

Package Leaflet: Information for the User
OESTROGEL® PUMP-PACK 750 MICROGRAMS/ACTUATION GEL
ESTRADIOL

Read all of this 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.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Oestrogel is and what it is used for
2. What you need to know before you use Oestrogel
3. How to use Oestrogel
4. Possible side effects
5. How to store Oestrogel
6. Contents of the pack and other information

What Oestrogel is and what it is used for

The full name of your medicine is Oestrogel Pump-Pack 750 micrograms/actuation gel. It is called Oestrogel in this leaflet.

Oestrogel is a Hormone Replacement Therapy (HRT). It contains the female hormone oestrogen. Oestrogel is used in postmenopausal women.

Oestrogel is used for:

Relief of symptoms occurring after menopause

During the menopause, the amount of the oestrogen produced by a woman's body drops. This can cause symptoms such as hot face, neck and chest ("hot flushes"). Oestrogel alleviates these symptoms after menopause. You will only be prescribed Oestrogel if your symptoms seriously hinder your daily life.

Prevention of osteoporosis

After the menopause some women may develop fragile bones (osteoporosis). You should discuss all available options with your doctor. If you are at an increased risk of fractures due to osteoporosis and other medicines are not suitable for you, you can use Oestrogel to prevent osteoporosis after menopause.

How Oestrogel works

Oestrogel works by replacing the oestrogen in your body. This is so that you have a similar amount of oestrogen as before your menopause.

What you need to know before you use Oestrogel

Medical history and regular check-ups

The use of HRT carries risks which need to be considered when deciding whether to start using it, or whether to carry on using 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 you 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 Oestrogel 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 Oestrogel.

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

Do not use Oestrogel

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 Oestrogel.

Do not use Oestrogel:

- 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 oestrogens**, 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 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 have ever 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 estradiol or any other ingredients of this medicine (listed in section 6).

If any of the above conditions appear for the first time while using Oestrogel, stop using 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 Oestrogel. If so, you should see your doctor more often for check-ups:

- fibrosis 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 oestrogen-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),
- a very high level of fat in your blood (triglycerides),
- fluid retention due to heart or kidney problems.

Stop using Oestrogel and see a doctor immediately

If you notice any of the following when taking HRT:

- any of the conditions mentioned in the 'Do not use Oestrogel' 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: Oestrogel 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)

Using oestrogen-only HRT will increase the risk of excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the womb lining (endometrial cancer).

Using a progestogen in addition to the oestrogen for at least 12 days of each 28 day cycle protects you from this extra risk. So your doctor will prescribe a progestogen separately if you still have your womb. If you have had your womb removed (a hysterectomy), discuss with your doctor whether you can safely take this product without a progestogen.

In women who still have a womb and who are not using HRT, on average, 5 in 1000 will be diagnosed with endometrial cancer between the ages of 50 and 65.

For women aged 50 to 65 who still have a womb and who take oestrogen-only HRT, between 10 and 60 women in 1000 will be diagnosed with endometrial cancer (i.e. between 5 and 55 extra cases), depending on the dose and for how long it is taken.

Unexpected bleeding

You will have a bleed once a month (so-called withdrawal bleed) while taking Oestrogel. But, if you have unexpected bleeding or drops of blood (spotting) besides your monthly bleeding, which:

- carries on for more than the first 6 months
- starts after you have been using Oestrogel for more than 6 months
- carries on after you have stopped using Oestrogel

see your doctor as soon as possible.

Breast cancer

Evidence shows that using combined oestrogen-progestogen and or oestrogen-only hormone replacement therapy (HRT) increases the risk of breast cancer. The extra risk depends on how long you use HRT. The additional risk becomes clear within 3 years of use. After stopping HRT the extra risk will decrease with time, but the risk may persist for 10 years or more if you have used for more than 5 years.

Compare

Women aged 50 to 54 who are not taking HRT, on average, 13 to 17 in 1000 will be diagnosed with breast cancer over a 5-year period.

For women aged 50 who start taking oestrogen-only HRT for 5 years, there will be 16-17 cases in 1000 users (i.e. an extra 0 to 3 cases).

For women aged 50 who start taking oestrogen-progestogen HRT over 5 years, there will be 21 cases in 1000 users (i.e. an extra 4 to 8 cases).

Women aged 50 to 59 who are not taking HRT, on average, 27 in 1000 will be diagnosed with breast cancer over a 10-year period.

For women aged 50 who start taking oestrogen-only HRT for 10 years, there will be 34 cases in 1000 users (i.e. an extra 7 cases)

For women aged 50 who start taking oestrogen-progestogen HRT for 10 years, there will be 48 cases in 1000 users (i.e. an extra 21 cases).

• **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. For mammogram screening, it is important that you inform the nurse/healthcare professional who is actually taking the x-ray that you use HRT, as this medication may increase the density of your breasts which may affect the outcome of the mammogram. Where the density of the breast is increased, mammography may not detect all lumps.

Ovarian cancer

Ovarian cancer is rare - much rarer than breast cancer. The use of oestrogen-only or combined oestrogen-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 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 using HRT for 5 years, there will be about 3 cases per 2000 users (i.e. 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 using 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 using Oestrogel and see a doctor immediately”.

Compare

Looking at women in their 50s who are not using 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 using oestrogen-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).

For women in their 50s who have had their womb removed and have been using oestrogen-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)

There is no evidence that HRT will prevent a heart attack.

Women over the age of 60 years who use oestrogen-progestogen HRT are slightly more likely to develop heart disease than those not using any HRT.

For women who have had their womb removed and are using oestrogen-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 using 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 using 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.

Other medicines and Oestrogel

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines including medicines obtained without a prescription, herbal medicines or natural products.

Some medicines may interfere with the effect of **Oestrogel**. This might lead to irregular bleeding.

This applies to the following medicines:

- Medicines for **epilepsy** (such as phenobarbital, phenytoin and carbamazepine).
- Medicines for **tuberculosis** (such as rifampicin, rifabutin).
- Medicines for **HIV infection** (such as nevirapine, efavirenz, ritonavir and nelfinavir).
- Herbal products containing **St John's wort** (*Hypericum perforatum*).
- Skin cleansers and detergents e.g. products containing benzalkonium chloride or sodium lauryl sulphate.
- Other skin products containing alcohol e.g. astringents or sunscreens.
- Products to treat skin and scalp disorders e.g. products to cure warts, acne or dandruff.
- Other skin medications which change how skin is made, e.g. anti-cancer products.

Laboratory tests

If you need a blood test, tell your doctor or the laboratory staff that you are using Oestrogel, because this medicine can affect the result of some tests.

Pregnancy and breast-feeding

Oestrogel is for use in postmenopausal women only. If you become pregnant, stop using Oestrogel and contact your doctor.

3. How to use Oestrogel

Always use Oestrogel exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Using this medicine

- If you have never used any other HRT medicines or you are switching to Oestrogel from a period-free HRT product, you can start using Oestrogel on any convenient day.
- If you are currently using another type of HRT where you have a period, finish your current medicine pack before you start using Oestrogel.
- Do not ask anyone else to apply the gel. Only you should apply your medicine.
- Do not use strong skin cleaners or detergents when washing the area where you will apply the gel.
- Avoid close skin contact with your partner for one hour after application.
- Do not wash the skin or apply other skin care products until at least one hour after application.
- If the prescribed dose does not provide relief, tell your doctor. Do not use more than the prescribed dose.

Your doctor will aim to prescribe the lowest dose to treat your symptoms for as short as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.

Preparing your new Pump Pack

Before using your **new Pump Pack for the first time**, you need to prepare it for use as follows:

- Remove the cap from the canister.
- Remove the stopper from the spout.
- Press the plunger down a few times until the gel comes out.
- Do not use this first dose of gel from your Pump Pack. This dose should be discarded.
- Your Pump Pack is now ready to use.

How much to use and when to use

- Apply the gel once a day, either in the morning or evening.
- Try to use the gel at about the same time each day.
- Your doctor will prescribe the lowest dose for the shortest time to treat your symptoms.
- One pump is equal to one measure
- The usual daily dose is 2 measures (i.e. 2 pumps) of gel. The Pump Pack will last four weeks.
- If 4 measures (i.e. 4 pumps) of gel have been prescribed, the Pump Pack will last two weeks.
- Spread the gel on a large area of skin on each shoulder, outer arm or each mid-inner thigh.

How to apply the gel

1. Make sure that your hands and the skin where you are going to apply the gel are clean, dry and unbroken.
2. Remove the canister cap to reveal the plunger.
3. Remove the stopper from the spout.
4. Hold the Oestrogel Pump Pack in one hand and place your other hand under the spout, ready to collect the gel.
5. Push the plunger down firmly. This will dispense one measure of the gel.
6. Apply the gel to either:
 - the outer arm and shoulder of both arms,
 or
 - the mid-inner thigh of both legs.
7. **Do not apply on or near the breasts, or near the genital area.**
8. Spread the gel over a large area of skin on each shoulder, outer arm or mid-inner thigh.
9. If your doctor has prescribed 2 measures of gel, spread 1 measure over each outer arm and shoulder, or each mid-inner thigh. If 4 measures of gel have been prescribed, spread 2 measures over each outer arm and shoulder or each mid-inner thigh. (See steps 4-8).
10. Cover the spout using the attached stopper.
11. Replace the cap.
12. Leave to dry for 5 minutes before covering with clothes.

13. Wash hands with soap and water after applying the gel.

If you believe Oestrogen has been transferred to another person (man or child):

Wash the area of skin onto which may have been affected immediately with soap and water.

How you know when your Pump Pack is empty

- The Pump Pack is nearly empty when the plunger does not return back to its original position after you have pushed it down.
- When this happens, do not use the Pump Pack any longer. Start using a new Pump Pack.

If you use more Oestrogen than you should

The effects of overdosing are generally: breast tenderness, nausea and vaginal bleeding. These symptoms disappear when treatment is stopped or the dose is reduced. In case of the accidental using of an excessive dose of the medicine tell your doctor immediately.

If you forget to use Oestrogen

- If it is more than 12 hours until your next dose, apply the gel as soon as you remember and apply the next dose at the normal time.
- If it is less than 12 hours until your next dose, skip the missed dose and apply the next dose at the normal time.
- Do not use a double dose (two doses at the same time) to make up for a forgotten dose.

If you forget a dose you may have breakthrough bleeding or spotting.

If you need to have surgery

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

4. Possible side effects

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

The following diseases are reported more often in women using HRT compared to women not using HRT:

- breast cancer,
- abnormal growth or cancer of 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,
- probable memory loss if HRT is started over the age of 65.

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

The following side effects have been reported since Oestrogen came on to the market:

Frequency not known (cannot be estimated from the available data):

- Nausea (sickness in the stomach)
- Dizziness
- Headache
- Hair loss (alopecia)
- Intense itching (pruritus)

During clinical trials, the following side effects have also been observed:

- **Frequency not known** (cannot be estimated from the available data)
- Breast pain
- Infection
- Pain
- Inflamed vagina causing discharge, itching and pain (vaginitis)

Side effects observed with HRT products used in menopause are reported below:

Common (may affect up to 1 in 10 people):

- Painful periods
- Menstrual periods which are heavier or last longer than usual
- Abnormal or irregular bleeding
- White or yellow vaginal discharge

Uncommon (may affect up to 1 in 100 people):

- Mood swings
- Migraine
- Vertigo
- Wind (flatulence)
- Increase in the volume of the uterus
- Vaginal yeast infection (candidiasis)
- Feeling of weakness

Rare (may affect up to 1 in 1000 people):

- Intolerance to glucose, which may affect your blood sugars
- If you have epilepsy, your symptoms may get worse
- High blood pressure
- A blood test may show changes in the way the liver is working
- Acne
- Unusual production of breast milk
- A type of allergic reaction called anaphylaxis (more likely if you have had allergic reactions in the past)

The following side effects have been reported with other HRTs:

- gall bladder disease
- various skin disorders:
 - discolouration 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)
- Rash
- Patchy brown or dark brown skin discoloration (melasma)
- Vomiting
- Abdominal pain
- Breast tenderness
- Breast enlargement
- Fluid retention (oedema)
- Weight changes
- Increase or decrease in sexual desire
- Depression

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist.

United Kingdom

This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Ireland

You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Oestrogel

- Keep this medicine out of the sight and the reach of children.
- Do not use this medicine after the expiry date which is stated on both the carton and the Oestrogel Pump Pack after “Exp”. The expiry date refers to the last day of that month.
- This medicinal product does not require any special storage conditions.
- Do not throw away via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Oestrogel Pump Pack contains

- The active ingredient is estradiol. This is a manmade form of the female hormone oestrogen.
- Each metered dose of 1.25g of gel (1 pump) of Oestrogel contains 750 micrograms of estradiol (as hemihydrate) 0.06% w/w.
- The other ingredients are: carbomer, trolamine, ethanol and purified water.

What Oestrogel Pump Pack looks like and contents of the pack

- Gel for transdermal use in 80 g bottle with metered-dose pump.
- Oestrogel is a non-greasy, non-staining, colourless, transdermal gel with an odour of alcohol.
- Oestrogel Pump Pack delivers 64 metered doses.

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