

### 3.3 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.

### 3.4 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.

### 3.5 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.

→ **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 (see Section 2.4 above)
- you have signs of a blood clot (see Section 2.4 above)
- you have any of the problems listed in Section 2.1 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.

→ 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. The risk of memory loss may be somewhat higher in women who start using HRT after the age of 65.

→ 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**.

## 5. How to store Ovestin

- Keep out of the sight and reach of children.
- Do not store above 30°C.
- Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of the month.
- If the medicine shows any other signs of deterioration, you should seek the advice of your pharmacist who will tell you what to do.
- 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

- Each gram of cream contains 1mg of estriol.
- The other ingredients are: eutanol G, lactic acid, sodium hydroxide, purified water, sorbitan monostearate, cetyl palmitate, glycerol, stearyl alcohol, cetyl alcohol, polysorbate 60 and chlorhexidine hydrochloride.

### What Ovestin looks like and contents of the pack

- Ovestin Cream is a white cream.
- There are 15 gm of cream in each tube.
- The pack contains a clear plastic applicator

### Product Licence holder

Procured from within the EU and repackaged by the Product Licence holder: S&M Medical Ltd, Chemilines House, Alperton Lane, Wembley, HA0 1DX.

### Manufacturer

This product is manufactured by Organon (Ireland) Ltd, Swords, Ireland.

**POM** PL No: 19488/1521

### Leaflet revision date: 21 July 2012

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S1521 LEAFLET 20120721

## PACKAGE LEAFLET: INFORMATION FOR THE USER

# OVESTIN® CREAM (estriol)

Your medicine is called Ovestin Cream but will be referred to as Ovestin throughout the following patient information leaflet.

### 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.

### In this leaflet:

1. What Ovestin is and what it is used for
2. 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

Ovestin contains a medicine called estriol. It belongs to a group of medicines called Hormone Replacement Therapy (HRT).

### What is Ovestin used for

Ovestin is used:

- For vaginal problems caused by having too little 'oestrogen'
- Before or after vaginal surgery to help wound healing.

### How Ovestin works

Estriol (the medicine in Ovestin) is one of the natural oestrogens.

- Oestrogens are female sex hormones.
- They are produced in the ovaries.
- They cause sexual development in women and control the menstrual cycle during the child-bearing years.

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.

## 2. Before you use Ovestin

As well as benefits, HRT has some risks that you need to consider when you're deciding whether to start taking it, or whether to carry on taking it. This is especially important if you are more than 60 years old.

### Before you start taking HRT

Your doctor should ask about you and your family's medical history. Your doctor may decide to examine your breasts or your stomach and may do an internal examination. They will only do this if it is necessary for you or you have any special concerns. Your doctor will tell you how often these tests should be performed

→ **Tell your doctor** if you have any medical problems or illnesses.

### Regular check-ups

Once you have started on HRT, see your doctor for regular check-ups (at least once a year). At these check-ups, 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.

### 2.1 Do not use Ovestin if:

- you are allergic (hypersensitive) to any of the ingredients of Ovestin (listed in Section 6)
- you have had a disease caused by blood clots in the arteries such as angina, stroke or a heart attack (myocardial infarction)
- you have had a blood clot (thrombosis)
- 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 vaginal bleeding that has not been explained by your doctor
- you have excessive thickening of the womb lining
- have a blood clotting disorder (thrombophilic disorder, such as protein C, protein S, or antithrombin deficiency)
- you 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.

### 2.2 Take special care with Ovestin

Check with your doctor or pharmacist before using your medicine if you have had:

- 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 2.4)
- relatives who have had blood clots
- asthma
- diabetes
- migraine or severe headaches
- epilepsy (fits)
- gallstones
- liver or kidney problems
- a rare problem called 'systemic lupus erythematosus' (SLE)
- otosclerosis (a hearing disorder).

→ **If you have any of these**, talk to your doctor or pharmacist before using Ovestin.

Ovestin contains cetyl alcohol and stearyl alcohol. This may cause local skin reactions (e.g. contact dermatitis).

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### 2.3 Ovestin and the risk of developing cancer

#### Breast cancer

- **Women who have ever had breast cancer should not take HRT.**

Taking HRT slightly increases the risk of breast cancer. The risk is also slightly increased if you have a later menopause. The risk after the menopause for a woman taking oestrogen-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 oestrogen plus progestogen HRT is higher than for oestrogen-only HRT. However, oestrogen plus progestogen HRT is beneficial for the endometrium.

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

Your risk of breast cancer is also higher if:

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

#### How likely is breast cancer?

Looking at **women aged 50 to 65**, on average, over a 5-year period:

- In women **not taking HRT: 9 to 12 in 1,000** will get breast cancer.
- In women **taking oestrogen-progestagen HRT: 15 to 18 in 1,000** will get breast cancer. This means **an extra 6 cases**, on average.

Looking at **women aged 50 to 79**, on average, over a 5-year period:

- In women **not taking HRT: 14 in 1,000** will get breast cancer.
- In women **taking oestrogen-progestagen HRT: 18 in 1,000** will get breast cancer. This means **an extra 4 cases**.

If you notice any changes in your breast, such as: dimpling of your skin, changes in your nipple or any lumps you can see or feel:

→ **Make an appointment to see your doctor** straight away.

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

**Taking oestrogen-only HRT tablets for a long time can increase the risk of developing cancer of the lining of the womb.** It is possible there may be a similar risk with oestrogen cream used directly in the vagina for repeated treatments or over a long time.

You do not need to take a separate progestogen with Ovestin.

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. Ovarian cancer is much rarer than breast cancer. 'Long-term (at least 5 to 10 years) use of oestrogen-only HRT products is thought to carry a slightly increased risk of ovarian cancer. Some studies suggest the long-term use of combined HRT may carry a similar, or slightly smaller risk. It is not yet known whether Ovestin increases the risk in the same way.

For women who have been taking HRT for over 5 years there will be one extra case per 2500 users.

### 2.4 Ovestin and the heart or circulation

#### Coronary artery disease (CAD)

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

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

Women taking oestrogen-progestagen HRT are slightly more likely to get heart disease during the first year of taking that type of HRT than those not taking any HRT. For other types of HRT (like Ovestin), the risk is likely to be similar. However this is not yet certain. As the risk of heart disease strongly depends on age, the number of extra cases of heart disease due to use of estrogen-progestagen HRT is very low in healthy women close to menopause, but will rise with more advanced age.

If you get a pain in your chest that spreads to your 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

Combined oestrogen-progestagen and oestrogen-only HRT increase the risk of stroke up to 1.5-fold. The comparable risk for users, versus non-users, does not change with age or time since menopause.

However, because the risk of stroke is strongly age-related, the overall general risk of stroke in women, who use HRT, will increase with age.

Other things that can increase the risk of stroke include:

- getting **older**
- **high blood pressure**
- **smoking**
- drinking too much **alcohol**
- an uneven **heartbeat**

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

#### How likely is a stroke?

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

- In women **not taking HRT: 8 in 1,000** would be expected to have a stroke.
- In women **taking HRT: 11 in 1,000** would be expected to have a stroke.

If you get 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 increases the risk of blood clots in the veins (also called deep vein thrombosis, or DVT) 1.3 to 3-fold. This is especially during the first year of taking it.

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

You are more likely to get a blood clot if:

- you are **older**
  - if you get **pregnant** or have **recently had a baby**
  - you have ever had a **miscarriage**
  - if you use **oestrogens**
  - you are **very overweight**
  - you have had a **blood clot before** in the leg, lung or other organ
  - any of your **close family** have had **blood clots**
  - you have any **blood clotting problem** that needs treatment with a medicine such as warfarin
  - you are off your feet for a long time because of **major surgery, injury or illness**
  - you have a rare problem called **SLE**.
  - you have **cancer**
- If any of these things apply to you, talk to your doctor to see if you should take HRT.

### How likely is a blood clot?

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

- In women **not taking HRT: 4 in 1,000** would be expected to get a blood clot in a vein.
- In women who have been **taking HRT for over 5 years, 9 in 1,000** would be expected to get a blood clot.

If you get painful swelling in your 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.

### 2.5 Taking other medicines

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription, including herbal medicines. 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.

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.

### 2.6 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.

### 2.7 Pregnancy and breast-feeding

- 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.

### 3.1 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.

- 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.

### 3.2 How to apply the cream

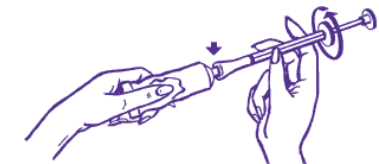
Ovestin comes in a pack together with a clear plastic applicator.

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

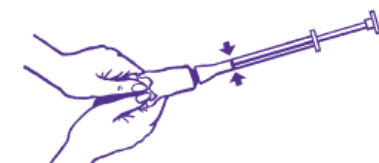
The applicator has a ring marked on the body. Fill the applicator up to the ring mark with Ovestin cream to get the correct dose.

→ **Follow these instructions:**

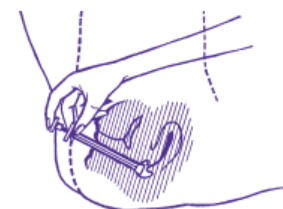
- 1 Remove the cap from the tube and turn the cap upside down. Then use the sharp point to open the tube.
- 2 Screw the end of the applicator onto the tube



- 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.

### 3.3 If you use more Estriol 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.

### 3.4 If you forget to use Estriol

- 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.

### 3.5 If you stop using Estriol

Keep using this medicine as prescribed by your doctor. Keep using Estriol, 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, Estriol can cause side effects, although not everybody gets them.

→ **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 (see Section 2.4 above)
- you have signs of a blood clot (see Section 2.4 above)
- you have any of the problems listed in Section 2.1 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 Estriol. 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.
- 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. The risk of memory loss may be somewhat higher in women who start using HRT after the age of 65.

→ 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**.

## 5. How to store Estriol

- **KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.**
- Do not store above 30°C.
- Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of the month.
- If the medicine shows any other signs of deterioration, you should seek the advice of your pharmacist who will tell you what to do.
- 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 Estriol contains

- Each gram of cream contains 1mg of estriol.
- The other ingredients are: eutanol G, lactic acid, sodium hydroxide, purified water, sorbitan monostearate, cetyl palmitate, glycerol, stearyl alcohol, cetyl alcohol, polysorbate 60 and chlorhexidine hydrochloride.

### What Estriol looks like and contents of the pack

- Estriol Cream is a white cream.
- There are 15 gm of cream in each tube.
- The pack contains a clear plastic applicator

### Product Licence holder

Procured from within the EU and repackaged by the Product Licence holder: S&M Medical Ltd, Chemilines House, Alperton Lane, Wembley, HA0 1DX.

### Manufacturer

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**Leaflet revision date: 21 July 2012**

S1521 LEAFLET Estriol 20120721

## PACKAGE LEAFLET: INFORMATION FOR THE USER

### ESTRIOL 0.1% VAGINAL CREAM (estriol)

Your medicine is called Estriol 0.1% Vaginal Cream but will be referred to as Estriol throughout the following patient information leaflet.

**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.

#### In this leaflet:

1. What Estriol is and what it is used for
2. Before you use Estriol
3. How to use Estriol
4. Possible side effects
5. How to store Estriol
6. Further information

## 1. What Estriol IS and what it is used for

Estriol contains a medicine called estriol. It belongs to a group of medicines called Hormone Replacement Therapy (HRT).

#### What is Estriol used for

Estriol is used:

- for vaginal problems caused by having too little 'oestrogen'
- before or after vaginal surgery to help wound healing.

#### How Estriol works

Estriol (the medicine in Estriol) is one of the natural oestrogens.

- Oestrogens are female sex hormones.
- They are produced in the ovaries.
- They cause sexual development in women and control the menstrual cycle during the child-bearing years.

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 Estriol which contain oestrogen. It may take several days or weeks before you notice an improvement.

## 2. Before you use Estriol

As well as benefits, HRT has some risks that you need to consider when you're deciding whether to start taking it, or whether to carry on taking it. This is especially important if you are more than 60 years old.

#### Before you start taking HRT

Your doctor should ask about you and your family's medical history. Your doctor may decide to examine your breasts or your stomach and may do an internal examination. They will only do this if it is necessary for you or you have any special concerns. Your doctor will tell you how often these tests should be performed

→ **Tell your doctor** if you have any medical problems or illnesses.

#### Regular check-ups

Once you have started on HRT, see your doctor for regular check-ups (at least once a year). At these check-ups, 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.

#### 2.1 Do not use Estriol if:

- you are allergic (hypersensitive) to any of the ingredients of Estriol (listed in Section 6)
  - you have had a disease caused by blood clots in the arteries such as angina, stroke or a heart attack (myocardial infarction)
  - you have had a blood clot (thrombosis)
  - 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 vaginal bleeding that has not been explained by your doctor
  - you have excessive thickening of the womb lining
  - have a blood clotting disorder (thrombophilic disorder, such as protein C, protein S, or antithrombin deficiency)
  - you 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 Estriol.

#### 2.2 Take special care with Estriol

Check with your doctor or pharmacist before using your medicine if you have had:

- 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 2.4)
- relatives who have had blood clots
- asthma
- diabetes
- migraine or severe headaches
- epilepsy (fits)
- gallstones
- liver or kidney problems
- a rare problem called 'systemic lupus erythematosus' (SLE)
- otosclerosis (a hearing disorder).

→ **If you have any of these**, talk to your doctor or pharmacist before using Estriol.

Estriol contains cetyl alcohol and stearyl alcohol. This may cause local skin reactions (e.g. contact dermatitis).

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### 2.3 Estriol and the risk of developing cancer

#### Breast cancer

- **Women who have ever had breast cancer should not take HRT.**

Taking HRT slightly increases the risk of breast cancer. The risk is also slightly increased if you have a later menopause. The risk after the menopause for a woman taking oestrogen-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 oestrogen plus progestogen HRT is higher than for oestrogen-only HRT. However, oestrogen plus progestogen HRT is beneficial for the endometrium.

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

Your risk of breast cancer is also higher if:

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

#### How likely is breast cancer?

Looking at **women aged 50 to 65**, on average, over a 5-year period:

- In women **not taking HRT: 9 to 12 in 1,000** will get breast cancer.
- In women **taking oestrogen-progestagen HRT: 15 to 18 in 1,000** will get breast cancer. This means **an extra 6 cases**, on average.

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5-year period:

- In women **not taking HRT: 14 in 1,000** will get breast cancer.
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**If you notice** any changes in your breast, such as: dimpling of your skin, changes in your nipple or any lumps you can see or feel:

→ **Make an appointment to see your doctor** straight away.

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

**Taking oestrogen-only HRT tablets for a long time can increase the risk of developing cancer of the lining of the womb.** It is possible there may be a similar risk with oestrogen cream used directly in the vagina for repeated treatments or over a long time.

You do not need to take a separate progestogen with Estriol.

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. Ovarian cancer is much rarer than breast cancer. ' Long-term (at least 5 to 10 years) use of oestrogen-only HRT products is thought to carry a slightly increased risk of ovarian cancer. Some studies suggest the long-term use of combined HRT may carry a similar, or slightly smaller risk. It is not yet known whether Estriol increases the risk in the same way.

For women who have been taking HRT for over 5 years there will be one extra case per 2500 users.

### 2.4 Estriol and the heart or circulation

#### Coronary artery disease (CAD)

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

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

Women taking oestrogen-progestagen HRT are slightly more likely to get heart disease during the first year of taking that type of HRT than those not taking any HRT. For other types of HRT (like Estriol), the risk is likely to be similar. However this is not yet certain. As the risk of heart disease strongly depends on age, the number of extra cases of heart disease due to use of estrogen-progestagen HRT is very low in healthy women close to menopause, but will rise with more advanced age.

**If you get a pain in your chest that spreads to your 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

Combined oestrogen-progestagen and oestrogen-only HRT increase the risk of stroke up to 1.5-fold. The comparable risk for users, versus non-users, does not change with age or time since menopause.

However, because the risk of stroke is strongly agerelated, the overall general risk of stroke in women, who use HRT, will increase with age.

Other things that can increase the risk of stroke include:

- getting **older**
- **high blood pressure**
- **smoking**
- drinking too much **alcohol**
- an uneven **heartbeat**

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

#### How likely is a stroke?

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

- In women **not taking HRT: 8 in 1,000** would be expected to have a stroke.
- In women **taking HRT: 11 in 1,000** would be expected to have a stroke.

**If you get** 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 increases the risk of blood clots in the veins (also called deep vein thrombosis, or DVT) 1.3 to 3-fold. This is especially during the first year of taking it.

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

You are more likely to get a blood clot if:

- you are **older**
  - if you get **pregnant** or have **recently had a baby**
  - you have ever had a **miscarriage**
  - if you use **oestrogens**
  - you are **very overweight**
  - you have had a **blood clot before** in the leg, lung or other organ
  - any of your **close family** have had **blood clots**
  - you have any **blood clotting problem** that needs treatment with a medicine such as warfarin
  - you are off your feet for a long time because of **major surgery, injury or illness**
  - you have a rare problem called **SLE**.
  - you have **cancer**
- If any of these things apply to you, talk to your doctor to see if you should take HRT.

### How likely is a blood clot?

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

- In women **not taking HRT: 4 in 1,000** would be expected to get a blood clot in a vein.
- In women who have been **taking HRT for over 5 years, 9 in 1,000** would be expected to get a blood clot.

**If you get** painful swelling in your 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.

### 2.5 Taking other medicines

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription, including herbal medicines. This is because Estriol can affect the way some other medicines work. Also some other medicines can affect the way Estriol 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.

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

If you have a vaginal infection, your doctor may also prescribe a medicine to treat the infection.

### 2.6 Operations

→ **Tell your doctor** you are using Estriol 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.

### 2.7 Pregnancy and breast-feeding

- Do not use Estriol 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

Estriol has no or little effect on the ability to drive or use machines

## 3. How to use Estriol

Always use Estriol 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 Estriol straight away.
- If you have never used HRT before or if you are changing over from a period-free HRT, you can also use Estriol straight away.
- If you are changing over from another type of HRT where you have a period, start taking Estriol one week after you finish the other HRT.

### 3.1 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.
- 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.

### 3.2 How to apply the cream

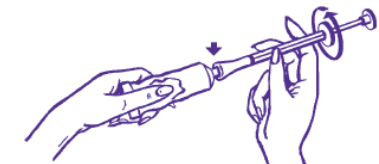
Estriol comes in a pack together with a clear plastic applicator.

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

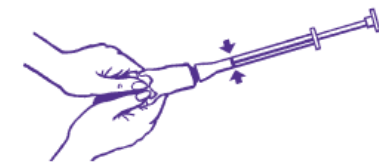
The applicator has a ring marked on the body. Fill the applicator up to the ring mark with Estriol cream to get the correct dose.

→ **Follow these instructions:**

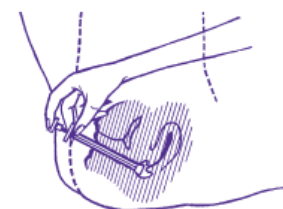
- 1 Remove the cap from the tube and turn the cap upside down. Then use the sharp point to open the tube.
- 2 Screw the end of the applicator onto the tube



- 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.

Estriol is easy to remove with water.