgot to insert the medicine on that day, insert one dose of the medicine the next day.

Adhere to the treatment regimen recommended by the doctor.

Do not stop treatment with the medicine without consulting 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 medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Crinone 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 experience an allergic effect. You may have, for example, an itchy skin rash.

The frequency of this side effect is unknown.

Additional side effects

Common side effects (occur in 1-10 out of 100 users):

Breast tenderness.

Side effects of unknown frequency:

Vaginal bleeding that causes spotting between periods, irritation or other mild reactions in or around the vagina.

Note:

Crinone gel can stay in the vagina for several days. You may have discharge that looks like beige-brown clumps or cloudy white discharge during this time. Such discharge may cause irritation, pain or swelling in the vagina, but this is nothing to worry about.

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the 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 homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il/>

5. HOW SHOULD THE MEDICINE BE STORED

- 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) that appears on the package. The expiry date refers to the last day of that month.
- Store the applicators in the original package, below 25°C. Do not store in a refrigerator.
- Each applicator is intended for single use. Dispose of the gel that remains in the applicator after use.
- Do not dispose of medicines via the wastewater (sewage) or household waste. Ask the pharmacist how to dispose of medicines that you no longer use. These measures will help to protect the environment.

6. FURTHER INFORMATION

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

Glycerin, Light Liquid Paraffin, Hydrogenated Palm Oil Glycerides, Carbomer 974P, Polycarbophil, Sorbic Acid, Sodium Hydroxide, Purified Water.

What the medicine looks like and the contents of the package:

Crinone is a smooth white/off-white gel in a capped, white, disposable vaginal applicator. Each applicator is individually wrapped.

Crinone comes in packs of 6 or 15 disposable applicators. Not all pack sizes may be marketed.

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

Manufacturer and address: Ares Trading S.A., Aubonne, Switzerland.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 120 01 29994 00

Revised in April 2021 according to MOH guidelines.