

**Patient leaflet in accordance with the Pharmacists' Regulations
(Preparations) - 1986**

This medicine is dispensed without a doctor's prescription

**Vagifem® 10 micrograms
Film-coated vaginal tablets**

**Active ingredient:
estradiol 10 mcg (as hemihydrate)**

Inactive ingredients and allergens in this medicine: see section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

Use this medicine according to the instructions in the section about dose in this leaflet. Consult your pharmacist if you need further information. Consult your doctor if your symptoms of illness get worse or do not improve after 2 to 4 weeks, or if other symptoms occur.

1. What is this medicine intended for?

Vagifem 10 micrograms is intended to treat vaginal atrophy that is caused by estrogen deficiency in women after the menopause.

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

Therapeutic group: estrogens, natural and semi-synthetic, simple.

Vagifem 10 mcg contains estradiol which is a female sex hormone that belongs to a group of hormones called estrogens. The estradiol in Vagifem 10 mcg is exactly the same as the estradiol produced in the ovaries of women.

Vagifem 10 mcg belongs to a group of medicines called vaginal hormone replacement therapy (HRT).

Vagifem 10 mcg is used to relieve menopausal symptoms in the vagina such as dryness and irritation. This condition is called 'vaginal atrophy', it is caused by a drop in the levels of estrogen in your body. This happens naturally after the menopause.

Vagifem 10 mcg 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. Before using this medicine

Do not use this medicine if:

- You are **sensitive** (allergic) to **estradiol** or any of the other ingredients in this medicine (see section 6 'Additional information').
- You have or have ever had **breast cancer**, or you are suspected of having **breast cancer**.
- 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 this type of cancer.
- You have **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.

If any of the above conditions appear for the first time while you are using Vagifem 10 mcg, stop using it at once and consult your doctor immediately.

Medical history and routine medical check ups

The use of HRT carries risks which need to be considered when deciding whether to start the treatment, or when deciding 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 consult 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 which may include an examination of your breasts and/or an internal examination, if necessary.

Once you have started taking Vagifem 10 mcg, 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 to use this medicine.

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

Special warnings about using this medicine

Before you start treatment with Vagifem 10 mcg, tell your doctor if you have or have ever had any of the following problems, as these problems may return or become worse during treatment with this medicine. 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 tumor
- 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 estrogen-sensitive cancer (for example if your mother, sister or grandmother 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 heart or kidney problems
- hereditary and acquired angioedema (see section 4, 'Side effects').

Note, Vagifem 10 mcg 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.

Hormone replacement therapy 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 Vagifem 10 mcg when it is used for repeated or long-term (more than one year) treatments. However, Vagifem 10 mcg 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 is 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 HRT medicines which circulate in the blood.

However, Vagifem 10 mcg is for local treatment in the vagina, and its 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 10 mcg, but you should see your doctor if you are concerned.

Breast cancer

Evidence suggests that using Vagifem 10 mcg does not increase the risk of breast cancer in women who have not had breast cancer in the past. It is not known if Vagifem 10 mcg 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 undergo mammogram screening 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 will be about 3 cases per 2,000 users (this means about one 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 women not using HRT, especially during the first year of treatment.

Blood clots can be serious, and if a blood clot reaches the lungs, it can cause chest pain, breathlessness, fainting and even death.

You are more likely to get a blood clot in your veins as you get older and also if any of the following conditions apply to you. Inform your doctor if any of these situations apply 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
- 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 section 4 'Stop using Vagifem 10 mcg and see a doctor immediately'.

Compare:

For 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 (this means one extra case).

Heart disease (heart attack)

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

Stroke

The risk of getting stroke is about 1.5 times higher in women using HRT than in women not using it. The number of extra cases of stroke due to use of HRT will increase with age.

Compare:

For 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 (this means 3 extra cases).

Other conditions

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

Drug interactions

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

Vagifem 10 mcg, which is used for local treatment in the vagina, is not likely to affect other medicines. Vagifem 10 mcg may affect other vaginally applied treatments.

Pregnancy and breastfeeding

Vagifem 10 mcg is for use in postmenopausal women only. If you become pregnant, stop using Vagifem 10 mcg and contact your doctor.

Driving and using machines

No known effect.

3. How to use this medicine?

Always use this medicine exactly as described in this leaflet or as instructed by your doctor or pharmacist. Check with your doctor or pharmacist if you are not sure about your dosage or about how to take this medicine.

The usual dosage is:

- Use one vaginal tablet each day during the first 2 weeks.
- Then use one vaginal tablet twice a week. Leave an interval of 3 or 4 days between each tablet and the next.

Do not exceed the recommended dose.

Treatment duration

If your condition has not improved, or if it gets worse after 2-4 weeks, or if you experience other symptoms, see a doctor.

General information about treating the symptoms of menopause

When using medicines for treating menopausal symptoms, it is advisable to use the lowest dose that is still effective, and to use the medicine for as short a time as it is needed.

Using this medicine

- You can start using Vagifem 10 mcg on any day which is best for you.
- For vaginal use only.
- Insert the vaginal tablet into your vagina with the applicator.
- This medicine is not for swallowing!

The 'USER INSTRUCTIONS' at the end of the leaflet tell you how to use Vagifem 10 mcg. Read the instructions carefully before using Vagifem 10 mcg.

If you have accidentally taken a higher dose

If you have used more Vagifem 10 mcg than required, consult a doctor or pharmacist.

Vagifem 10 mcg is for local treatment inside the vagina. The dose of estradiol in Vagifem 10 mcg 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 a child has accidentally swallowed some medicine, immediately see a doctor

or go to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine

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

If you stop taking this medicine

Consult your doctor if you have any questions about the duration of treatment or to discuss alternative treatments.

If you need to have surgery

If you are going to have surgery, tell the surgeon that you are using Vagifem 10 mcg. You may need to stop using Vagifem 10 mcg for about 4 to 6 weeks before the surgery 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 10 mcg again.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Vagifem 10 mcg may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

The following diseases are reported more often in women using HRT medicines that circulate in the blood compared to women not using HRT. These risks are lower for vaginally administered treatments such as Vagifem 10 mcg:

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

For more information about these side effects, see section 2, 'Before using this medicine'.

Stop using Vagifem 10 mcg and see a doctor immediately

If you experience any of the following conditions during use of HRT:

- migraine-like headaches that happen for the first time
- yellowing of the skin or the white of the eye (jaundice); these could be signs of liver disease
- Swollen face, tongue and/or throat and/or difficulty swallowing or hives,

- together with difficulty breathing which are suggestive of an angioedema
- significant increase in blood pressure (possible symptoms are headache, fatigue, dizziness)
 - any of the conditions mentioned in section 2 under 'Do not use this medicine if'
 - if you become pregnant
 - if you notice signs of a blood clot, such as:
 - swelling associated with pain and redness in the legs
 - sudden chest pain
 - difficulty breathing
- For additional information see section 2 under 'Blood clots in a vein (thrombosis)'.

Common side effects: may affect up to 1 in 10 women

- headache
- stomach pain
- vaginal bleeding, discharge or discomfort.

Uncommon side effects: may affect up to 1 in 100 women

- an infection of the genitals caused by a fungus
- nausea
- rash
- weight gain
- hot flushes
- high blood pressure.

Very rare side effects: may affect up to 1 in 10,000 women

- diarrhea
- fluid retention
- migraine aggravated
- generalized hypersensitivity (for example anaphylactic reaction/shock).

The following side effects have been reported with oral 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).

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You

can also follow this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the blister card and the outer carton. The expiry date refers to the last day of that month.

Storage conditions:

Store below 25°C.

Do not refrigerate.

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. Additional information

Each vaginal tablet contains 10 micrograms estradiol (as estradiol hemihydrate).

In addition to the active ingredient, this medicine also contains: hypromellose, lactose monohydrate, maize starch, magnesium stearate.

The tablet coating contains:

hypromellose, macrogol 6000.

What the medicine looks like and contents of the pack:

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

The Vagifem 10 mcg is debossed 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.

Registration holder's name and address:

Novo Nordisk Ltd.

1 Atir Yeda Street

Kfar-Saba 4464301.

Manufacturer's name and address:

Novo Nordisk A/S, Novo Allé,

DK-2880 Bagsværd, Denmark.

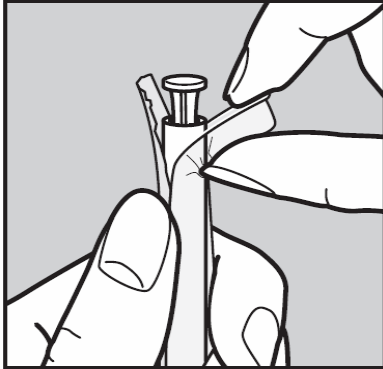
This leaflet was revised in August 2022 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 146-89-33241

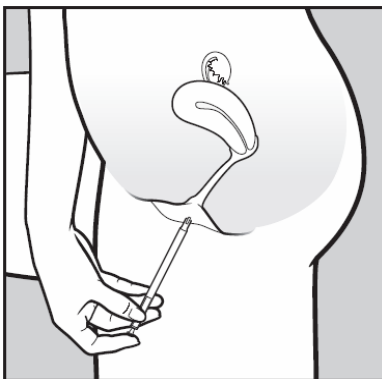
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USER INSTRUCTIONS

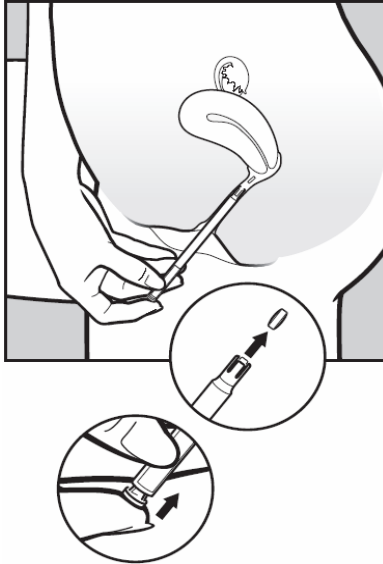
How to use Vagifem 10 mcg



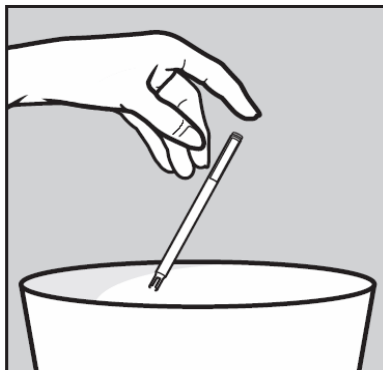
1. Tear off one single blister pack.
Open the end as shown in the picture.



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.