

PACKAGE LEAFLET: INFORMATION FOR THE USER
Ovestin® 1mg Cream
(Estriol)

- Read all of this leaflet carefully before you start using this medicine.**
- Keep this leaflet. You may need to read it again.
 - 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 symptoms are the same as 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.

The name of your medicine is Ovestin Cream, but will be referred to as Ovestin throughout the remainder of the leaflet.

- In this leaflet:**
1. What Ovestin is and what it is used for
 2. What you need to know before you use Ovestin
 3. How to use Ovestin
 4. Possible side effects
 5. How to store Ovestin
 6. Further information

1. What Ovestin is and what it is used for
The name of your medicine is Ovestin 1 mg cream. Ovestin contains a medicine called estriol. It belongs to a group of medicines called Hormone Replacement Therapy (HRT).

It is used to relieve menopausal symptoms in the vagina such as dryness or irritation. In medical terms this is known as 'vaginal atrophy'. It is caused by a drop in the levels of oestrogen in your body. This happens naturally after the menopause. Ovestin works by replacing the oestrogen which is normally produced in the ovaries of women. It is inserted into your vagina, so the hormone is released where it is needed. This may relieve discomfort in the vagina.

- When women get older the ovaries gradually produce less oestrogen.
- This happens at the menopause (usually around the age of 50).
 - If the ovaries are removed before the menopause, oestrogen production stops very suddenly.

Shortage of oestrogens may cause the vaginal wall to become thin and dry. So sexual intercourse may become painful and you may get vaginal infections. These problems can be relieved by using medicines like Ovestin which contain oestrogen. It may take several days or weeks before you notice an improvement.

- Ovestin is used:
- Before or after vaginal surgery to help wound healing.

2. What you need to know before you use Ovestin
Medical history and regular check-ups
The use of HRT carries risks which need to be considered when deciding whether to start taking it, or whether to carry on taking it.

The experience in treating women with a premature menopause (due to ovarian failure or surgery) is limited. If you have a premature menopause the risks of using HRT may be different. Please talk to your doctor.

Before you start (or restart) HRT, your doctor will ask about your own and your family's medical history. Your doctor may decide to perform a physical examination. This may include an examination of your breasts and/or an internal examination, if necessary. Once you have started on Ovestin you should see your doctor for regular check-ups (at least once a year). At these check-ups, discuss with your doctor the benefits and risks of continuing with Ovestin.

Go for regular breast screening, as recommended by your doctor.

Do not use Ovestin
If any of the following applies to you. If you are not sure about any of the points below, **talk to your doctor** before using Ovestin,

- Do not use Ovestin:
- If you have or have ever had **breast cancer**, or if you are suspected of having it
 - If you have **cancer which is sensitive to estrogens**, such as cancer of the womb lining (endometrium), or if you are suspected of having it
 - If you have **any unexplained vaginal bleeding**

- If you have **excessive thickening of the womb lining** (endometrial hyperplasia) that is not being treated
- If you have or have ever had a **blood clot in a vein** (thrombosis), such as in the legs (deep venous thrombosis) or the lungs (pulmonary embolism)
- If you have a **blood clotting disorder** (such as protein C, protein S, or antithrombin deficiency)
- If you have or recently have had a disease caused by blood clots in the arteries, such as a **heart attack, stroke** or **angina**
- If you have or ever have had a liver disease and your liver function tests have not returned to normal
- If you have a rare blood problem called “porphyria” which is passed down in families (inherited)
- If you are **allergic** (hypersensitive) to estriol or any of the other ingredients of Ovestin (listed in section 6 Contents of the pack and further information)

If any of the above conditions appear for the first time while using Ovestin, stop taking it at once and consult your doctor immediately.

- Warnings and precautions**
Tell your doctor if you have ever had any of the following problems, before you start the treatment, as these may return or become worse during treatment with Ovestin. If so, you should see your doctor more often for check-ups:
- fibroids inside your womb
 - growth of womb lining outside your womb (endometriosis) or a history of excessive growth of the womb lining (endometrial hyperplasia)
 - increased risk of developing blood clots (see “Blood clots in a vein (thrombosis)”)
 - increased risk of getting an estrogen-sensitive cancer (such as having a mother, sister or grandmother who has had breast cancer)
 - high blood pressure
 - a liver disorder, such as a benign liver tumor
 - diabetes
 - gallstones
 - migraine or severe headaches
 - a disease of the immune system that affects many organs of the body (systemic lupus erythematosus, SLE)
 - epilepsy
 - asthma
 - a disease affecting the eardrum and hearing (otosclerosis)
 - fluid retention due to cardiac or kidney problems

Tell your doctor if you have Hepatitis C and you are taking the combination drug regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir. Taking the combination of these drugs with some oestrogen-containing products may cause increases in liver function blood test results (increase in ALT liver enzyme); the risk of this happening with Ovestin is currently unknown. Ovestin contains cetyl alcohol and stearyl alcohol. This may cause local skin reactions (e.g.contact dermatitis).

- Stop using Ovestin and see a doctor immediately**
If you notice any of the following when taking HRT:
- any of the conditions mentioned in the ‘DO NOT take Ovestin’ section
 - yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease
 - a large rise in your blood pressure (symptoms may be headache, tiredness, dizziness)
 - migraine-like headaches which happen for the first time
 - if you become pregnant
 - if you notice signs of a blood clot, such as:
 - painful swelling and redness of the legs
 - sudden chest pain
 - difficulty in breathing
- For more information, see ‘Blood clots in a vein (thrombosis)’.

Note: Ovestin is not a contraceptive. If it is less than 12 months since your last menstrual period or you are under 50 years old, you may still need to use additional contraception to prevent pregnancy. Speak to your doctor for advice.
HRT and cancer
Excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)
Taking oestrogen-only HRT tablets for a long time can increase the risk of developing cancer of the womb lining (the endometrium).

It is uncertain whether there is a similar risk with Ovestin if used for repeated or long term (more than one year) treatments. However, Ovestin has been shown to have very low absorption into the blood, therefore the addition of a progestagen is not necessary.

If you get bleeding or spotting, it’s usually nothing to worry about, but you should make an appointment to see your doctor. It could be a sign that your endometrium has become thicker.

The following risks apply to hormone replacement therapy (HRT) medicines which circulate in the blood. However Ovestin is for local treatment in the vagina and the absorption into the blood is very low. It is less likely that the conditions mentioned below will get worse or come back during treatment with Ovestin, but you should see your doctor if you are concerned.

Breast cancer
Evidence suggests that using Ovestin does not increase the risk of breast cancer in women who had no breast cancer in the past. It is not known if Ovestin can be safely used in women who had breast cancer in the past.

Regularly check your breasts. See your doctor if you notice any changes such as:

- dimpling of the skin
- changes in the nipple
- any lumps you can see or feel

Additionally, you are advised to join mammography screening programs when offered to you.

Ovarian cancer
Ovarian cancer is rare – much rarer than breast cancer. The use of oestrogen-only HRT has been associated with a slightly increased risk of ovarian cancer.

The risk of ovarian cancer varies with age. For example, in women aged 50 to 54 who are not taking HRT, about 2 women in 2000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there will be about 3 cases per 2000 users (i.e. about 1 extra case).

Effect of HRT on your heart or circulation
Blood clots in a vein (thrombosis)
The risk of **blood clots in the veins** is about 1.3 to 3-times higher in HRT users than in non-users, especially during the first year of taking it.

Blood clots can be serious, and if one travels to the lungs, it can cause chest pain, breathlessness, fainting or even death.

- You are more likely to get a blood clot in your veins as you get older and if any of the following applies to you. Inform your doctor if any of these situations applies to you:
- you are unable to walk for a long time because of major surgery, injury or illness (see also section 3, If you need to have surgery)
 - you are seriously overweight (BMI >30 kg/m2)
 - you have any blood clotting problem that needs long-term treatment with a medicine used to prevent blood clots
 - if any of your close relatives has ever had a blood clot in the leg, lung or another organ
 - you have systemic lupus erythematosus (SLE)
 - you have cancer.

For signs of a blood clot, see “Stop taking Ovestin and see a doctor immediately”.

Compare
Looking at women in their 50s who are not taking HRT, on average, over a 5-year period, 4 to 7 in 1000 would be expected to get a blood clot in a vein. For women in their 50s who have been taking estrogen-only HRT for over 5 years, there will be 5 to 8 cases in 1000 users (i.e. 1 extra case).

Heart disease (heart attack)
For women taking estrogen-only therapy there is no increased risk of developing a heart disease.

Stroke The risk of getting stroke is about 1.5 times higher in HRT users than in non-users. The number of extra cases of stroke due to use of HRT will increase with age.

Compare
Looking at women in their 50s who are not taking HRT, on average, 8 in 1000 would be expected to have a stroke over a 5-year period. For women in their 50s who are taking HRT, there will be 11 cases in 1000 users, over 5 years (i.e. an extra 3 cases).

Other conditions
HRT will not prevent memory loss. There is some evidence of a higher risk of memory loss in women who start using HRT after the age of 65. Speak to your doctor for advice.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription, herbal medicines or other natural products. This is because Ovestin can affect the way some other medicines work. Also some other medicines can affect the way Ovestin works.

- Tell your doctor** or pharmacist if you are taking any of the following:
- 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*) - a herbal medicine used for depression.
 - one of the following medicines: corticosteroids, succinylcholine,theophyllines or troleandomycin.

Tell your doctor if you have Hepatitis C and you are taking the combination drug regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir. Taking the combination of these drugs with some oestrogen-containing products may cause increases in liver function blood test results (increase in ALT liver enzyme); the risk of this happening with Ovestin is currently unknown.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before using Ovestin.

If you have a vaginal infection, your doctor may also prescribe a medicine to treat the infection.
Operations
→ **Tell your doctor** you are using Ovestin if you are going to have surgery. You may need to stop using HRT 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 taking HRT again.

Pregnancy and breast-feeding
Ovestin is for use in postmenopausal women only. If you become pregnant, stop taking Ovestin and contact your doctor.

- Do not use Ovestin if you are pregnant or might become pregnant. This is because it may affect the baby.
- Do not breast-feed if you are using this medicine.

Ask your doctor or pharmacist for advice before taking any medicine, if you are pregnant or breast-feeding.

Driving and using machines
Ovestin has no or little effect on the ability to drive or use machines.

- 3. How to use Ovestin**
Always use Ovestin exactly as your doctor or pharmacist has told you. You should check with your doctor or pharmacist if you are not sure.
- If you have had your womb and ovaries removed, you can start using Ovestin straight away.
 - If you have never used HRT before or if you are changing over from a period-free HRT, you can also use Ovestin straight away.
 - If you are changing over from another type of HRT where you have a period, start taking Ovestin one week after you finish the other HRT.

How much to use
For vaginal problems

- The usual dose is 1 applicator up to the ring (0.5 mg estriol in 0.5 g of cream) a day for the first 2 to 3 weeks (maximally 4 weeks).
- Then the dose is 1 applicator up to the ring twice a week.

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

- Before or after vaginal surgery**
- Before surgery – the dose is 1 applicator up to the ring (0.5 mg estriol in 0.5 g of cream) a day for 2 weeks before the operation.
 - After surgery – do not use the cream again for at least 2 weeks. Then use 1 applicator up to the ring twice a week.

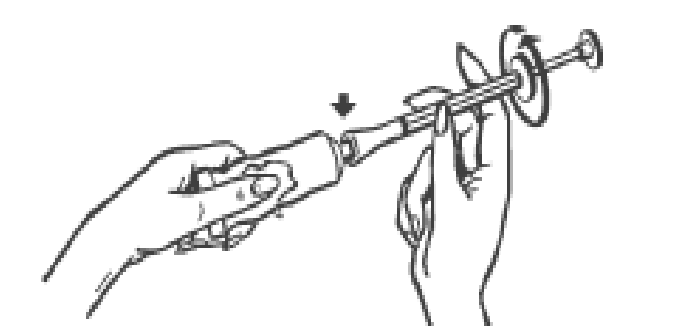
How to apply the cream
Ovestin comes in a pack together with a clear plastic applicator.

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

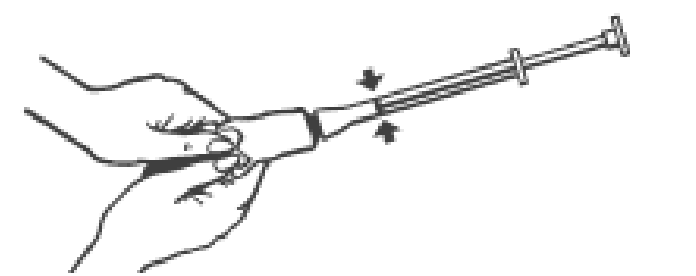
The applicator has a ring marked on the body. Fill the applicator up to the ring mark with Ovestin cream to get the correct dose.

→ **Follow these instructions:**

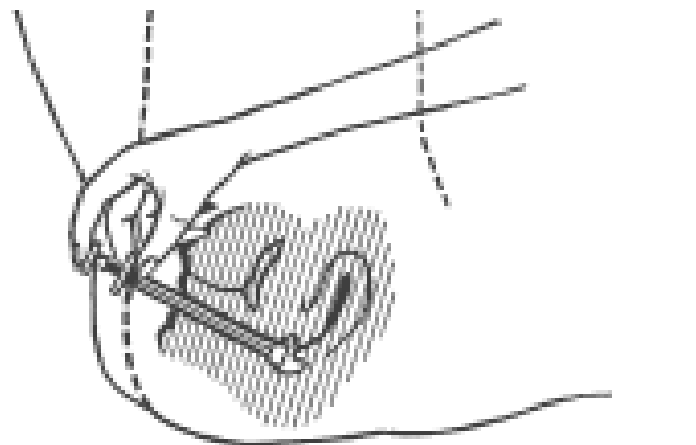
- 1 Remove the cap from the tube and turn the cap upside down. Then use the sharp point to open the tube.
- 2 Screw the end of the applicator onto the tube.



- 3 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).



- 4 Unscrew the applicator from the tube and put the cap back on the tube.
- 5 To apply the cream, lie down, 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 in hand hot, soapy water.
- Do not use detergents. Rinse well with clean water afterwards.
- Do not put the applicator in boiling water.

Ovestin is easy to remove with water.

If you use more Ovestin than you should or if you swallow it accidentally

If someone has swallowed some cream by accident, or too much cream is applied at any time, there is no need to worry. However, you should talk to your doctor. The person may feel sick or be sick. Women may have some vaginal bleeding after a few days.

If you forget to use Ovestin

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

If you stop using Ovestin

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

4. Possible side effects

Like all medicines, Ovestin can cause side effects, although not everybody gets them.

The following diseases are reported more often in women using HRT which circulate in the blood compared to women not using HRT. These risks apply less to vaginally administered treatments such as Ovestin:

- ovarian cancer
- blood clots in the veins of the legs or lungs (venous thromboembolism)
- stroke
- probable memory loss if HRT is started over the age of 65

For more information about these side effects, see Section 2.

→ **See your doctor straight away, if you notice any of the following serious side effects – your doctor may decide to stop you using the cream:**

- your blood pressure rises
- your skin or the whites of your eyes go yellow (jaundice)
- you suddenly have migraine-type headaches
- you have signs of a blood clot
- you have any of the problems listed in Section 2 above.

These side effects are rare.

Other side effects include:

- irritation or itching of the skin in or around your vagina when you start to use Ovestin. This usually gets better after a few weeks.
- increased vaginal discharge, bleeding or spotting
- gall bladder problems
- skin problems such as a rash or an allergy to the sun
- breasts become swollen, tender or painful
- headaches
- feeling sick or being sick.
- flu-like symptoms

→ If you have any of these side effects **tell your doctor**. They may decide to stop your treatment for a while.

Dementia

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

→If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, **tell your doctor or pharmacist**.

The following side effects have been reported with other HRTs:

- gall bladder disease
- various skin disorders:
 - discoloration of the skin especially of the face or neck known as "pregnancy patches" (chloasma)
 - painful reddish skin nodules (erythema nodosum)
 - rash with target-shaped reddening or sores (erythema multiforme)

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the **Google Play** or **Apple App Store**. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Ovestin

Keep out of the sight and reach of children.
Do not use this medicine after the "expiry" date on the pack.
Do not store above 25°C. Do not freeze. Keep the tube in the original box where children cannot see or reach it.
If your cream shows any signs of deterioration or discoloration please consult your pharmacist for advice.
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

What Ovestin cream contains

- The active substance is estriol. Each gram of cream contains 1 milligram of estriol.
- The other ingredients are octyldodecanol, glycerol, cetyl alcohol, stearyl alcohol, polysorbate 60, sorbitan stearate, chlorhexidine hydrochloride, lactic acid, sodium hydroxide, purified water and synthetic spermaceti.

What Ovestin cream looks like and the contents of the pack

Ovestin Cream is a white cream. There are 15 grams of cream in each tube and comes with a plastic applicator.

Manufactured by: Organon Ireland Ltd. PO Box 2857, Drynam Road, Swords, Co. Dublin. Ireland or Aspen Bad Oldesloe GmbH, Industriestrasse 32-36, D-23843 Bad Oldesloe, Germany. Procured from within the EU. Product Licence holder: Quadrant Pharmaceuticals Ltd, Lynstock House, Lynstock Way, Lostock, Bolton BL6 4SA. Repackaged by Maxearn Ltd, Unit 29, Oakhill Trading Estate, Devonshire Road, Worsley, Manchester, M28 3PT.

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Ovestin Cream

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Ovestin is a registered trademark.

Blind or partially sighted?
Is this leaflet hard to see or read?
Contact Quadrant Pharmaceuticals
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