

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

***Pr*Vagifem® 10**
Estradiol vaginal inserts USP
10 mcg
with applicators

Read this carefully before you start taking **Vagifem® 10** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your doctor or pharmacist about your medical condition and treatment and ask if there is any new information about **Vagifem® 10**.

Serious Warnings and Precautions

In postmenopausal women taking oral estrogen-alone, who had a prior surgery removal of the uterus (called a hysterectomy), there is an increased risk of:

- stroke and blood clots in the large veins (**deep vein thrombosis**).

Estrogens with or without progestins should:

- NOT be used for the prevention of heart disease or stroke.
- be used at the **lowest effective dose** and for the **shortest period of time** possible. You should have regular medical check-ups.

What is Vagifem® 10 used for?

Vagifem®10 is used to treat symptoms of vaginal atrophy due to low levels of estrogen.

How does Vagifem® 10 work?

Vagifem® 10 provides a sex hormone called estradiol, which is a type of estrogen, to the vagina. This may help reduce dryness and discomfort around your vagina. After menopause, your body makes less or no estrogen. Vagifem® 10 replaces the estrogen that are missing in some women.

What are the ingredients in Vagifem® 10?

Medicinal ingredients: Estradiol (as estradiol hemihydrate)

Nonmedicinal ingredients: Hypromellose, lactose monohydrate, magnesium stearate, maize starch and polyethylene glycol 6000

Vagifem® 10 comes in the following dosage forms:

Vaginal inserts, each containing 10 mcg estradiol. Each insert is pre-loaded into the applicator.

Do not use Vagifem® 10 if:

- You have or might have estrogen-dependent cancers;

- Your uterus lining is thicker than normal (endometrial hyperplasia);
- You have, might have or have had breast cancer;
- You have unexplained or unusual bleeding from the vagina;
- You are or may be pregnant or breastfeeding;
- You have or have had blood clotting problems:
 - deep vein thrombosis (blood clots in big veins);
 - pulmonary embolism (blood clots in the lung);
 - thrombophlebitis (inflammation of a vein caused by a blood clot);
- You have porphyria (blood pigment disease);
- You have or had liver problems. This includes blood tests showing your liver is not working properly;
- You have or had a heart attack, stroke, a blockage or narrowing of the arteries around the heart (called coronary heart disease);
- You have eye problems that are caused by low blood flow to the eye;
- You are allergic to estradiol or any of the ingredients in this drug or the container.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Vagifem® 10. Talk about any health conditions or problems you may have, including if you:

- have a history of allergy or intolerance to any drugs or other substances;
- have a personal history of breast disease (including breast lumps) and/or breast biopsies, or a family history of breast cancer;
- had any vaginal bleeding that is not normal;
- have or had uterus problems:
 - Fibroids (growths) inside your uterus
 - Endometriosis (growth of the uterine lining outside your uterus)
 - A history of endometrial hyperplasia (overgrowth of the lining of the uterus);
 - have had a hysterectomy (surgical removal of the uterus).
- have a history of liver problems, jaundice (yellowing of the eyes and/or skin) or itching;
- have a history of migraine headache;
- have a disease called systemic lupus erythematosus, an autoimmune disease;
- have high calcium in the blood as a result of kidney disease or cancer;
- have or had high blood pressure;
- have symptoms of blood blockage to the brain;
 - migraine, headaches, trouble speaking, paralysis, loss of consciousness.
- have a history of high cholesterol or high levels of other fats (such as triglycerides) in the blood;
- have or have a history of kidney disease;
- have or have a history of asthma;
- have or have a history of epilepsy (seizures);
- have otosclerosis, an ear problem;
- have been diagnosed with diabetes;
- if you think you may have a vaginal infection;
- smoke.

Other warnings you should know about:

Vagifem® 10 has benefits and risks. Consider them when deciding to start taking Vagifem® 10 or to carry on taking it. You should talk with your healthcare professional regularly about whether you still need treatment with hormone therapy (HT).

Breast Cancer: For breast cancer, there is:

- An increased risk of breast cancer in postmenopausal women taking combined estrogen plus progestin.
- No difference in the risk of breast cancer in postmenopausal women with a previous hysterectomy taking estrogen-alone.

If you have or had breast cancer, you should not take estrogens with or without progestins.

If you have a family history of breast cancer or have had breast lumps, breast biopsies or abnormal mammograms (breast x-rays), talk to your healthcare professional before starting HRT.

You should have regular breast exams done by your healthcare professional and by yourself. You should review technique for breast self-exams with your healthcare professional. See your healthcare professional if you notice any changes such as:

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

You should have a mammogram before starting HT and at regular intervals during treatment. You should join mammography screening programs. For mammogram screening, it is important that you inform the healthcare professional who is taking the x-ray that you use HT. Mammography may not detect all lumps.

Overgrowth of the lining of the uterus and cancer of the uterus:

The use of systemic estrogen-alone therapy increases the risk of developing endometrial hyperplasia (overgrowth of the lining of the uterus). The risk of endometrial cancer (cancer of the lining of the uterus) increases the longer you use estrogen alone. These risks apply to postmenopausal women with a uterus.

Vagifem® 10 has not been shown to increase risk of overgrowth of the lining of the uterus and cancer of the uterus.

Talk to your healthcare professional about the risk factors for overgrowth and cancer of the uterus lining. They should discuss ways to reduce the risks, including progestin treatments. You should report any unexpected or unusual vaginal bleeding to your healthcare professional right away while you are using Vagifem® 10.

Ovarian Cancer:

- Women who take estrogen alone or combined HRT for 5 or more years have a slightly higher chance of ovarian cancer.

Heart Disease and Stroke: There is an increased risk of:

- stroke and coronary heart disease in post-menopausal women taking combined oral estrogen plus progestin.

- stroke in post-menopausal women taking oral estrogen-alone HT. There is no difference in the risk of coronary heart disease in post-menopausal women with prior hysterectomy taking oral estrogen-alone.

Abnormal Blood Clotting:

- In postmenopausal women taking combined estrogen plus progestin: there is an increased risk of pulmonary emboli and deep vein thrombosis (blood clots in the lung and in big veins).
- In postmenopausal women, with previous hysterectomy, taking estrogen-alone: there is an increased risk of deep vein thrombosis.

You are more likely to get a blood clot in your veins as you get older. Talk to your healthcare professional if any of the below situations apply to you. Blood clots can be life-threatening or cause serious disability if:

- You use estrogens;
- You are unable to walk for a long time because of a major surgery, injury or sickness;
- You are overweight and your BMI is greater than 30;
- 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 smoke;
- You have systemic lupus erythematosus (an autoimmune disease);
- You have cancer.

If you are going to have a surgery, tell your healthcare professional that you are taking Vagifem® 10. You may need to stop taking Vagifem® 10 at least 4 weeks before the surgery to reduce the risk of a blood clot. Ask your healthcare professional when you can start taking Vagifem® 10 again.

Gallbladder Disease:

- The use of estrogens by postmenopausal women has been associated with an increased risk of gallbladder disease that needs surgery.

Dementia (loss of memory and intellectual function):

- There is an increased risk of dementia in women age 65 and older who are taking combined oral estrogen plus progestin.

Physical exam, tests, and check-ups:

- Before you start taking Vagifem® 10, your healthcare professional should:
 - Do a physical exam, a Pap smear and a breast exam
 - Do blood pressure tests, blood tests and a mammogram (breast x-ray).
 - Ask you about your personal and your family’s health history.
- Your healthcare professional may take samples of your uterus tissue if needed.
- While you are taking Vagifem® 10, check your breasts often and get regular check-ups with your healthcare professional.
- Your first check-up should be within 3 to 6 months of starting Vagifem® 10. Thereafter, these should be scheduled at least once a year. These check-ups will help to detect any side effects you may have. Your visits may include:
 - a blood pressure check, a breast exam, a Pap smear, pelvic exam, mammograms and blood tests. Your healthcare professional will decide when these are necessary

and will interpret the results.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Vagifem® 10:

- Medicines that impact liver enzymes;
- Phenobarbital, phenytoin, carbamazepine, used to treat epilepsy and seizures;
- Ritonavir and nelfinavir, used to treat HIV/AIDS;
- Anti-infective medicines such as rifampicin, rifabutin, nevirapine, efavirenz;
- St. John's Wort, used to treat depression.

How to take Vagifem® 10:

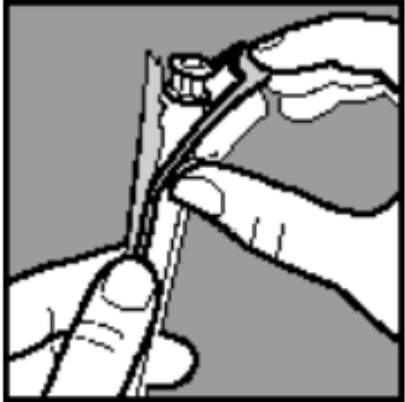
- Ask your healthcare professional to show you how to use the Vagifem® 10 applicator.
- Use Vagifem® 10 exactly as directed by your healthcare professional.
- Do not use more than the recommended dose prescribed by your healthcare professional.
- Do not change the dose or schedule unless your healthcare professional tells you to.
- Vagifem® 10 is a vaginal insert that you place in your vagina.
- **Do not take Vagifem® 10 by mouth (orally).**

Steps:



The vaginal insert is pre-loaded into the applicator. You can see this through the plastic bubble in the package.

1. Wash your hands.



2. Push the Vagifem[®] 10 applicator through the foil backing (not through the plastic bubble) that says Vagifem[®] 10 and Novo Nordisk.

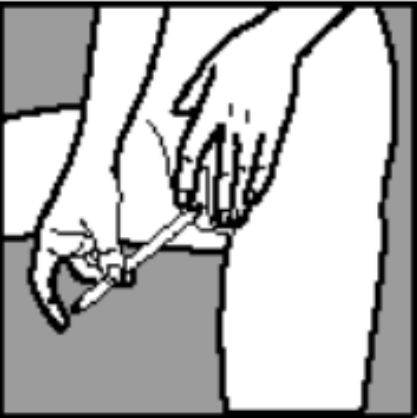


3. Choose the position that is most comfortable for you. You may want to:
 - sit on the edge of a chair with your knees apart,
 - stand up with one foot raised on the edge of the tub or bed,
 - squat,
 - lie down.

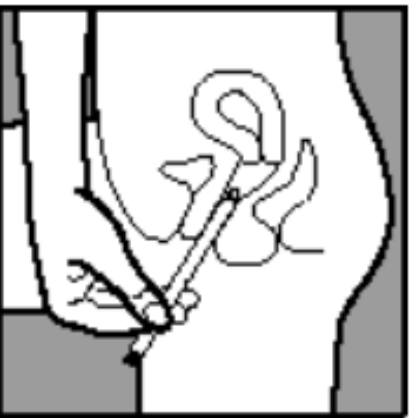
Inserting Vagifem[®] 10 is like inserting a tampon.



4. Hold the applicator with your thumb and middle finger. Leave your index finger free to press the applicator plunger.



5. With your free hand, hold open the skin at the vaginal opening.



6. Gently slide the vaginal insert end of the applicator into the vagina as far as it will comfortably go. This will be no more than 8 cm. Aim towards your lower back. **DO NOT FORCE.** You do not need to insert the entire applicator into your body. The plunger end of

the applicator will be outside your body. The words Vagifem® 10 and Novo Nordisk on the applicator will be outside your body.



7. Use your index finger to gently push the plunger. This will release the vaginal insert from the applicator onto the vaginal tissues. You will hear a clicking sound when the insert is released.



8. Withdraw the applicator and discard in a waste basket. Do not flush the applicator down the toilet.

If Vagifem® 10 comes out right after use, it is recommended to insert another vaginal insert.

Recommended Adult Dose:

- **Initial dose:** 1 vaginal insert daily for two weeks.
- **Maintenance dose:** 1 vaginal insert every three or four days between doses (2 vaginal inserts per week).

Overdose:

Signs of overdose may include feeling sick or vomiting, breast pain, swelling, bloating, cramps, headache, dizziness, general ill feeling or vaginal bleeding.

If you think you, or a person you are caring for, have taken too much Vagifem® 10, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed dose:

- If you forget to use a vaginal insert, use one as soon as you remember. However, if the dose is close to the next scheduled dose, skip the missed insert and continue with your next scheduled insert.
- Do not use two vaginal inserts to make up for a missed dose.

What are possible side effects from using Vagifem® 10?

These are not all the possible side effects you may feel when taking Vagifem® 10. If you experience any side effects not listed here, contact your healthcare professional.

- Breast edema, breast enlargement, breast pain or pain tenderness
- Peripheral edema (swelling of arms or legs)
- Genital infection with a fungus or vaginal inflammation
- Headache, dizziness
- Nausea
- Diarrhea
- Feeling tired
- Abdominal pain (stomach), distension or discomfort
- Vaginal bleeding, discharge or discomfort
- Back pain
- Weight gain
- Acne, rash, itchy skin
- Muscle spasms, pain in extremities
- Anxiety, trouble sleeping

Vagifem® 10 can cause abnormal blood test results. Your healthcare professional will decide when these are necessary and will interpret the results. They will tell you if your test results are abnormal and if you need treatment.

Serious side effects and what to do about them			
Symptom / effect	Talk with your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Gastrointestinal problems: Abdominal pain, nausea or vomiting		✓	
Palpitation (fast-beating, fluttering or pounding heart): skipping beats, beating too fast, pounding, fluttering rapidly		✓	
Urinary tract infection (infection in urinary system including kidneys, ureters, bladder and urethra): Pain or burning sensation while urinating, frequent urination, blood in urine, pain in the pelvis, strong smelling urine, cloudy urine		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk with your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Vaginal bleeding changes: increased or decreased menstrual bleeding, spotting, infrequent periods or absence of bleeding, severe vaginal bleeding		✓	
UNCOMMON			
Allergic reaction: Hives, itching, swelling, low blood pressure (paleness and coldness of skin, rapid heartbeat), sweating			✓
Application Site reaction around vagina: itching, burning, redness, swelling, rash, or discharge from the vagina, injury from applicator		✓	
Blood clot in the eye: Sudden partial or complete loss of vision			✓
Breast abnormalities (including breast cancer): dimpling or sinking of the skin, changes in the nipple, or any lumps you can see or feel		✓	
Cholestasis (decrease in bile flow from the liver): jaundice (yellowing of the skin or whites of eyes), dark urine, light coloured stools		✓	
Cystitis (bladder infection): increased need to urinate, pain in the pelvis or lower back, frequent urination during the night, cloudy urine that may contain blood, burning sensation when passing urine		✓	
Deep vein thrombosis (blood clot in the legs) or Thrombophlebitis (inflammation of a vein often in the leg): Leg swelling or pain, redness, warmth, tenderness and pain in affected area			✓
Depression (sad mood that won't go away): difficulty sleeping or sleeping too much, changes in appetite or weight, feelings of worthlessness, guilt, regret, helplessness or hopelessness, withdrawal from social situations, family, gatherings and activities with friends, reduced libido (sex drive) and thoughts of death or suicide.		✓	
Heart attack: Crushing chest pain or chest heaviness			✓

Serious side effects and what to do about them			
Symptom / effect	Talk with your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Hypertension (high blood pressure): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or heart palpitations		✓	
Migraine: severe headache often accompanied by nausea, vomiting and sensitivity to light		✓	
Ovarian cancer: abdominal pain or bloating, quickly feeling full after eating, weight loss, pain in pelvis, change in bowel habits, need to urinate often		✓	
Pulmonary embolism (blood clot in the lungs): Pain in the chest, coughing blood, sudden shortness of breath, or difficulty in breathing			✓
Stroke (blood clot in the brain): Sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech or weakness or numbness in face, arm or leg			✓
Urinary tract disorders: difficulty and pain when passing urine, blood in urine		✓	
Vaginal infection (inflammation of the vagina): itching, burning, soreness, odor or discharge from the vagina		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Keep out of the reach of children.
- Store in a dry place, between 15° and 25°C. Protect from light. Do not refrigerate.

If you want more information about Vagifem® 10:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website <http://www.novonordisk.ca>, or by calling 1-800-465-4334.

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