

PART III: CONSUMER INFORMATION**P^rESTRACE[®]**
(17 β -estradiol Tablets)

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

ABOUT THIS MEDICATION**What the medication is used for:**

- Symptomatic relief of menopausal symptoms (hot flashes, dryness, itching and burning in and around the vagina)
- ESTRACE[®] may also contribute to the prevention of osteoporosis, when combined with other important therapeutics such as diet, calcium and vitamin D intake, smoking cessation and regular physical weight bearing exercises. Osteoporosis is a thinning of the bones that makes them weaker and easier to break.

Use of ESTRACE[®] is to be considered in light of other available therapies for the prevention of postmenopausal osteoporosis. Adequate diet, calcium and vitamin D intake, cessation of smoking as well as regular physical weight bearing exercise are required in addition to the administration of ESTRACE[®].

ESTRACE[®] 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 replacement therapy (HRT) with your doctor. You should regularly talk with your doctor about whether you still need treatment with HRT.

Important

If you still have your uterus (womb), talk to your doctor about adding a progestin (another female hormone) to ESTRACE[®] to prevent cancer of the uterus.

What it does:

ESTRACE[®] replaces diminishing estrogen production by the body.

Estrogens are female hormones that are produced by the body and are necessary for the normal sexual development and the regulation of menstrual periods during the childbearing years.

Low estrogen levels in menopause can also cause osteoporosis, which is a thinning of the bones that make them weaker and easier to break. Estrogens can help prevent osteoporosis related to menopause.

When it should not be used:

You should not take ESTRACE[®] if you:

- have liver disease
- have (or have had) a personal history of known or suspected estrogen-dependent cancer such as cancer of the uterus (endometrial cancer)
- have abnormal growth of the lining of the uterus (endometrial hyperplasia)
- have (or have had) a personal history of known or suspected breast cancer
- have unusual or undiagnosed genital bleeding
- may be pregnant or are nursing
- have (or have had) a stroke or coronary heart disease (including heart attack and/or angina)
- have migraines
- have (or have had) blood clot disorders, including blood clots in the legs or lungs or thrombophlebitis (blood clot and inflammation of the veins).
- have partial or complete loss of vision due to blood vessel disease in the eye
- are allergic to estradiol or any other ingredient in ESTRACE[®] tablets (see **What the medicinal ingredient is** and **What the important nonmedicinal ingredients are**)

What the medicinal ingredient is:

17 β -estradiol

What the important nonmedicinal ingredients are:

Acacia, cornstarch, dibasic calcium phosphate, lactose, magnesium stearate, silicon dioxide, talc and colour dyes {FD&C Blue #1 and D&C Red #27 aluminum lake (1 mg tablet), FD&C Blue #1 and FD&C Yellow #5 aluminum lake (tartrazine) (2 mg tablet)}.

What dosage forms it comes in:

The dosage form is a tablet. ESTRACE[®] is provided in 0.5 mg, 1 mg and 2 mg strength tablets.

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 *estrogen-alone* therapy compared with placebo (a pill with no active ingredients) in postmenopausal women.

The WHI trial indicated an increased risk of myocardial infarction (heart attack), stroke, breast cancer, pulmonary emboli (blood clots in the lungs) and deep vein thrombosis (blood clots in the large veins) in postmenopausal women taking oral combined *estrogen plus progestin*.

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 developing invasive breast cancer, heart attack, stroke and blood clots in both lungs and large veins with the use of estrogen plus progestin therapy.
- 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.

Breast Cancer

The results of the WHI trial indicated an increased risk of breast cancer in post-menopausal women taking combined *estrogen plus progestin* compared to women taking placebo.

The results of the WHI trial indicated no difference in the risk of breast cancer in post-menopausal women with prior hysterectomy taking *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 hormone replacement therapy (HRT).

Women should have a mammogram before starting HRT 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 the technique for breast self-examination with your doctor.

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

The use of *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). If you still have your uterus you should take a progestin medication (another hormone drug) regularly for a certain number of days of each month to reduce the risk of endometrial hyperplasia.

You should discuss progestin therapy and risk factors for endometrial hyperplasia and endometrial carcinoma with your doctor. You should also report any unexpected or unusual vaginal bleeding to your doctor.

If you have had your uterus removed, you are not at risk of developing endometrial hyperplasia or endometrial carcinoma. Progestin therapy is therefore not generally required in women who have had a hysterectomy.

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 *estrogen plus progestin* compared to women taking placebo.

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

Abnormal Blood Clotting

The results of the WHI trial indicated an increased risk of blood clots in the lungs and large veins in post-menopausal women taking combined *estrogen plus progestin* compared to women taking placebo.

The results of the WHI trial indicated an increased risk of blood clots in the large veins, but no difference in the risk of blood clots in the lungs in post-menopausal women with prior hysterectomy taking *estrogen-alone* compared to women taking placebo.

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

Dementia

The Women’s Health Initiative Memory Study (WHIMS) was a substudy of the WHI trial and indicated an increased risk of dementia (loss of memory and intellectual function) in post-menopausal women age 65 and over taking oral combined *estrogen plus progestin* compared to women taking placebo.

The WHIMS indicated no difference in the risk of dementia in post-menopausal women age 65 and over with prior hysterectomy taking oral *estrogen-alone* compared to women taking placebo.

BEFORE you use ESTRACE® 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 (tissue from the endometrium, found outside the uterus (generally in the pelvic cavity)).
- 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 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 kidney disease, asthma or epilepsy (seizures)
- Have a history of bone disease (this includes certain metabolic conditions or cancers that can affect blood levels of calcium or phosphorus)
- Have been diagnosed with diabetes
- Have been diagnosed with porphyria (a disease of blood pigment)
- Have a history of high cholesterol or high triglycerides
- Are pregnant or may be pregnant
- Have had a hysterectomy (surgical removal of the uterus)
- Smoke
- Recent or future surgery

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with ESTRACE® include:

- Certain drugs used to:
 - Prevent blood clots
 - Control diabetes
 - Control high blood pressure
 - Prevent inflammation (containing phenylbutazone)
 - Control epilepsy (e.g. phenobarbital, phenytoin, or carbamazepine)
 - Control anxiety (e.g. meprobamate)

- Treat bacterial infection such as antibiotics containing rifampicin (also called rifampin)
- Grapefruit juice and some herbal products (e.g. St. John’s wort) available over-the-counter may also interact with ESTRACE®.

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:

Your doctor will prescribe the lowest dose of estrogen needed to prevent menopausal symptoms or the development of osteoporosis. Estrogen is usually administered for the first 21 days to 25 days of each month. Take one tablet of ESTRACE® at the same time each day.

- Treatment of menopausal symptoms: Initial treatment consists of a 1mg tablet per day. Every 3 to 6 months, you and your doctor should discuss whether you should reduce the dose of ESTRACE® or stop taking ESTRACE®.
- Prevention of osteoporosis: Initial treatment consists of a 0.5 mg tablet per day as soon as possible after menopause.

If your uterus has been removed (hysterectomy) you will take ESTRACE® every day of the month. If you have a uterus, you will take ESTRACE® on certain days of the month as directed by your doctor. You will also take a progestin on certain days of the month to prevent abnormal growth of the lining of your uterus. Your doctor may adjust the dose according to your individual needs.

Overdose:

In women, overdosage of ESTRACE® may cause nausea, breast discomfort, fluid retention, and vaginal bleeding. In case of overdose call the nearest hospital or poison control center.

Missed Dose:

If you miss a dose, take it as soon as possible. However, if it is almost time to take your next dose, skip the missed dose and go back to the regular dosing schedule. Do not double dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Women rarely have severe side effects from taking estrogens. However if you have any of the symptoms listed below you must speak with your doctor immediately.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Frequency (common or uncommon)	Symptom/possible side effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Abdominal pain, nausea or vomiting		✓	
Uncommon	Lumps or discharge from the breast		✓	✓
	Crushing chest pain or chest heaviness			✓
	Pain or swelling in the leg or feet			✓
	Pain in groin		✓	
	Persistent sad mood			✓
	Sharp pain in the chest, coughing blood or sudden shortness of breath			✓
	Sudden partial or complete loss of vision			✓
	Sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech or weakness or numbness in an arm or leg			✓
	Sudden loss of coordination			✓
	Unexpected vaginal bleeding		✓	
	Yellowing of the skin (jaundice)			✓

- Headaches (mild)
- Dizziness (mild)

Also, many women who are taking estrogens with a progestin will start having monthly vaginal bleeding, similar to menstrual periods again. This effect will continue for as long as the medicine is taken. However, monthly bleeding should not occur in women who have had their uterus removed by surgery (hysterectomy).

Other possible side effects

- Breast pain and swelling
- Irregular vaginal bleeding or spotting
- Vaginal itching/discharge or pain
- Depression, nervousness, and/or irritability
- Allergic reaction and rash
- Hair loss or abnormal hair growth
- Increased blood sugar levels
- Change in blood pressure
- Acne
- Change in cholesterol and/or triglyceride levels
- Change in weight

This is not a complete list of side effects. For any unexpected effects while taking ESTRACE®, contact your doctor or pharmacist.

HOW TO STORE IT

Store the bottle at room temperature (15°-30°C). Keep container tightly closed and protect from light. **Keep out of the reach of children.**

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs . If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345
toll-free fax 866-678-6789
By email: cadrmpp@hc-sc.gc.ca

By regular mail:
Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
Health Canada
Tunney's Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.

Side effects that usually do not need medical attention

These side effects go away during treatment as your body adjusts to the medicine. However, check with your doctor if they continue or become bothersome:

- Bloating
- Stomach cramps

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be obtained by contacting the sponsor, Shire Canada Inc., at: 1-800-268-2772

This leaflet was prepared by Shire Canada Inc.

Last revised: October 15, 2007.