

PART III: CONSUMER INFORMATION

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

This leaflet is Part III of a three-part "Product Monograph" published when Vagifem® 10 was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Vagifem® 10. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Vagifem® 10 (estradiol vaginal inserts USP) is used for the treatment of the symptoms of vaginal atrophy due to estrogen deficiency.

Vagifem® 10 should be used only under the supervision of a doctor, with regular follow-up at least once a year to identify side effects associated with its use. Your first follow-up visit should be within 3 to 6 months of starting treatment. Your visit may include a blood pressure check, a breast exam, a Pap smear and pelvic exam. You should have a mammogram before starting treatment and at regular intervals as recommended by your doctor. Your doctor may recommend some blood tests.

You should carefully discuss the risks and benefits of hormone therapy (HT) with your doctor. You should regularly talk with your doctor about whether you still need treatment with HT.

What it does:

Vagifem® 10 provides estrogen in and around the vagina. This helps to reduce dryness and discomfort you are experiencing in the urinary and genital area. Estrogen is made in your body by your ovaries. At some point, usually between the ages of 45 and 55, the ovaries decrease the amount of estrogen produced or stop producing estrogen all together. At this time, women go through the "change of life" or menopause. Monthly periods stop. Some women experience irritating feelings of warmth, heat and sweating (hot flashes).

Others find that the tissues of the vagina and urinary tract become thin and dry. This can be very uncomfortable and you may feel itching, burning and pain. Some women feel pain during sex. The same feelings may occur if the ovaries are surgically removed.

When it should not be used:

Vagifem® 10 should NOT be used under these conditions:

- Known or suspected estrogen-dependent carcinoma
- Overgrowth of the lining of the uterus (endometrial hyperplasia)
- Known or suspected, or past history of breast cancer
- Unexpected or unusual vaginal bleeding
- Known or suspected pregnancy
- Breastfeeding
- Have or have had blood clot disorders, including blood clots in the leg, lung or thrombophlebitis
- Porphyria (a disease of blood pigment)
- Liver dysfunction or disease as long as liver function tests have failed to return to normal
- Active or past history of arterial thromboembolic disease (e.g. stroke, myocardial infarction and/or coronary disease)
- Partial or complete loss of vision due to ophthalmic vascular disease
- Allergy to estradiol or any of the ingredients in Vagifem® 10

What the medicinal ingredient is:

Estradiol hemihydrate

What the important nonmedicinal ingredients are:

Lactose monohydrate, maize starch, hypromellose, magnesium stearate and polyethylene glycol 6000

What dosage forms it comes in:

Vagifem[®] 10 is available as vaginal inserts, supplied in cartons of 18 vaginal inserts. Each insert is pre-loaded into the applicator and contains 10 µg estradiol.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

The Women's Health Initiative (WHI) trial is a large clinical study that assessed the benefits and risks of oral combined *estrogen plus progestin* therapy and oral *estrogen-alone* therapy compared with placebo (a pill with no active ingredients) in postmenopausal women.

The WHI trial indicated an increased risk of stroke and deep vein thrombosis in postmenopausal women with prior hysterectomy (surgical removal of the uterus) taking oral *estrogen-alone*.

Therefore, you should highly consider the following:

- There is an increased risk of stroke and blood clots in the large veins with the use of estrogen-alone therapy.
- Estrogens with or without progestins should not be used for the prevention of heart disease or stroke.
- Estrogens with or without progestins should be used at **the lowest effective dose** and for the **shortest period of time** possible. Regular medical follow-up is advised.

Vagifem[®] 10 is a locally administered vaginal treatment containing 10 µg of estradiol and therefore the occurrence of the conditions mentioned in the box above, is less likely than with estrogen products used for systemic treatment. However, since Vagifem[®] 10 is a hormone therapy product these risks should be considered.

Breast Cancer

The results of the WHI trial indicated no difference in the risk of breast cancer in post-menopausal women with prior hysterectomy taking oral estrogen-alone compared to women taking placebo.

Estrogens should not be taken by women who have a personal history of breast cancer.

In addition, women with a family history of breast cancer or women with a history of breast lumps, breast biopsies or abnormal mammograms (breast x-rays) should consult with their doctor before starting HT.

Women should have a mammogram before starting HT and at regular intervals during treatment as recommended by their doctor.

Regular breast examinations by a doctor and regular breast self-examinations are recommended for all women. You should review technique for breast self-examination with your doctor.

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 HT, 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.

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

The use of systemic estrogen-alone therapy by post menopausal women who still have a uterus increases the risk of developing endometrial hyperplasia (overgrowth of the lining of the uterus), which increases the risk of endometrial cancer (cancer of the lining of the uterus).

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

It is important to report any unusual vaginal bleeding to your doctor right away while you are using Vagifem[®] 10. Vaginal bleeding after menopause may be a warning sign of cancer of the uterus (womb). Your doctor should check any unusual vaginal bleeding to find out the cause.

Ovarian Cancer

Use of estrogen alone and estrogen plus progestin therapies for 5 or more years has been associated with increased risk of ovarian cancer.

Heart Disease and Stroke

The results of the WHI trial indicated an increased risk of stroke and coronary heart disease in post-menopausal women taking combined oral estrogen plus progestin compared to women taking placebo.

In postmenopausal women taking oral estrogen-alone HT, the results of the WHI indicated an increased risk of stroke, but no difference in the risk of coronary heart disease in post-menopausal women with prior hysterectomy taking oral estrogen-alone compared to women taking placebo.

Abnormal Blood Clotting

Use of oral estrogen with or without progestin by menopausal women is associated with increased risk of blood clots.

The risk of blood clots also increases with age, if you or a family member has had blood clots, if you smoke or if you are severely overweight. The risk of blood clots is also temporarily increased if you are immobilized for long periods of time and following major surgery. You should discuss risk factors for blood clots with your doctor since blood clots can be life-threatening or cause serious disability.

Gallbladder Disease

The use of oral estrogens by postmenopausal women has been associated with an increased risk of gallbladder disease requiring surgery.

Dementia

Use of combined oral estrogen plus progestin in women age 65 and over is associated with increased risk of probable dementia.

BEFORE you use Vagifem[®] 10 talk to your doctor or pharmacist if you:

- have a history of allergy or intolerance to any medications or other substances
- have a personal history of breast disease (including breast lumps) and/or breast biopsies, or a family history of breast cancer
- have experienced any unusual or undiagnosed vaginal bleeding
- have a history of uterine fibroids or endometriosis
- have a history of liver disease, jaundice (yellowing of the eyes and/or skin) or itching related to estrogen use or during pregnancy
- have a history of migraine headache

- have a disease called systemic lupus erythematosus for which the most common symptoms are joint pain, skin rash and fever
- have a history of high blood pressure
- have a personal or family history of blood clots, or a personal history of heart disease or stroke
- have a history of high cholesterol or high levels of other fats (such as triglycerides) in the blood
- have a history of kidney disease, asthma or epilepsy (seizures)
- have a condition called otosclerosis that can affect one or both ears and for which the most common symptoms are hearing loss, ringing in the ears and dizziness
- have been diagnosed with diabetes
- are pregnant or may be pregnant
- If you think you may have a vaginal infection

Therapy should be discontinued if any of the following situations is discovered:

- Jaundice or deterioration of liver function
- Significant increase in blood pressure
- New onset of migraine-type headache
- Pregnancy

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or pharmacist if you are taking any other medications, including prescription medications, over-the-counter medications, vitamins or herbal products.

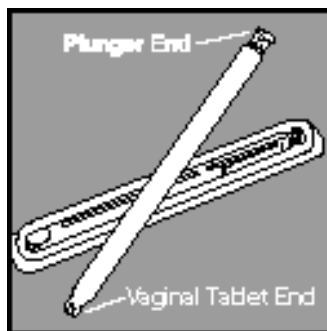
PROPER USE OF THIS MEDICATION

Usual dose:

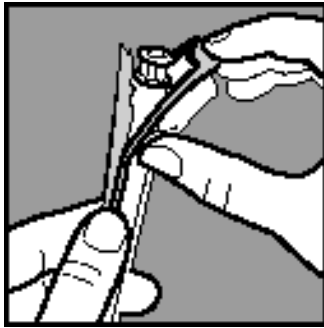
In order to prevent injury, you need to be shown how to use Vagifem[®] 10 correctly. Ask your doctor or pharmacist to demonstrate the proper use of Vagifem[®] 10 applicator.

You can start using Vagifem[®] 10 on any day of the week at any time of day you like. Once started, it is recommended that Vagifem[®] 10 be used at that same time each day. Use 1 vaginal insert each day for the first 2 weeks (7 vaginal inserts per week, a total of 14 vaginal inserts). Then, use 1 vaginal insert twice a week with 3 or 4 days between doses (2 vaginal inserts per week).

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



1. Wash your hands.

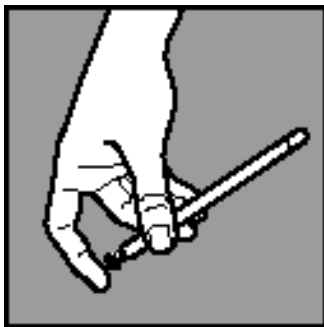


2. Push the Vagifem[®] 10 applicator through the foil backing (not through the plastic bubble) that says Vagifem[®] 10 and Novo Nordisk.

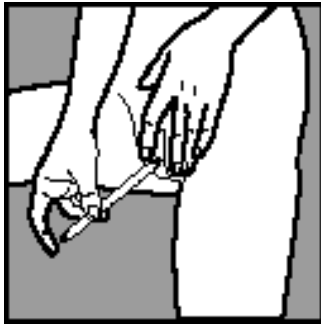


3. Choose the position that is most comfortable for you. You may want to:
 - sit on the edge of a chair with your knees apart,
 - stand up with one foot raised on the edge of the tub or bed,
 - squat,
 - lie down.

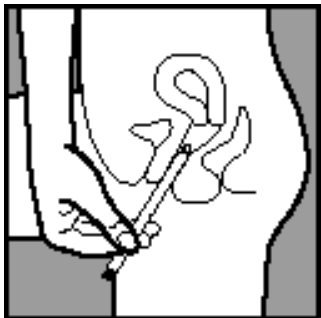
Inserting Vagifem[®] 10 is like inserting a tampon.



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 is expelled immediately after use, it is recommended to insert another vaginal insert.

Overdose:

No cases of overdose have been reported. In general, excessive doses of estrogen may result in nausea, vomiting, abdominal cramps, headache, dizziness, and general ill feeling (malaise). Call your doctor if you suspect an overdose.

If you think you have taken too much Vagifem[®] 10, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If a dose is forgotten, it should be taken as soon as the patient remembers. A double dose should be avoided.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The following adverse reactions have been reported with estrogen/progestin combination in general:

- Breast edema, breast enlargement, breast pain or pain tenderness
- Peripheral edema (swelling of arms or legs)

The following side effects were reported during clinical trials conducted on Vagifem[®] 10:

- Genital infection with a fungus or vaginal inflammation
- Headache
- Nausea
- Abdominal pain (stomach), distension or discomfort
- Vaginal bleeding, discharge or discomfort
- Back pain
- Weight gain

Although Vagifem[®] 10 is only used in the vagina to treat local urogenital symptoms of menopause, the risks associated with oral estrogen therapy in general should be taken into account.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Abdominal pain, nausea or vomiting		✓	
Unexpected vaginal bleeding		✓	
UNCOMMON			
Allergic reaction: Hives, itching, swelling, low blood pressure (paleness and coldness of skin, rapid heartbeat), sweating			✓
Genital infection with a fungus or vaginal inflammation	✓		
Breast lump		✓	
Heart attack: Crushing chest pain or chest heaviness			✓
Blood clot in the leg (deep vein thrombosis): Leg swelling or pain			✓
Depression: Persistent sad mood			✓
Blood clot in the lungs (pulmonary embolism): Pain in the chest, coughing blood, sudden shortness of breath, or difficulty in breathing			✓
Blood clot in the eye: Sudden partial or complete loss of vision			✓
Stroke: Sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech or weakness or numbness in face, arm or leg			✓
Jaundice: Yellowing of the skin or eyes			✓

These are not all the possible side effects of Vagifem® 10. For more information, ask your healthcare provider or pharmacist.

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect (<http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php>);
- By calling 1-866-234-2345 (toll-free);
- By completing a Patient Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 0701E
Ottawa, ON
K1A 0K9

Postage paid labels and the Patient Side Effect Reporting Form are available at MedEffect (<http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php>).

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.

HOW TO STORE IT

Keep out of the reach of children. Keep Vagifem[®] 10 at room temperature, between 15° and 25°C (59 - 77°F), away from heat and humidity. Do not refrigerate. Store away from direct sunlight. Do not store any of your medications near the cooking area of the kitchen, the shower area of the bathroom, or the glove compartment of your car as the temperature in these areas may go above normal room temperature from time to time.

Do not use Vagifem[®] 10 after the expiration date printed on the package.

Speak to your doctor or pharmacist if you have further questions after reading this information.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: <http://www.novonordisk.ca> or by contacting Novo Nordisk Canada Inc., at: 1-800-465-4334

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Last revised: March 2017