

Package leaflet: Information for the user

Vagifem 10 micrograms 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, 'Possible side effects'.

What is in this leaflet

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

1. What Vagifem is and what it is used for

Vagifem contains estradiol

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

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

It 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 oestrogen in your body. This happens naturally after the menopause.

Vagifem works by replacing the oestrogen 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.

The experience of treating women older than 65 years is limited.

2. What you need to know before you use Vagifem

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 Vagifem 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 Vagifem.

Go for regular breast screening as recommended by your doctor.

Do not use Vagifem:

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 Vagifem.

Do not use Vagifem if:

- You are **allergic** (hypersensitive) to **estradiol** or any of the other ingredients of Vagifem (listed in section 6 'Contents of the pack and other information').
- You have or have ever had **breast cancer**, or you are suspected of having it.
- You have or have ever had **cancer which is sensitive to oestrogens**, such as cancer of the womb lining (endometrium), or you are suspected of having it.
- You have **any unexplained vaginal bleeding**.
- You have excessive **thickening of the womb lining** (endometrial hyperplasia) that is not being treated.
- 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).
- You have a **blood clotting disorder** (such as protein C, protein S or antithrombin deficiency).
- You have or have recently had a disease caused by blood clots in the arteries, such as a **heart attack, stroke or angina**.
- You have or have ever had a **liver disease** and your liver function tests have not returned to normal.
- You have a rare blood problem called '**porphyria**', which is passed down in families (inherited).

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

- Asthma
- Epilepsy
- Diabetes
- Gallstones
- High blood pressure
- Migraines or severe headaches
- A liver disorder, such as a benign liver tumour
- Growth of womb lining outside your womb (endometriosis) or a history of excessive growth of the womb lining (endometrial hyperplasia)
- A disease affecting the eardrum and hearing (otosclerosis)
- A disease of the immune system that affects many organs of the body (systemic lupus erythematosus, SLE)
- Increased risk of getting an oestrogen-sensitive cancer (such as having a mother, sister or grandmother who has had breast cancer)
- Increased risk of developing blood clots (see 'Blood clots in a vein (thrombosis)')
- Fibroids inside your womb

- A very high level of fat in your blood (triglycerides)
- Fluid retention due to cardiac or kidney problems.

Stop using Vagifem and see a doctor immediately

If you notice any of the following when using HRT:

- Migraine-like headaches which happen for the first time
- 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)
- Any of the conditions mentioned in the ‘Do not use Vagifem’ section above
- 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: Vagifem 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 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 Vagifem when it is used for repeated or long term (more than one year) treatments. However, Vagifem 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, Vagifem 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 Vagifem, but you should see your doctor if you are concerned.

Breast cancer

Evidence suggests that using Vagifem does not increase the risk of breast cancer in women who had no breast cancer in the past. It is not known if Vagifem 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 oestrogen-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 Vagifem 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 oestrogen-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 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 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 Vagifem

Please tell your doctor or pharmacist if you are using or have recently used any other medicines,

including medicines obtained without a prescription, herbal medicines or other natural products. However, Vagifem is used for a local treatment in the vagina and is not likely to affect other medicines. Vagifem may affect other vaginally applied treatments.

Pregnancy and breast-feeding

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

Driving and using machines

No known effect.

3. How to use Vagifem

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 Vagifem on any day which is best for you.
- Insert the vaginal tablet into your vagina with the applicator.

The 'USER INSTRUCTIONS' at the end of the leaflet tell you how to do this. Read the instructions carefully before using Vagifem.

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

For OTC-products

- When using medicines for any menopausal symptoms, it is recommended to use the lowest dose that works, and to use the medicine for as short a time as it is needed.

For prescription only products

- Your doctor will aim to prescribe the lowest dose of Vagifem 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 Vagifem than you should

- If you have used more Vagifem than you should, talk to a doctor or pharmacist.
- Vagifem 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 mouth.

If you forget to use Vagifem

- 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 Vagifem

Do not stop using Vagifem without talking to your doctor. Your doctor will explain the effects of stopping treatment. He or she 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 Vagifem. You may need to stop

using Vagifem 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 Vagifem 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 Vagifem:

- 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 Vagifem'.

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 oestrogen 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:

HPRA Pharmacovigilance

Website: www.hpra.ie

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

5. How to store Vagifem

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

Do not refrigerate.

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 Vagifem contains

- The active substance is estradiol 10 micrograms (as estradiol hemihydrate). Each vaginal tablet contains 10 micrograms estradiol (as estradiol hemihydrate).
- Other ingredients are: hypromellose, lactose monohydrate, maize starch and magnesium stearate.
- The film-coating contains: hypromellose and macrogol 6000.

What Vagifem looks like and contents of the pack

Each white vaginal tablet comes in an applicator which is used once only.

Vagifem is engraved with NOVO 278 on one side.

Pack sizes:

18 vaginal tablets with applicators.

24 vaginal tablets with applicators.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

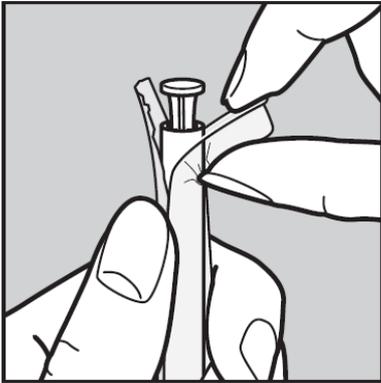
Further information on Vagifem is available to the medical and allied professionals from:

Novo Nordisk Limited
1st Floor, Block A, The Crescent Building,
Northwood Business Park,
Santry, Dublin 9
Phone 1850 665 665

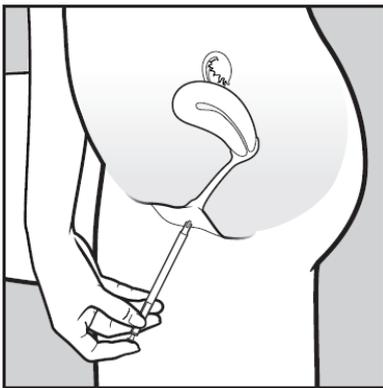
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USER INSTRUCTIONS

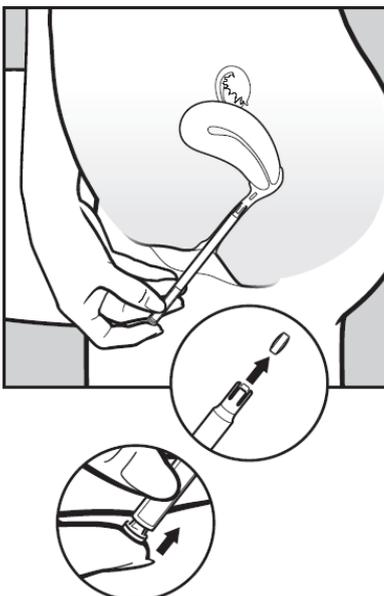
How to use Vagifem



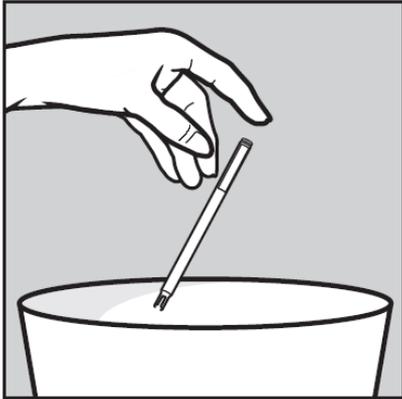
1. Tear off one single blister pack.
Open the end as shown in the picture.



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



3. To release the tablet, gently press the push-button until you feel a click. The tablet will stick to the wall of the vagina straight away. It will not fall out if you stand up or walk.



4. Take out the applicator and throw it away.

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