PART III: CONSUMER INFORMATION

Premarin® Vaginal Cream
(Conjugated Estrogens CSD 0.625 mg/g)

IMPORTANT: PLEASE READ

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

ABOUT THIS MEDICATION

What the medication is used for:

- To treat vulvar and vaginal atrophy and kraurosis vulvae (itching, burning, dryness in or around the vagina, difficulty or burning on urination) associated with menopause.

- To treat dyspareunia (pain during intercourse) associated with menopause.

Premarin® Vaginal Cream should not be used by women with intact uteri unless it is prescribed in association with a progestin.

Premarin® Vaginal Cream 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 menopausal hormone therapy (MHT) with your doctor. You should regularly talk with your doctor about whether you still need treatment with MHT.

What it does:

When using Premarin® Vaginal Cream women are using a hormone, estrogen (i.e. conjugated estrogens CSD 0.625 mg/g). Premarin® Vaginal Cream replaces estrogen specifically in and around the vagina which naturally decreases at menopause.

Estrogens are female hormones that are produced by a woman's ovaries and are necessary for normal sexual development and the regulation of menstrual periods during the childbearing years.

When a woman is between the ages of 45 and 55, the ovaries normally stop making estrogens. This leads to a drop in body estrogen levels and marks the beginning of menopause (the end of monthly menstrual periods). A sudden drop in estrogen levels also occurs if both ovaries are removed during an operation before natural menopause takes place. This is referred to as surgical menopause.

When the estrogen levels begin dropping, some women develop very uncomfortable symptoms, such as feelings of warmth in the face, neck, and chest, or sudden intense episodes of heat and sweating ("hot flashes") as well as vaginal symptoms. In some women the symptoms are mild; in others they can be severe. These symptoms may last a few months or longer.

When it should not be used:

Before using Premarin® Vaginal Cream be sure to tell your doctor if you have any of the following medical problems, as Premarin® Vaginal Cream should not be used under these conditions:

- **Known, suspected, or past history of breast cancer.**
- **Known or suspected hormone-dependent cancer.** Estrogens may increase the chances of getting certain types of cancers, including cancer of the breast or uterus. If you have or had cancer, talk with your healthcare provider about whether you should take Premarin® Vaginal Cream.
- **Unexpected or unusual vaginal bleeding**
- **Have (or have had) blood clot disorders, including blood clots in the legs or lungs or thrombophlebitis (inflammation of the veins).**
- **Serious liver disease**
- **Active or past history of heart disease, heart attacks or stroke.**
- **If you are allergic to Premarin® Vaginal Cream or any of its ingredients, or have had any unusual reactions to its ingredients (see What the medicinal ingredients are and What the nonmedicinal ingredients are).**
- **If you are pregnant or suspect you may be pregnant.** Since pregnancy may be possible early in pre-menopause while you are still having spontaneous periods, the use of non-hormonal birth control should be discussed with your physician at this time. If you accidentally take estrogen during pregnancy, there is a small risk of your unborn child having birth defects.
- If you have partially or completely lost vision due to blood vessel disease of the eye.
- If you have overgrowth of the lining of the uterus.
- Have known abnormality of the blood clotting system that increases your risk for having a blood clot (e.g. protein C, protein S, or antithrombin deficiency).
- If you experience migraines with or without aura.

What the medicinal ingredients are:
Conjugated equine estrogens

What the nonmedicinal ingredients are:

The cream contains the following inactive ingredients: Cetyl Alcohol, Cetyl Esters Wax, Glycerin, Glyceryl Monostearate, Methyl Stearate, Mineral Oil, Phenylethyl Alcohol, Propyl Glycol

Monostearate, Sodium Lauryl Sulfate, Water Purified, White Wax.

What dosage forms it comes in:

Premarin® Vaginal Cream is available in tubes of 14 g and 30g, each gram containing 0.625 mg of conjugated estrogens CSD. Each tube is accompanied with one (14g tube) or two (30g tube) calibrated plastic applicators.

Serious Warnings and Precautions

In postmenopausal women taking *estrogen with progestin*, there is an increased risk of:

- Heart attack
- Stroke (bleeding or blot clot in the brain),
- Breast cancer,
- Pulmonary emboli (blood clots in the lungs), and
- Deep vein thrombosis (blood clots in the deep veins of the leg or arm).

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

- Stroke (bleeding or blot clot in the brain),
- Deep vein thrombosis (blood clots in the deep veins of the leg or arm).

Therefore, you should highly consider the following:

- 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.

WARNINGS AND PRECAUTIONS

Breast Cancer

There is an increased risk for breast cancer in women taking menopausal MHT for many years. The risk increases the longer you take MHT and persists for more than 10 years after stopping treatment with both *estrogen plus progestin* therapy and *estrogen-alone* therapy.

Talk to your doctor before starting MHT if you have:

- a family history of breast cancer or have had breast lumps, breast biopsies or abnormal mammograms (breast x-rays)
- Never had a baby before or had your first full-term pregnancy at an older age
- You are overweight
- You started menstruating at an early age

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

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

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

Ovarian Cancer

In some studies, the use of estrogen-alone and estrogen plus progestin therapies for 5 or more years has been associated with an 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 *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 Premarin® Vaginal Cream 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 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 and 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
- have been diagnosed with otosclerosis (hearing loss due to a problem with the bones in your ear)
- have been told that you have a condition called hereditary angioedema or if you have had episodes of rapid swelling of the hands, feet, face, lips, eyes, tongue, throat (airway blockage), or digestive tract.
- have been diagnosed with lupus.
- Premarin® Vaginal Cream may weaken and contribute to the failure of condoms, diaphragms, or cervical cap made of latex or rubber.

Other existing conditions you should discuss with your health professional include lupus, very low calcium levels, thyroid problems, fluid retention, gallbladder disease, depression, and breastfeeding. If you have upcoming surgery or prolonged bedrest, you should also discuss these.

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 (such as St. John's wort). Some medications (such as medications for high blood pressure, diabetes, blood clots, sleeping, anxiety, seizures, pain-relief and tuberculosis) may affect how Premarin® Vaginal Cream works. Premarin® Vaginal Cream may also affect how other medicines work.

You should also tell your doctor or pharmacist if you use latex or rubber diaphragms or cervical caps.

PROPER USE OF THIS MEDICATION

Usual Dose:
You should follow the dosage regimen prescribed by your healthcare provider.

Estrogens should be used at the lowest dose possible for your treatment only as long as needed. You and your healthcare provider should talk regularly (for example every 3 to 6 months) about the dose you are taking and whether you still need treatment with Premarin® Vaginal Cream.

Do not give Premarin® Vaginal Cream to other people, even if they have the same symptoms you have. It may harm them.

Instructions for Use of Applicator:
1. Remove cap.
2. Screw nozzle end of applicator onto the tube.
3. Gently squeeze tube to force sufficient cream into the barrel to provide the prescribed dose.
4. Unscrew applicator from tube.
5. Place the applicator into the vaginal opening.
6. To release medication, press plunger downward.

TO CLEANSE: Pull plunger out from barrel. Wash with mild soap and warm water. DO NOT BOIL.

Overdose:

If you think you, or a person you are caring for, have taken too much Premarin® Vaginal Cream, contact a healthcare professional, hospital emergency department, regional poison control center or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Overdosage with estrogens may cause nausea and vomiting, breast discomfort, fluid retention, bloating or vaginal bleeding may occur in women. There is no specific antidote and further treatment if necessary should be symptomatic.

Overdosage may result in a period of amenorrhea (lack of menses) of a variable length and may be followed by irregular menses for several cycles. No cases of overdosage in male patients have been reported.

Missed Dose:

If you miss a dose, use it as soon as possible. If it is almost time for your next dose, skip the missed dose and go back to your normal schedule. Do not use 2 doses at the same time.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects may include:

- Breast pain, leaking of milk from the nipple
- Inflammation of the vagina, vaginal itching and/or discharge
- Breakthrough bleeding, spotting, changes in menstrual flow, painful periods
- Joint pain, leg pain
- Hair loss
- Changes in weight (increase or decrease)
- Nausea, vomiting, bloating, abdominal pain
- Dizziness
- Headache (including migraine)
- Changes in libido
- Mood disturbances, irritability
- Rash, itching, hives, tender red nodules on the shins and legs, acne

If any of these affects you severely, tell your doctor, nurse or pharmacist.

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

Frequency	Symptom / possible side effect	Talk with your doctor or pharmacist		Stop taking drug and seek immediate medical help
		Only if severe	In all cases	
Common	**Blood clot:** Pain or swelling in the leg.			√
	Breast Cancer: Breast lump, unusual discharge.		√	
	Edema: Swelling of the hand and/or feet.	√		
	High Blood Pressure: headaches, dizziness, vision problems, shortness of breath		√	
	Persistent sad mood.			√
	Unexpected vaginal bleeding.		√	
Rare	**Blood clot in the lung:** Sharp pain in the chest, coughing blood or sudden shortness of breath.			√
	Stroke: Sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech or weakness or numbness in an arm or leg.			√
Very rare	**Blood clot in the eye:** Sudden partial or complete loss of vision.			√

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Frequency	**Symptom / possible side effect**	**Talk with your doctor or pharmacist**		**Stop taking drug and seek immediate medical help**
		Only if severe	**In all cases**	
Very rare	**Liver disorder:** Yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite.			√
Unknown	**Angioedema and Severe Allergic Reactions:** swelling of the face, eyes, or tongue, difficulty swallowing, wheezing, hives and generalized itching, rash, fever, abdominal cramps, chest discomfort or tightness, difficulty breathing, unconsciousness.			√
	Cerebrovascular insufficiency: visual disturbances, migraines, trouble speaking, paralysis or loss of consciousness.			√
	Gallbladder disorder: severe pain in the upper right abdomen, pain in the back between the shoulder blades, nausea and vomiting.		√	
Unknown	**Heart Attack:** Crushing chest pain or chest heaviness, pain in the arm, back, neck or jaw, shortness of breath, cold sweat, nausea, light-headedness.			√

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Frequency	**Symptom / possible side effect**	**Talk with your doctor or pharmacist**		**Stop taking drug and seek immediate medical help**
		Only if severe	**In all cases**	
	Heart palpitations	√		
	Increased blood sugar: frequent urination, thirst, and hunger.	√		
	Worsening of asthma: wheezing, coughing, shortness of breath, difficulty breathing			√

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

HOW TO STORE IT

Store Premarin® Vaginal Cream at 15° C to 30° C (room temperature).

Keep out of reach and sight of children.

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 (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

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

MORE INFORMATION

If you want more information about Premarin® Vaginal Cream:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Part III: Consumer Information by visiting the Health Canada Drud Product Database website (Drug Product Database: Access the database);the manufacturer's website (http//www.pfizer.ca) or by calling: 1-800-463-6001.

This leaflet was prepared by
Pfizer Canada ULC
17,300 Trans-Canada Highway
Kirkland, QC H9J 2M5

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