B651/04
Package leaflet: Information for the patient

Oestrogel 0.75 mg/dose, transdermal gel
estradiol

Read the entire leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Do you have any questions? Contact your doctor or pharmacist.
- Do not pass this medicine on to others, as it has been prescribed for you only. It may harm them, even if their symptoms are the same as yours.
- Do you experience any side effects listed in section 4? Or do you experience a side effect not listed in this leaflet? Then contact your doctor or pharmacist.

Oestrogel 0.75 mg/dose, transdermal gel is abbreviated in this text to Oestrogel or 'this medicine'.

Contents of this leaflet:
1. What is Oestrogel and what is it used for?
2. When should you not use this medicine or be extra careful?
3. How to use this medicine?
4. Possible side effects
5. How to store this medicine?
6. Contents of the package and other information

1. What is Oestrogel and what is this medicine used for?

Oestrogel is a hormone replacement therapy (HRT). This medicine contains the female hormone estradiol. When you apply the gel to your skin, this hormone is absorbed through the skin and enters your bloodstream.

This medicine is used in women after menopause. These women have not had a menstrual period for at least 6 months.

This medicine is used for:

Reduction of your symptoms that occur after menopause
During menopause, your body produces less estrogen. This can cause symptoms such as a warm face, warm neck, and chest ("hot flashes"). This medicine reduces these symptoms after menopause. You will only be prescribed this medicine if you are significantly troubled by your symptoms in daily life.

Prevention of bone loss (prevention)
After menopause, some women may develop fragile bones (osteoporosis). You should discuss all available options with your doctor.
If you are at increased risk of fractures due to osteoporosis and other medications are not suitable for you, you can use this medicine to prevent osteoporosis after menopause.

2. When should you not use this medicine or be extra careful with it?

Medical history (diseases and conditions you have ever had) and regular check-ups The use of hormone replacement therapy (HRT) carries risks. These risks should be considered when deciding to start or continue using this medicine.
The experience with treating women with premature menopause (you enter menopause earlier because your ovaries do not function properly) or due to surgery. If you have premature menopause, the risks of using HRT may be different. Talk to your doctor.

Before you start (or restart) HRT, your doctor will ask about the diseases and conditions you and your family have had in the past. Your doctor may decide to perform a physical examination. If necessary, this may include a breast examination and/or an internal examination.

Once you have started this medicine, you should regularly visit your doctor for check-ups (at least once a year). Discuss with your doctor during these check-ups the pros and cons of continuing treatment with this medicine.
Have your breasts examined regularly on the advice of your doctor or nurse.

When should you not use this medicine?
When you have one of the following conditions. If you are unsure about any of the conditions listed below, talk to your doctor before using this medicine.

- If you have or have had breast cancer or if you think you have breast cancer
- If you have a cancer that is sensitive to estrogens, such as cancer of the uterine lining (endometrium), or if you think you have it
- If you are losing blood from your vagina without a known cause
- If you have a severe thickening of the uterine lining (endometrial hyperplasia) and if you are not being treated for it;
- If you have or have ever had a blood clot in a vein (thrombosis), such as in the legs (deep vein thrombosis) or in the lungs (pulmonary embolism)
- If you have a blood clotting disorder (your blood does not clot properly) (such as protein C, protein S, or antithrombin deficiency)
- If you have or have recently had a disease caused by blood clots in the arteries, such as a heart attack, stroke, or a painful and pressing feeling in the chest (angina pectoris)
- If you have or have ever had liver disease and the results of tests that measure how well your liver is working are still not normal
- If you have a rare blood problem called porphyria that is passed down in families (inherited)
- If you are allergic (hypersensitive) to any of the ingredients in this medicine. You can find these ingredients in section 6.

If you develop any of the conditions above for the first time while using this medicine, stop using it immediately and contact your doctor right away.

When should you be extra careful with this medicine?
Contact your doctor if you have or have ever had any of the following problems before starting treatment. These conditions may return or worsen during treatment with this medicine.

If any of the following conditions apply to you, you should see your doctor more often for check-ups:

fibroids in your uterus
growth of the uterine lining outside your uterus (endometriosis) or you have previously had extensive growth of the uterine lining (endometrial hyperplasia)
increased risk of developing blood clots (see the section "Blood clots in a vein (thrombosis)")
increased risk of developing an estrogen-sensitive cancer (for example, if you have 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 headache
a disease where your immune system does not function properly. Your body makes itself sick (systemic lupus erythematosus, SLE)
epilepsy
asthma
an ear condition where bone grows in your middle ear, you may become deaf (otosclerosis)
you have too much fat (triglycerides) in your blood;
you retain fluid (fluid retention) because you have heart or kidney problems.
Hereditary and acquired angioedema

Stop using this medicine and see a doctor immediately

If you develop any of the following conditions while using HRT:

any of the conditions listed in the section 'When should you not use this medicine?'
your skin or the whites of your eyes turn yellow (jaundice). These may be signs of a liver disease.
Swelling of the face, tongue and/or throat and/or difficulty swallowing or a skin rash with pink bumps and severe itching (hives or welts), along with difficulty breathing; these symptoms indicate angioedema;
a severe increase in your blood pressure (symptoms may include headache, fatigue, dizziness)
migraine-like headache occurring for the first time

if you become pregnant

- if you show signs of a blood clot, such as:
- painful swelling and redness of the legs
- sudden chest pain
- you have difficulty breathing

See the section 'Blood clots in a vein (thrombosis)' for more information.

Note: this medicine is not a contraceptive. If it has been less than 12 months since your last period or if you are under 50 years old, you may still need contraception. Consult your doctor for advice.

HRT and cancer

Thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)
If you receive estrogen-only HRT, the risk of thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer) will increase.

A cycle lasts 28 days, if you take progestogen for at least 12 days of that cycle in addition to estrogen, you protect yourself against this extra risk. If you still have your womb, your doctor will therefore prescribe a progestogen separately. If your womb has been removed (a hysterectomy), discuss with your doctor whether you can safely take this medicine without a progestogen.
In women who still have a womb and do not receive HRT, on average 5 out of 1,000 women aged 50 to 65 will develop endometrial cancer.
For women aged 50 to 65 who still have a womb and receive estrogen-only HRT, between 10 and 60 out of 1,000 women will develop endometrial cancer (that is, between 5 and 55 extra cases), depending on the dose and how long the medicine is taken.

This medicine contains a higher dose of estrogen than other estrogen-only HRT medicines. The risk of developing endometrial cancer from using this medicine with a progestogen is unknown.

Irregular bleeding
You may experience irregular bleeding or spotting during the first 3-6 months of using this medicine. But if the irregular bleeding;
- lasts longer than 6 months;
- starts after you have used this medicine for more than 6 months;
- does not stop after you have stopped using this medicine;

contact your doctor as soon as possible.

Unexpected bleeding
You will have a bleeding once a month (so-called withdrawal bleeding) while using this medicine in combination with a progestogen (e.g., progesterone). But if you have unexpected spotting outside your monthly bleeding, which:
lasts longer than the first 6 months;
starts after you have taken this medicine for more than 6 months;
does not stop after you have stopped taking this medicine;

then contact your doctor as soon as possible.

Breast cancer

Evidence shows that taking a combination of estrogen-progestogen or estrogen-only HRT increases the risk of breast cancer. The extra risk depends on how long you take HRT. The extra risk becomes apparent within 3 years of use.
After stopping HRT, the additional risk will decrease over time, but the risk will persist for 10 years or longer if you have used HRT for 5 years.

Comparison

In women aged between 50 and 54 who do not take HRT, an average of 13 to 17 out of 1000 are diagnosed with breast cancer over a 5-year period.diagnosis of breast cancer established.
In women aged 50 who start taking combined estrogen-progestogen HRT for 5 years, there are 21 cases per 1000 users (i.e., 4 to 8 extra cases).

In women aged between 50 and 59 who do not take HRT, an average of 27 out of 1000 are diagnosed with breast cancer over a 10-year period.

In women aged 50 who start taking estrogen-only HRT for 10 years, there will be 34 cases per 1000 users (an extra 7 cases).

In women aged 50 who start taking combined estrogen-progestogen HRT for 10 years, there are 48 cases per 1000 users (i.e., 21 extra cases).

Check your breasts regularly. See your doctor if you notice changes such as:

dimpling of the skin;
changes in the nipple;
changes in the nipple;
lumps that you can see or feel.

If mammography screening programs (your breasts are examined) are offered, it is advised that you participate. For mammogram screening, it is important to inform the nurse/healthcare professional taking the X-rays (mammogram) that you are using HRT. This medication can increase the density of your breasts (higher density means a breast contains relatively more milk glands and less fatty tissue), which can affect the mammogram result. When breast density is increased, mammography may not detect all lumps.

Ovarian cancer
Ovarian cancer is rare and much less common than breast cancer. The use of estrogen-only HRT or combined estrogen-progestogen 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 do not use HRT, about 2 out of 2,000 women will develop ovarian cancer over a 5-year period. For women who have taken HRT for 5 years, about 3 out of 2,000 women will develop ovarian cancer (that is, about 1 extra case).
Effect of HRT on heart and 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 use.

Blood clots can be serious, and if one travels to the lungs, you may experience: chest pain, breathlessness, or fainting. It can even be fatal.

You are more likely to get a blood clot in your veins as you get older and if any of the following apply to you. Contact your doctor if any of the following apply to you:

- you cannot walk for long periods because you have had surgery, are injured, or are ill (see also section 3: if you need to have surgery)
- you are severely overweight (BMI over 30 kg/m^2)
- you have a blood clotting disorder that requires long-term treatment with medication to prevent clots.
- if you or any of your family members have ever had a blood clot in the leg, lung, or another organ
- you have a disease where your immune system does not work properly. Your body attacks itself (systemic lupus erythematosus)
- you have cancer

For signs of a blood clot, see the section "Stop using this medicine and see a doctor immediately."

When looking at women in their fifties who do not take HRT, an average of 4 to 7 out of 1,000 women would be expected to develop a blood clot in a vein over a 5-year period.
For women in their 50s who have taken combination estrogen-progestogen HRT for more than 5 years, 9 to 12 out of 1,000 women (that is, 5 extra cases) will develop a blood clot in a vein.
For women in their 50s who have had their uterus removed and have taken estrogen-only HRT for more than 5 years, there will be 5 to 8 out of 1,000 women (that is, 1 extra case).

Heart disease (myocardial infarction/heart attack)
There is no evidence that HRT will prevent a heart attack.
In women over 60 who use combination estrogen-progestogen HRT, the chance of developing heart disease is slightly higher than in women who do not use HRT.
For women who have had their uterus removed and use estrogen-only HRT, there is no increased risk of developing heart disease.

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

In women in their 50s who do not take HRT, it is expected that on average 8 out of 1,000 women will have a stroke over a 5-year period.
For women in their 50s who take HRT, there will be 11 out of 1,000 women who have a stroke over a 5-year period (that is, 3 extra cases).

Children
This medicine can accidentally be transferred from the skin to other people. Do not let others, especially children, come into contact with the area of your skin where this medicine is applied and cover the area, if necessary with clothing, after the gel has dried. If a child comes into contact with the skin where this medicine is applied, wash the child's skin as soon as possible with water and soap. The transfer of estradiol can cause young children to show signs of puberty that are not expected (e.g., breast development). In most cases, the symptoms will disappear when children are no longer exposed to this medicine.

Contact your doctor if you see signs and symptoms (breast development or other sexual changes) in a child who may have been accidentally exposed to this medicine.

Other conditions

If you use this medicine, you may experience fluid retention in the body. If your heart or kidneys do not work well, you should be regularly monitored during treatment with this medicine.

HRT does not prevent memory loss. There may be a higher risk of memory loss in women who start HRT after the age of 65. Contact your doctor for advice.

Are you using any other medicines?

Some medicines can interfere with the effect of Oestrogel. This may cause irregular vaginal bleeding. This applies to the following medicines:

Other medicines for use on the skin (such as cancer medications)

Medications for epilepsy (medications such as phenobarbital, phenytoin, and carbamazepine)

Medications for tuberculosis, a disease caused by a bacterium (medications such as rifampicin,
rifabutin)

Medications for HIV infection, the virus that can cause AIDS (medications such as nevirapine, efavirenz, ritonavir, nelfinavir).

Herbal medicines containing St. John's wort (Hypericum perforatum).

HRT may affect the action of other medicines:

A medicine used for epilepsy (lamotrigine); this may increase the frequency of epileptic seizures

Medicines used for an infection with the hepatitis C virus (HCV) (such as the combination ombitasvir/paritaprevir/ritonavir with or without dasabuvir, as well as treatment with the combination glecaprevir/pibrentasvir) can lead to increased liver function blood test results (increase of the liver enzyme ALT) in women using oral contraceptives containing ethinylestradiol. This medicine contains estradiol instead of ethinylestradiol. It is not known whether an increase in the ALT liver enzyme occurs when using this medicine in combination with this HRT treatment.

Are you using or have you recently used any other medicines besides Oestrogel? If so, tell your doctor or pharmacist. This also applies to medicines for which you do not need a prescription and to herbal medicines, other natural products, or medical skincare products containing alcohol or cleansing agents. Your doctor will inform you about this.

Laboratory tests

If you are having a blood test, tell your doctor or the laboratory staff that you are using this medicine. This medicine can affect the results of certain tests.

Pregnancy, breastfeeding, and fertility

This medicine should only be used by women who have gone through menopause (postmenopausal women).

If you become pregnant, stop using this medicine and contact your doctor.

Oestrogel contains ethanol

This medicine contains 500 mg of alcohol (ethanol) in each dose of 1.25 grams, equivalent to 400 mg/g,

(40% w/w). This product may cause a burning sensation on your skin if your skin is damaged. This medicine is flammable until it has dried.

3. How to use this medicine?

Always use this medicine exactly as your doctor or pharmacist has told you. If you are unsure about the correct use, contact your doctor or pharmacist.

Your doctor will try to prescribe the lowest dose to treat your symptom for as short a time as possible. Contact your doctor if you think this dose is too strong or not strong enough.

This medicine is a gel that contains the female hormone estradiol. When you apply the gel to your skin, it will dry within 5 minutes. This hormone is then quickly absorbed through the skin and enters your bloodstream.

Spread the gel as thinly as possible over the entire skin on the inside and outside of your arm from your wrist to your shoulder and/or on the inside of your thighs. Rub it in as much as possible.

DO NOT apply this medicine on or near the breasts or mucous membranes or near the pubic area or vagina.

Before using a new bottle of the gel, you must first prime the pump. To do this, press the pump and discard the first dose of gel.

Each time you press the pump, it delivers a dose of 1.25 grams of this medicine (1 actuation). This corresponds to 0.75 mg estradiol.

Where should this medicine be applied:

Arms from wrist to shoulder Inside of your thighs

The usual dose is 1 actuation of the pump (1.25 grams of gel); to be applied to your arm from your wrist to your shoulder and/or the inside of your thighs.

Each bottle contains at least 60 doses of the gel (actuations).
Apply 1 actuation of the pump of this medicine every day, do this for 21 days (3 weeks) in a row and then stop using the gel for 7 days (1 week) (see below in the section “The application of this medicine should be performed”

The application of this medicine should be performed:
by the woman herself,
in the morning or evening, preferably after washing, at the same time every day.
The woman should not have skin contact with other adults or children for 1 hour after applying the gel.

Spread the gel as widely as possible, on the arm and shoulders and/or the inside of the thighs on a large area of undamaged skin.

If the gel is still sticky five minutes after application, you probably have not spread it widely enough over your skin. Spread the gel more widely over your arms and shoulders and/or the inside of your thighs next time.

Always wash your hands with water and soap after applying the gel.

Do not let others come into contact with the area where this medicine has been applied until the gel is completely dry and covered with clothing, if applicable.

Women who still have their uterus:
Your doctor will always prescribe the lowest effective dose that you need to use.

Apply 1 pump release of this medicine every day, do this for 21 days (3 weeks) in a row, and then stop using the gel for 7 days (1 week).
If estrogens are used for a long time without adding progestogen (such as progesterone) to the treatment, the risk of endometrial cancer increases in women with a uterus. To counteract this, estrogens should be used with a progestogen for at least 12 to 14 days per monthly cycle (21 days).

Your doctor will likely prescribe a treatment with progesterone.

You take the progestogen for at least 12 to 14 days per monthly cycle. During the 4th week, in the week you do not use estrogens, you also do not take any medicine containing progesterone. During that period without treatment, a withdrawal bleeding ("menstruation") may occur.

Women without a uterus:
Only if you have a condition where cells from the uterine lining are located in certain places outside the uterus (endometriosis), estrogen therapy should not be combined with progestogens when you no longer have a uterus.

If you are using this medicine for the treatment of symptoms caused by menopause and you notice that this medicine is too strong or too weak, contact your doctor.

Duration of the treatment
Your doctor will tell you how long you need to use this medicine. It is important that you adhere to this. Do not stop the treatment too early; discuss it with your doctor first.
Have you used too much of this medicine?
An unpleasant feeling in the breasts (painful tension), bleeding, and nervousness are possible signs of overdose, which usually disappear when less gel is applied. In that case, you should apply a smaller amount of gel after consulting the treating physician.

If you have used too much of this medicine, contact your doctor or pharmacist immediately.

Have you forgotten to use this medicine?
Do not take a double dose the next day to make up for a forgotten dose. If the next dose is to be applied within 12 hours, wait until it is time to apply the next dose of gel. If the next dose is to be administered more than 12 hours later, apply the missed dose immediately and apply the next dose at the normal time.

If you need to have surgery
If you need to have surgery, tell the surgeon that you are using this medicine. To reduce the risk of a blood clot, you may need to stop using this medicine about 4 to 6 weeks before the surgery (see section 2: Blood clots in a vein). Ask your doctor when you can start taking this medicine again.

Do you have any other questions about the use of this medicine? Then contact your doctor or pharmacist.

4. Possible side effects
Like any medicine, this medicine can cause side effects, although not everyone will experience them.

The following diseases are more commonly seen in women using HRT compared to women not using HRT:
- breast cancer;
- abnormal growth or cancer in the lining of the womb (endometrial hyperplasia or cancer);
- ovarian cancer;
- blood clots in the veins of the legs or lungs (venous thromboembolism);
- heart disease;
- stroke;
- possible memory loss when HRT is started after the age of 65.

See section 2 for more information about these side effects.

Common side effects (occur in less than 1 in 10 users): painful menstruation (dysmenorrhea), heavy bleeding during menstruation (menorrhagia), light bleeding (spotting), menstrual problems, vaginal discharge (leukorrhea), unexpected vaginal bleeding, abnormal thickening of the cells of the womb (endometrial hyperplasia), abdominal pain and cramps, abdominal swelling, nausea or vomiting, headache, muscle cramps, pain in the arms and legs, nervousness, depression.

Uncommon side effects (occur in less than 1 in 100 users): benign breast tumor, uterine polyp, the number of uterine fibroids (benign tumors) increases, a condition where cells from the lining of the womb are found outside the womb and cause pain (endometriosis), breast pain (mastodynia), worsening of
estrogen-dependent tumors, migraine, dizziness, drowsiness, joint pain (arthralgia), superficial or deep vein thrombosis, pain and swelling of the veins (thrombophlebitis), swelling of feet, hands, ankles (peripheral edema), itching (pruritus), salt retention in the body, bloated feeling, change in body weight, skin rash, itching, brown spots on the skin (chloasma), abnormal liver test results, liver tumors, gallstones.

Rare side effects (occur in less than 1 in 1000 users): Sensitivity to contact lenses, severe allergic (life-threatening) reactions, liver test problems, yellowing of the skin or whites of the eyes indicating a liver problem, glucose intolerance (especially in diabetes), bone pain, worsening of epilepsy (seizures), change in sexual desire, skin discoloration, pimples (acne), increased blood pressure.

The following side effects may occur with HRT:

benign and malignant tumors that can be influenced by estrogen hormones, such as cancer of the lining of the womb (endometrial cancer)
heart attack (myocardial infarction) and stroke
gallbladder diseases
skin conditions such as: vascular purpura (small blood spots under the skin)
symptoms of dementia
women using HRT are more likely to develop a venous thrombosis or a pulmonary embolism than women who do not receive HRT. For more information, see "When should you not use this medicine?" and "HRT and venous thrombosis" in section 2.
Women using HRT have a slightly higher risk of breast cancer. The risk increases with the number of years they use HRT. Out of 1,000 women who do not use HRT, approximately 32 in the age group of 50-64 years are estimated to develop breast cancer. Out of 1,000 women who use HRT for 5 years or have recently used it, about 2 to 6 additional women will develop breast cancer. If HRT is used for 10 years, this number can increase to 5 to 19 additional women per 1,000 women. The number of additional cases of breast cancer does not depend on the age at which you started HRT (provided you started HRT between the ages of 45 and 65). For more information, see "When should you not use this medicine?" and "HRT and breast cancer" in section 2.
In women who still have their uterus and use HRT with only estrogens, the risk of endometrial cancer increases with the duration of HRT. Of the 1,000 women who do not use HRT, it is estimated that about 5 in the age group of 50-65 years will develop endometrial cancer. Depending on the duration and dose, approximately 10-60 additional cases of endometrial cancer are expected per 1,000 women using only estrogen. If a progestogen is also used, this risk is largely eliminated.

The following side effects have been reported with other HRTs:
gallbladder disease
various skin conditions:
- skin discoloration, especially of the face or neck, known as "pregnancy patches" (chloasma);
- painful reddish skin nodules (erythema nodosum);
- skin rash with red spots or target-shaped red discoloration spots (erythema multiforme).

Reporting side effects
If you experience side effects, contact your doctor or pharmacist. This also applies to possible side effects not listed in this leaflet. You can also report side effects directly via the Netherlands Pharmacovigilance Centre Lareb, website: www.lareb.nl.

By reporting side effects, you can help us obtain more information about the safety of this medicine.

5. How to store this medicine?

Keep out of the sight and reach of children.

There are no special storage conditions for this medicine.

Do not use this medicine after the expiry date. This can be found on the label after Exp. It includes a month and a year. The last day of that month is the expiry date.

Do not flush medicines down the sink or toilet and do not throw them in the trash. Ask your pharmacist what to do with medicines you no longer use. They will then be destroyed responsibly and will not enter the environment.

6. Contents of the package and other information

What substances are in this medicine?
- The active substance in this medicine is estradiol.
- The other substances in this medicine are: carbomer, trolamine, ethanol, and purified water. See also section 2 "Oestrogel contains ethanol".

What does Oestrogel look like and how much is in a package?
This medicine is available in a package of 1 or 3 multidose bottles. Each 80 gram package consists of a bottle with a calibrated dosing pump. One pump activation dispenses exactly 1.25 grams of gel containing 0.75 mg estradiol. Each 80 gram gel package provides at least 60 doses of 1.25 grams.

Marketing authorization holder and manufacturer

Registration holder/repacker
BModesto B.V.
Minervaweg 2
8239 DL Lelystad

Manufacturer
Besins Manufacturing Belgium
Groot-Bijgaardenstraat 128
B-1620 Drogenbos Belgium

Or

Laboratoires Besins International
13 Rue Perrier,
92120 Montrouge
France

Registered under:
RVG 129564//123203 - Oestrogel 0.75 mg/dose, transdermal gel. Country of origin: Belgium.

The product from this leaflet is marketed in the country of origin under the name Oestrogel 0.75 mg/dose Transdermal Gel.

This leaflet was last approved in January 2025.