

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

## OVESTIN® CREAM

Estriol 0.1% w/w

### The active ingredient and its quantity:

Each gram of cream contains 1 mg Estriol.

One dose (when the amount of cream in the applicator reaches the ring mark) contains 0.5 g **Ovestin Cream** corresponding to 0.5 mg Estriol.

For a list of inactive ingredients, see section 6 “**Further information**”. Also see section 2 “**Important information regarding some of the ingredients of the medicine**”.

**Read this leaflet carefully in its entirety before using the medicine.** This leaflet contains concise information about the medicine. If you have further questions, ask the doctor or pharmacist.

This medicine has been prescribed for your treatment. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

If any of the side effects worsen, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

### 1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is intended for the treatment of vaginal disorders due to estrogen deficiency.

**Therapeutic group: Ovestin Cream** contains an active ingredient called estriol. It belongs to a group of medicines called **Hormone Replacement Therapy (HRT)**.

Estriol (the active ingredient in **Ovestin Cream**) is one of the natural estrogens.

- Estrogens are female sex hormones.
- Estrogens are produced in the ovaries.
- Estrogens cause sexual development in women and control the menstrual cycle during the child-bearing years.
- When women get older, the ovaries gradually produce less estrogen.
- This process happens at menopause (usually around the age of 50).
- If the ovaries are removed before the menopause, estrogen production stops suddenly.

Shortage of estrogens may cause the vaginal wall to become thin and dry, so that sexual intercourse may become painful and you may get vaginal infections. These problems can be relieved by using medicines like **Ovestin Cream**, which contains estrogen. Several days or weeks may pass before you notice an improvement.

### 2. BEFORE USING THE MEDICINE

#### ❗ Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient Estriol or to any of the additional ingredients contained in the medicine (listed in section 6).
- You are pregnant or may be pregnant or if you are breastfeeding.
- You have a hormone-dependent tumor (e.g., endometrial cancer).
- You have had angina pectoris or a heart attack (myocardial infarction).
- You have had a blood clot (thrombosis) (deep vein thrombosis, pulmonary embolism) or currently have venous thrombosis.
- You have a blood-clotting problem (e.g., deficiency in protein C, protein S or antithrombin).
- You have had breast cancer or suspect that you have breast cancer.
- You have had cancer of other sex organs, such as cancer of the womb lining or ovary.
- You have unexplained vaginal bleeding.
- You have excessive thickening of the womb lining.
- You have or have had a liver disease, and your liver is still not working properly.
- You have a rare blood problem called “porphyria”.

Do not use this medicine if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before using **Ovestin Cream**.

#### Special warnings regarding use of the medicine

##### ❗ Before treatment with Ovestin Cream, tell your doctor if you have or have had in the past:

- a problem caused by growth of the womb lining outside the womb (fibroids or endometriosis)
- any problem with your heart or circulation (including high blood pressure or risk factors for a blood clot – see section “**Ovestin Cream and the heart or circulation**”)
- vaginal bleeding
- relatives who have had blood clots
- asthma
- diabetes
- migraine or severe headaches
- epilepsy (epileptic fits)
- gallstones
- liver or kidney problems
- a rare problem called ‘systemic lupus erythematosus’ (SLE)
- risk factors for an estrogen-dependent tumor (first-degree hereditary breast cancer)
- otosclerosis (a hearing disorder)

If you have any of the above, talk to your doctor before using **Ovestin Cream**.

Tell the doctor if you have hepatitis C and if you are taking a combination of the following medicines: ombitasvir, paritaprevir or ritonavir, with or without dasabuvir. Taking a combination of these medicines with estrogen-containing preparations may cause increases in liver function blood test results (increase in ALT liver enzyme); the risk of this happening with **Ovestin Cream** is currently unknown.

#### Tests and follow-up

##### Routine checkups

Once you start treatment with HRT, visit your doctor for routine tests (at least once a year). In these tests, your doctor may discuss the benefits and risks of continuing to take HRT.

##### Make sure that you:

- go for **regular breast screening** and **cervical smear tests**
- regularly check your breasts** for any changes such as: dimpling of the skin, changes in the nipple, or any lumps you can see or feel.

In addition to the benefits of **Hormone Replacement Therapy (HRT)**, there are risks to consider when deciding whether to start or continue with this treatment. This is especially important if you are over 60 years of age.

##### Before you start taking HRT

Your doctor should ask you about your medical history and your family's medical history. Your doctor may decide to check your breasts or abdomen and may perform an internal examination. The tests will be performed only if they are necessary for you or there are any special concerns.

##### Ovestin Cream and the risk of developing cancer

###### **Breast cancer**

- Women who have ever had breast cancer should not take Hormone Replacement Therapy (HRT).**

Taking HRT slightly increases the risk of breast cancer. Also, the risk is slightly increased if you have a later menopause. The risk after the menopause for a woman taking estrogen-only HRT for 5 years is about the same as for a woman of the same age who is still having periods over that time and not taking HRT. The risk for a woman who is taking estrogen plus progestogen HRT is higher than for a woman taking estrogen-only HRT. However, estrogen plus progestogen HRT is beneficial for the endometrium.

For all kinds of HRT, the extra risk of breast cancer increases the longer you take it. However, it returns to normal about 5 years after stopping HRT.

Your risk of getting breast cancer is even higher if:

- you have a first- or second-degree relative (mother, sister or grandmother) who has had breast cancer.
- you are seriously overweight.

###### **What are the chances of getting breast cancer?**

Looking at **women aged 50**, on average, by the time they reach the age of 65:

- In women **not taking HRT: 32 in 1,000** will get breast cancer.
- In women **who start taking estrogen-only HRT** at age 50 and take it for **5 years: between 33 and 34 in 1,000** will get breast cancer. This means an **extra 1 to 2 cases**.
- In women **taking estrogen-only HRT for 10 years: 37 in 1,000** will get breast cancer. This means an **extra 5 cases**.

If you **notice** any changes in your breast, such as: dimpling of the skin, changes in the nipple or any lumps you can see or feel, **make a doctor's appointment immediately!**

###### **Endometrial cancer (cancer of the lining of the womb)**

**Taking estrogen-only HRT tablets for a long time can increase the risk of developing cancer of the lining of the womb.** There may be a similar risk with estrogen cream administered directly into the vagina in repeated treatments or over a long time.

You do not need to take progestogen when using **Ovestin Cream**.

If you get breakthrough bleeding or spotting, it is usually nothing to worry about, but you **should talk to your doctor**. It could be a sign that your endometrium has become thicker.

###### **Ovarian cancer**

Ovarian cancer (cancer of the ovaries) is very rare, but it is serious. It can be difficult to diagnose, because there are often no obvious signs of the problem. Some studies have shown that taking estrogen-only HRT for more than 5 years may increase the risk of ovarian cancer. It is not yet known whether other kinds of HRT increase the risk in the same way.

##### Ovestin Cream and the heart or circulation

###### **Heart disease**

**HRT is not recommended for women who have recently had heart disease.** If you have ever had heart disease, talk to your doctor to see if you can take HRT.

###### **HRT will not help prevent heart disease.**

Studies with one type of HRT (containing a progestogen, and a different estrogen than the one in **Ovestin Cream**) have shown that women may be slightly more likely to get heart disease during the first year of taking that type of HRT. For other types of HRT (like **Ovestin Cream**), the risk is likely to be similar, however this is not yet certain. **If you have chest pain that spreads to the arm or neck, see a doctor as soon as possible!**

Do not use any more HRT until a doctor says you can. This pain could be a sign of heart disease.

###### **Stroke**

Studies show that HRT **slightly increases** the risk of having a stroke. Other factors that can increase the risk of stroke include: **aging, high blood pressure, smoking, drinking too much alcohol, an uneven heartbeat.**

If you are worried about any of these factors, or if you have had a stroke in the past, talk to your doctor to see if you can take HRT.

###### **What are the chances of getting a stroke?**

Looking at **women in their 50s**, on average, over 5 years:

- In women **not taking HRT: 3 in 1,000** are expected to have a stroke.
- In women **taking HRT: 4 in 1,000** are expected to have a stroke.

Looking at **women in their 60s**, on average, over 5 years:

- In women **not taking HRT: 11 in 1,000** are expected to have a stroke.
- In women **taking HRT: 15 in 1,000** are expected to have a stroke.

If you **have** an unexpected migraine-type headache, with or without disturbed vision, **see a doctor straight away**, and do not use any more HRT until a doctor says you can. These headaches may be an early warning sign of a stroke.

###### **Blood clots**

HRT may increase the risk of blood clots in the veins (also called deep vein thrombosis - DVT), especially during the first year of taking it.

**These blood clots are not always serious.** However, if a blood clot travels to the lungs, it can cause chest pain, feeling breathless, collapse or even death. This condition is called a pulmonary embolism or PE.

You are more likely to get a blood clot if:

- you are **very overweight**; you have had a **blood clot before**; any of your **close family** have had **blood clots**; you have ever had a **miscarriage**; you have any **blood clotting problem** that requires treatment with a medicine such as warfarin; you are in a **lying position** for a long time because of **major surgery, injury or illness**; you have a rare problem called **systemic lupus erythematosus (SLE)**.

If any of the listed above apply to you, talk to your doctor to see if you should take HRT.

###### **What are the chances of getting a blood clot?**

Looking at **women in their 50s**, on average, over 5 years:

- In women **not taking HRT: 3 in 1,000** are expected to get a blood clot.
- In women **taking HRT: 7 in 1,000** are expected to get a blood clot.

Looking at **women in their 60s**, on average, over 5 years:

- In women **not taking HRT: 8 in 1,000** are expected to get a blood clot.
- In women **taking HRT: 17 in 1,000** are expected to get a blood clot.

If you have painful swelling in the leg, sudden chest pain or have problems breathing, **see a doctor straight away!**

Do not use any more HRT until a doctor says you can. These may be signs of a blood clot.

#### ❗ Drug interactions

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

**Tell your doctor** or pharmacist if you are taking any of the following medicines:

- medicines for epilepsy - such as barbiturates, hydantoins and carbamazepine.
- medicines for infections - such as griseofulvin and rifamycins.
- medicines for viral infections - such as nevirapine, efavirenz, ritonavir or nelfinavir.
- herbal preparations containing St. John's wort (Hypericum perforatum) - an herbal medicine used to treat depression.
- any one of the following medicines: corticosteroids, succinylcholine, theophylline or troleandomycin.

Tell the doctor if you have hepatitis C and if you are taking a combination of the following medicines: ombitasvir, paritaprevir or ritonavir, with or without dasabuvir. Taking a combination of these medicines with estrogen-containing preparations may cause increases in liver function blood test results (increase in ALT liver enzyme); the risk of this happening with **Ovestin Cream** is currently unknown.

If you are not sure if you are using any of the medicines mentioned above, talk to your doctor before using **Ovestin Cream**.

If you have a vaginal infection, it should be treated before using **Ovestin Cream**.

#### ❗ Operations

If you are about to undergo surgery, **tell your doctor** you are using **Ovestin Cream**. You may need to stop using HRT for about 4 to 6 weeks before the operation to reduce the risk of a blood clot. Your doctor will tell you when you can start using HRT again.

#### ❗ Pregnancy and breastfeeding

- Do not use **Ovestin Cream** if you are pregnant or may be pregnant. This is because it may affect the baby.
- Do not breastfeed if you are using this medicine.

If you are pregnant or breastfeeding, ask your doctor or pharmacist for advice before taking any medicine.

#### ❗ Driving and using machines

**Ovestin Cream** has no effect or may have little effect on the ability to drive or use machines.

#### ❗ Important information regarding some of the ingredients of the medicine

**Ovestin Cream** contains cetyl alcohol and stearyl alcohol. These can cause localized skin reactions (for example, contact dermatitis).

### 3. HOW SHOULD YOU USE THE MEDICINE?

Always use **Ovestin Cream** according to the doctor's instructions. You should check with the doctor or pharmacist if you are not sure about the dosage and treatment regimen of the medicine.

- If you have had your womb and ovaries removed, you can start using **Ovestin Cream** straight away.
- If you have never used HRT or if you are changing over from another type of HRT during which you did not have a monthly period, you can start using **Ovestin Cream** immediately.
- If you are changing over from another type of HRT during which you have a period, start taking **Ovestin Cream** one week after you finish the other HRT.

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

#### Do not exceed the recommended dose.

Note: This medicine is intended for vaginal use.

The recommended dosage is generally:

##### For vaginal problems

- The usual dose is 1 applicator filled up to the ring mark (0.5 mg estriol in 0.5 g of cream) a day, for the first 2 to 3 weeks.
- Then, the dose is 1 applicator filled up to the ring mark, twice a week.

Your doctor will prescribe the lowest dose that relieves your symptoms. Your doctor may want you to stop the treatment from time to time (every 2 to 3 months for a period of 4 weeks). This is to check if you still need treatment.

##### Instructions for use:

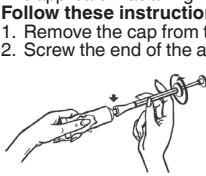
**Ovestin Cream** comes in a package that includes a clear plastic applicator.

Use the applicator to apply the cream in the vagina. **A good time to do this is before going to bed.**

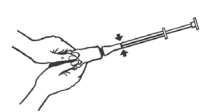
The applicator has a ring marked on the body. Fill the applicator up to the ring mark with **Ovestin Cream** to get the correct dose.

##### Follow these instructions:

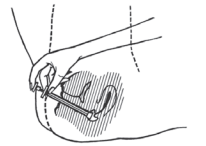
- Remove the cap from the tube and turn the cap upside down. Then use the sharp point on the cap to open the tube.
- Screw the end of the applicator onto the tube.



- Squeeze the tube to fill the applicator with the cream, up to the red ring mark (the plunger will stop at the red ring mark).



- Unscrew the applicator from the tube and put the cap back on the tube.
- To apply the cream, lie down on your back, put the end of the applicator deep into your vagina and slowly push the plunger all the way in.



#### Cleaning the applicator

- After use, pull the plunger out of the barrel.
- Wash the plunger and barrel with warm soapy water.
- Do not use detergents. Rinse well with clean water afterwards.
- Do not put the applicator in boiling water.

**Ovestin Cream** is easily removed with water.

For tests to perform before using the medicine, see section 2.

**If you accidentally took a higher dosage or if you swallowed or someone has swallowed some cream by accident**, talk to your doctor, as you/the person may feel nauseated or vomit. A little vaginal bleeding may occur after several days.

If you took an overdose or if a child or anyone else 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

- If you forgot to take this medicine at the required time, do not take a double dose.
- Apply the missed dose when you remember and consult with the doctor, unless you are more than 12 hours late after the required time.

- If you are more than 12 hours late, just skip the missed dose.

Adhere to the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with this medicine without consulting your doctor.

##### If you stop taking the medicine

Keep using this medicine as prescribed for you by the doctor, even if you seem to feel better. If you stop too early or suddenly, your problem may return.

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

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

### 4. SIDE EFFECTS

Like all medicines, use of **Ovestin Cream** may cause side effects in some users.

Do not be alarmed by the list of side effects. You may not suffer from any of them.

**Refer to the doctor straight away, if you notice any of the following serious side effects – your doctor may decide to discontinue use of the cream:**

- your blood pressure rises.
- your skin or the whites of your eyes become yellow (jaundice).
- you suddenly have migraine-type headaches (see section 2 “**Ovestin Cream and the heart or circulation**”, above).
- you have signs of a blood clot (see section 2 “**Ovestin Cream and the heart or circulation**”, above).
- you have one or more of the problems listed in section 2 (see above “**Do not use the medicine if:**”).

These side effects are rare.

##### Additional side effects:

- irritation or itching of the skin in or around your vagina when you start using **Ovestin Cream**. This effect usually gets better after a few weeks.
- increased vaginal discharge, bleeding or spotting.
- gallbladder problems.
- skin problems such as a rash or an allergy to the sun.
- breasts become swollen, tender or painful.
- headaches.
- nausea or vomiting.
- flu-like symptoms.

**Tell your doctor** if you get any of these side effects; he may decide to stop the treatment for a while.

##### Dementia

HRT will not prevent memory loss. In one study of women who started treatment with combined HRT after the age of 65, a small increase in the risk of dementia was observed.

**If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult with your doctor.**

##### 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](http://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>

In addition, you can report to the company via the following address: [www.perrigo-pharma.co.il](http://www.perrigo-pharma.co.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.

**Storage conditions:** Store below 25°C. Do not freeze. Can be used within 35 days of first opening, and no later than the expiration date of the medicine, whichever comes first.

Do not dispose of medicines into wastewater or household waste. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help protect the environment.

### 6. FURTHER INFORMATION

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

Purified water, glycerol, stearyl alcohol, octyldodecanol, cetyl alcohol, polysorbate 60, cetyl palmitate, sorbitan stearate, lactic acid, chlorhexidine dihydrochloride, sodium hydroxide.

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

**Ovestin Cream** is a homogeneous, smooth, white to almost-white mass of creamy consistency, with a mild characteristic odor. **Ovestin Cream** is contained in a 15-gram aluminum tube.

Each tube is packed in a cardboard package containing a transparent plastic applicator.

**Registration Holder and address:** Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.

**Manufacturer name and address:** Aspen Pharma Trading Ltd., Dublin, Ireland.

Revised in December 2021 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 6560.21266