

Package leaflet: Information for the user

<Invented Name> film-coated tablets

estradiol valerate and dienogest

Read all of this leaflet carefully before you start taking 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. 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.

What is in this leaflet

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

1. What <Invented Name> is and what it is used for

<Invented Name> is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an oestrogen and a progestogen. <Invented Name> is used in postmenopausal women with at least 12 months since their last natural period-

<Invented Name> is used for:

Relief of symptoms occurring after menopause

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

2. What you need to know before you take <Invented Name>

Medical history and regular check-ups

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

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

your doctor.

Before you start (or restart) HRT, your doctor will ask about your own and your family's medical history. Your doctor may decide to perform a physical examination. This may include an examination of your breasts and/or an internal examination, if necessary.

- Once you have started on <Invented Name> 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 <Invented Name>.
- Go for regular breast screening, as recommended by your doctor.

Do not take <Invented Name>

if any of the following applies to you. If you are not sure about any of the points below, **talk to your doctor** before taking <Invented Name>.

Do not take <Invented Name>:

- 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 the lungs (pulmonary embolism);
 - If you have a **blood clotting disorder** (such as protein C, protein S, or antithrombin deficiency);
 - If you have or recently have had a disease caused by blood clots in the arteries, such as a **heart attack, stroke or angina**;
 - If you have or 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 **oestrogens, progestogens** or any of the other ingredients of <Invented Name> (listed in section 6 Further information).
- If any of the above conditions appear for the first time while taking <Invented Name>, stop taking it at once and consult your doctor immediately.

Warnings and precautions

Tell your doctor if you have ever had any of the following problems, before you start the treatment, as these may return or become worse during treatment with <Invented Name>. If so, you should see your doctor more often for check-ups:

- fibroids inside your womb;
- growth of womb lining outside your womb (endometriosis) or a history of excessive growth of the womb lining (endometrial hyperplasia);
- increased risk of developing blood clots (see “Blood clots in a vein (thrombosis)”);
- increased risk of getting a 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 tumour;
- 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 cardiac or kidney problems.

Stop taking <Invented Name> and see a doctor immediately

If you notice any of the following when taking HRT:

- any of the conditions mentioned in the ‘DO NOT take <Invented Name>’ 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: <Invented Name> is not a contraceptive. If it is less than 12 months since your last menstrual period or you are under 50 years old, you may still need to use additional contraception to prevent pregnancy. Speak to your doctor for advice.

HRT and cancer

Excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)

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

The progestogen in <Invented Name> protects you from this extra risk.

Irregular bleeding

You may have irregular bleeding or drops of blood (spotting) during the first 3-6 months of taking <Invented Name>. However, if the irregular bleeding:

- carries on for more than the first 6 months;
- starts after you have been taking <Invented Name> for more than 6 months;
- carries on after you have stopped taking <Invented Name>;

see your doctor as soon as possible.

Breast cancer

Evidence shows that taking 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 HRT for more than 5 years.

Compare

In 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-progestogen 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 for 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-progestagen HRT has been associated with a slightly increased risk of ovarian cancer.

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

Effect of HRT on 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 taking it.

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

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

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

For signs of a blood clot, see “Stop taking <Invented Name> and see a doctor immediately”.

Compare

Looking at women in their 50s who are not taking HRT, on average, over a 5-year period, 4 to 7 in 1000 would be expected to get a blood clot in a vein.

For women in their 50s who have been taking oestrogen-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).

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 taking any HRT.

Stroke

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

Compare

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

Other conditions

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

Other medicines and <Invented Name>

Some medicines may interfere with the effect of <Invented Name>. This might lead to irregular bleeding. This applies to the following medicines:

- Medicines for **epilepsy** (such as phenobarbital, phenytoin, carbamazepine);
 - Medicines for **tuberculosis** (such as rifampicin and rifabutin);
 - Medicines for **HIV infection** (such as nevirapine, efavirenz, ritonavir and nelfinavir);
 - Herbal remedies containing **St. John's Wort** (*Hypericum perforatum*).
- Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines including medicines obtained without a prescription, herbal medicines or other natural products.

Laboratory tests

If you need a blood test, tell your doctor or the laboratory staff that you are taking <Invented Name>, because this medicine can affect the results of some tests.

Pregnancy and breast-feeding

<Invented Name> is for use in post-menopausal women only. If you become pregnant, stop taking <Invented Name> and contact your doctor.

Driving or using machines

There is nothing to suggest that the use of <Invented Name> affects driving and use of machines.

Important information about some of the ingredients of <Invented Name>

<Invented Name> contains lactose (type of sugar). If you have an intolerance to some sugars, check with your doctor before taking <Invented Name>.

3. How to take <Invented Name>

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.

Always take <Invented Name> exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. Your doctor will decide how long you should take <Invented Name> for.

Take one tablet each day, preferably at the same time. Swallow the tablet whole with a drink of water. You can take <Invented Name> with or without food. Start your next calendar pack of tablets the day after you finish your current pack.

Do not take a break between packs.

If you have been taking other HRT preparations: carry on until you have finished your current pack and have taken all the tablets for that month. Take your first <Invented Name> tablet the next day. Do not leave a break between your old tablets and the <Invented Name> tablets.

If you have been using a HRT treatment with a gap week: begin the day after the treatment-free period.

If this is your first HRT treatment: you can start your <Invented Name> tablets at any time.

If you take more <Invented Name> than you should

If you have taken too many <Invented Name> tablets by mistake, you may feel sick, vomit or have some menstruation-like bleeding. No specific treatment is necessary but you should consult your doctor or pharmacist if you are worried.

If you forget to take <Invented Name>

If you forget to take a tablet at your usual time and you are less than 24 hours late, take it as soon as possible. Take the next tablet at the usual time.

If you are more than 24 hours late, leave the forgotten tablet in the pack. Continue to take the rest of the tablets at the usual time every day. Do not take a double dose to make up for a forgotten tablet.

If you forget to take your tablet for several days you may experience bleeding.

If you stop taking <Invented Name>

You may begin to feel the usual symptoms of menopause again, which may include hot flushes, trouble sleeping, nervousness, dizziness or vaginal dryness. You will also start to lose bone mass when you stop taking <Invented Name>. Consult your doctor or pharmacist if you want to stop taking <Invented Name> tablets.

If you need to have surgery

If you are going to have surgery, tell the surgeon that you are taking <Invented Name>. You may need to stop taking <Invented Name> 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 taking <Invented Name> again.

4. Possible side effects

Like all medicines, <Invented Name> can cause side effects, although not everybody gets them. Unexpected menstruation-like bleeding occurs during the first few months of treatment with <Invented Name>. It is usually temporary and normally disappears with continued treatment. If it does not, contact your doctor.

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 is a list of side effects that have been linked to the use of <Invented Name>:

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

- headache,
- feeling sick,
- breast pain, vaginal bleeding, hot flushes

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

- weight increase
- sleeplessness, nervousness, loss of appetite leading to weight loss, aggression, depression, inability to sleep, decrease in sex drive, inability to achieve orgasm
- dizziness, migraine, hyperactivity, pins and needles
- high blood pressure, venous blood clot (leg pain) (see also under section 2 “<Invented name> and venous blood clots (venous thromboembolism)), nose bleeds
- high blood pressure, venous blood clot (leg pain) (see also under section 2 “<Invented name> and venous blood clots (venous thromboembolism)), nose bleeds
- wind, abdominal pain, constipation, diarrhea, dry mouth, vomiting
- biliary pain
- increased sweating, acne, itchy skin, dry skin with red scaly patches called psoriasis
- muscle pain, leg cramps
- problems with the lining of the womb, painful periods, genital itching, vaginal thrush
- tiredness, generalized fluid retention, facial swelling

The following side effects have been reported with other HRTs:

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

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V*. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store <Invented Name >

Keep out of reach and sight of children.

Do not use <Invented Name> after the expiry date which is stated on the label, carton and blister after "EXP". The expiry date refers to the last day of that month.

Store <Invented Name> in the original package to protect from light.

<Invented Name> does not require any special temperature storage conditions.

Medicines should not be disposed via the waste water or the household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Content of the pack and other information

What <Invented Name> contains

The active substances are estradiol valerate and dienogest. Each tablet contains 1.0 mg estradiol valerate (equivalent to 0.764 mg estradiol) and 2.0 mg dienogest.

The other ingredients are: Lactose monohydrate, Maize starch, Pregelatinized maize starch, Povidone K30, Magnesium stearate, Polyvinyl alcohol, Titanium dioxide (E171), Macrogol/PEG 3350, Talc, Iron oxide red (E172), Black iron oxide (E172).

What <Invented Name> looks like and contents of the pack

<Invented Name> are round pink film-coated tablets.

<Invented Name> is available in packages containing 28, 3x28 and 6x28 film-coated tablets

Not all pack sizes may be marketed

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

<{To be completed nationally}>

Manufacturer:

Laboratorios León Farma S.A.

La Vallina s/n, Pol. Ind. Navatejera, Navatejera-

24008 León Spain

This medicinal product is authorised in the Member States of the EEA under the following names:

Netherland: Estradiol Valeraat 1 mg / Dienogest 2 mg Laboratorios León Farma,

Germany, Austria, Hungary, Czech Republic, Slovakian, Estonia, Lithuania, Romania: Velbienne

Poland: Velbienne mini

Latvia: Linelle

France, Belgium, Luxembourg: Dienogest / Valérate d'estradiol EFFIK

Spain: Dienogest / Estradiol Valerato EFFIK

Portugal: Dienogest / Valerato de estradiol EFFIK

This leaflet was last approved in {MM/YYYY}.

<[To be completed nationally]>