

Package leaflet: Information for the user

Vagirux 10 microgram vaginal tablets

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

1. What Vagirux is and what it is used for

Vagirux contains estradiol.

- Estradiol is a female sex hormone.
- It belongs to a group of hormones called estrogens.
- It is exactly the same as the estradiol produced by the ovaries of women.

Vagirux belongs to a group of medicines called vaginal Hormone Replacement Therapy (HRT).

Vagirux is used to relieve menopausal symptoms in the vagina such as dryness or irritation. In medical terms this is known as “vaginal atrophy”. It is caused by a drop in the levels of estrogen in your body. This happens naturally after the menopause.

Vagirux works by replacing the estrogen, which is normally produced in the ovaries of women. It is inserted into your vagina, so the hormone is released where it is needed. This may relieve discomfort in the vagina.

2. What you need to know before you use Vagirux

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 internal examination, if necessary.

Once you have started on Vagirux, you should see your doctor for check-ups at least once a year. At

these check-ups, discuss with your doctor the benefits and risks of continuing with Vagirux.

Go for regular breast screening as recommended by your doctor.

Do not use Vagirux

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 Vagirux.

Do not use Vagirux:

- if you have or have ever had **breast cancer**, or you are suspected of having it.
- if you have or have ever had **cancer, which is sensitive to estrogens**, such as cancer of the womb lining (endometrium), or 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 have recently 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 to estradiol** or any of the other ingredients of this medicine (listed in section 6).

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

Warnings and precautions

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

- Fibroids inside your womb;
- Growth of womb lining outside your womb (endometriosis) or a history of excessive growth of the womb lining (endometrial hyperplasia);
- Increased risk of developing blood clots (see 'Blood clots in a vein (thrombosis)');
- Increased risk of getting an estrogen-sensitive cancer (such as having a mother, sister or grandmother who has had breast cancer);
- High blood pressure;
- A liver disorder, such as a benign liver tumour;
- Diabetes;
- Gallstones;
- Migraines 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;
- Hereditary and acquired angioedema.

Stop using Vagirux and see a doctor immediately

If you notice any of the following when using HRT:

- Any of the conditions mentioned in the ‘Do not use Vagirux’ section above;
 - Yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease.
 - Swollen face, tongue and/or throat and/or difficulty swallowing or hives, together with difficulty breathing which are suggestive of an angioedema.
 - 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: Vagirux 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 estrogen-only HRT tablets for a long time can increase the risk of developing cancer of the womb lining (the endometrium).

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

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

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

Breast cancer

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

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

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

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

Ovarian cancer

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

Compare

The risk of ovarian cancer varies with age. For example, in women aged 50 to 54 who do not take HRT, about 2 women in 2,000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there are about 3 cases per 2,000 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 using Vagirux and see a doctor immediately”.

Compare

Looking at women in their 50s who do not take HRT, on average, over a 5-year period, 4 to 7 in 1,000 would be expected to get a blood clot in a vein.

For women in their 50s who have been taking estrogen-only HRT for over 5 years, there will be 5 to 8 cases in 1,000 users (i.e. 1 extra case).

Heart disease (heart attack)

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

Stroke

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

Compare

Looking at women in their 50s who do not take HRT, on average, 8 in 1,000 would be expected to have a stroke over a 5-year period. For women in their 50s who take HRT, there will be 11 cases in 1,000 users, over 5 years (i.e. 3 extra 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 Vagirux

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 other natural products.

However, Vagirux is used for a local treatment in the vagina and is not likely to affect other medicines. Vagirux may affect other vaginally applied treatments.

Pregnancy and breast-feeding

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

Driving and using machines

No known effect.

3. How to use Vagirux

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

Using this medicine

- You can start using Vagirux on any day which is best for you.
- For vaginal use only. Do not take the tablet by mouth.
- Insert the vaginal tablet into your vagina with the applicator.

The “USER INSTRUCTIONS” at the end of the leaflet tells you how to do this. Read the instructions carefully before using Vagirux.

The vaginal tablet applicator is intended for multiple use up to 24 times for a single patient (one tablet per application). Thereafter, throw away the applicator via the household waste. Do not use applicators that show obvious signs of damage.

How much to use

- Use one vaginal tablet each day for the first 2 weeks.
- Then use one vaginal tablet twice a week. Leave 3 or 4 days between each dose.

General information about treating symptoms of the menopause

- Your doctor will aim to prescribe the lowest dose of Vagirux to treat your symptom for as short as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.
- Treatment should only be continued if the benefit is greater than the risk. Talk to your doctor about this.

If you use more Vagirux than you should

- If you have used more Vagirux than you should, talk to your doctor or pharmacist.
- Vagirux is for local treatment inside the vagina. The dose of estradiol is so low that a considerable number of tablets would have to be taken to approach the dose normally used for treatment taken by the mouth.

If you forget to use Vagirux

- If you forget a dose, use the medicine as soon as you remember.
- Do not use a double dose to make up for a forgotten dose.

If you stop using Vagirux

Do not stop using Vagirux without talking to your doctor. Your doctor will explain the effects of stopping treatment. They will also discuss other possibilities for treatment with you.

If you need to have surgery

If you are going to have surgery, tell the surgeon that you are using Vagirux. You may need to stop using Vagirux 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 Vagirux again.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

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 medicines, which circulate in the blood, compared to women not using HRT. These risks apply less to vaginally administered treatments

such as Vagirux:

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

For more information about these side effects, see section 2. 'What you need to know before you use Vagirux'.

Common: may affect up to 1 in 10 people

- Headache;
- Stomach pain;
- Vaginal bleeding, discharge or discomfort.

Uncommon: may affect up to 1 in 100 people

- An infection of the genitals caused by a fungus;
- Feeling sick (nausea);
- Rash;
- Weight increase;
- Hot flush;
- Hypertension.

Very rare: may affect up to 1 in 10,000 people

- Diarrhoea;
- Fluid retention;
- Migraine aggravated;
- Generalised hypersensitivity (e.g. anaphylactic reaction/shock).

The following side effects have been reported with systemic estrogen treatment

- 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

Ireland
HPRA Pharmacovigilance
Website: <https://www.hpra.ie>

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal.

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

5. How to store Vagirux

Keep this medicine out of the sight and reach of children.

Keep the blisters in the outer carton in order to protect from light.

Do not use this medicine after the expiry date which is stated on the carton label and blister after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment. This medicine may cause risk to the aquatic environment.

6. Contents of the pack and other information

What Vagirux contains

- The active substance is estradiol. Each vaginal tablet contains estradiol hemihydrate equivalent to 10 microgram estradiol.
- Other ingredients are: hypromellose, lactose monohydrate, maize starch and magnesium stearate.
The film-coating contains: hypromellose and macrogol.

What Vagirux looks like and contents of the pack

The vaginal tablets are white, round, film-coated tablets embossed with “E” on one side. The diameter of the tablet is approximately 6 mm.

Pack sizes:

18 vaginal tablets per blister with multiple use applicator.

24 vaginal tablets per blister with multiple use applicator.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Gedeon Richter Plc.

Gyömrői út 19-21.

Budapest H-1103

Hungary

Manufacturer

Haupt Pharma Münster GmbH (Member of the Aenova Group)

Schleebrüggenkamp 15

48159 Münster

Germany

Gedeon Richter Plc.

Gyömrői út 19-21.

Budapest H-1103

Hungary

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

Austria:	Rewellfem 10 Mikrogramm Vaginaltabletten
Croatia:	Vagirux 10 mikrograma tablete za rodnicu
Czech Republic:	Vagirux
Denmark:	Rewellfem
Estonia:	VAGIRUX
Finland:	Vagirux
Hungary:	Vagirux 10 mikrogramm hüvelytabletta
Iceland:	Rewellfem
Ireland:	Vagirux
Italy:	Vagirux

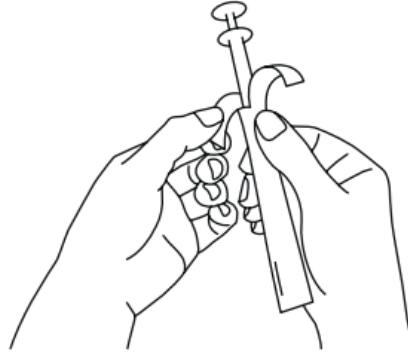
Latvia:	Vagirux 10 mikrogrami vaginālās tabletes
Liechtenstein:	Rewellfem
Lithuania:	VAGIRUX 10 mikrogramų makšties tabletės
Norway:	Vagirux
Poland:	Vagirux
Portugal:	Formyra
Malta:	Vagirux 10 microgram vaginal tablets
Romania:	ESTRADIOL RICHTER 10 micrograme comprimate vaginale
Slovakia:	Vagirux 10 mikrogramov vaginálne tablety
Slovenia:	Vagirux 10 mikrogramov vaginalne tablete
Spain:	Vagirux 10 microgram vaginal tablets
Sweden:	Vagirux

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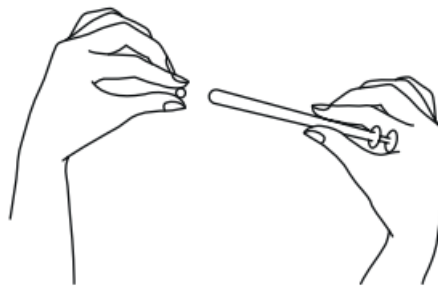
USER INSTRUCTIONS

How to use Vagirux

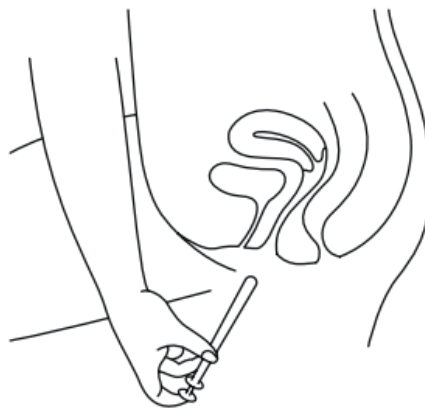
1. Remove the applicator from its sealing foil.
Open the end as shown in the picture.



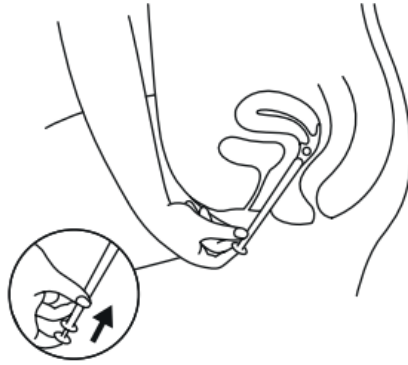
2. While holding the tube, pull the plunger of the applicator until it comes to a stop. Press one vaginal tablet out from the separate blister and place it firmly into the holder (wide end) of the applicator tube.



3. Insert the applicator carefully into the vagina.
Stop when you can feel some resistance (8–10 cm).



4. To release the vaginal tablet, press the plunger until it stops.
The tablet will stick to the wall of the vagina straight away. It will not fall out if you stand up or walk.



5. After each use, prior to a subsequent use, clean the applicator according to the following cleaning procedure:
 - Withdraw the plunger from the applicator.
 - Clean both the tube and the plunger using mild soap and rinse them with warm tap water thoroughly. Rinse both the tube's inner and outer surface.
 - If necessary, remove larger amounts of remaining water from both the tube and the plunger by shortly shaking them.
 - Air dry both the tube and the plunger on a clean surface (e.g. paper towel).
 - Reintroduce the plunger into the applicator tube for subsequent uses.

6. Use the applicator until the pack becomes empty (18 or 24 times). Thereafter, throw it away via the household waste.