

PART III: CONSUMER INFORMATION

Premarin®
conjugated estrogens tablets CSD
0.3 mg, 0.625 mg, and 1.25 mg

IMPORTANT: PLEASE READ

This leaflet is part III of a three-part "Product Monograph" published when Premarin® 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®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

- To relieve menopausal and post-menopausal symptoms (vasomotor symptoms like hot flashes and night sweats).
- To prevent osteoporosis caused by low estrogen levels associated with menopause. Osteoporosis is a thinning of the bones that makes them weaker and easier to break.
- To treat certain types of abnormal uterine bleeding due to hormonal imbalance when your doctor has found no serious cause of the bleeding.
- To treat vulva and vaginal atrophy associated with menopause (itching, burning, dryness in or around the vagina, difficulty or burning on urination)

Premarin® tablets for the prevention of osteoporosis is recommended only for women who are at risk of developing this condition.—Talk to your doctor about whether a different treatment or medicine without estrogens might be better for you.

Adequate diet, calcium and vitamin D intake, cessation of smoking as well as regular weight-bearing exercise should be discussed with your doctor or pharmacist in addition to taking Premarin.

If you use Premarin® tablets only to treat symptoms of vulvar and vaginal atrophy associated with menopause, talk with your healthcare provider about whether a vaginal (topical) treatment might be better for you.

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

Premarin® 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.

What it does:

When taking Premarin® women are using a hormone, estrogen (i.e. conjugated equine estrogen tablets). Premarin® replaces estrogen in your body, 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"). In some women the symptoms are mild; in others they can be severe. These symptoms may last only a few months or longer. Taking Premarin® can alleviate these symptoms. If you are not taking estrogen for other reasons, such as the prevention of osteoporosis, you should take Premarin® only as long as you need it for relief from your menopausal symptoms.

After menopause, some women develop osteoporosis. This is a thinning of the bones that makes them weaker and allows them to break more easily, often leading to fractures of the vertebrae, hip and wrist bones.

Using Premarin® Tablets, in addition to taking adequate calcium (1000 milligrams to 1500 milligrams per day) and vitamin D, and regular weight-bearing exercise, slows down bone thinning and may prevent bones from breaking.

When it should not be used:

Before using Premarin® be sure to tell your doctor if you have any of the following medical problems, as Premarin® 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®.
- 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® 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 the 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.

What the medicinal ingredients are:

Conjugated equine estrogens

What the nonmedicinal ingredients are:

Each Premarin® Tablet contains the following nonmedicinal ingredients:

Calcium Sulphate Anhydrous, Carnauba Wax, Glyceryl Monooleate, Lactose, Magnesium Stearate, Methylcellulose, Microcrystalline Cellulose, Pharmaceutical Glaze, Polyethylene Glycol, Stearic Acid, Sucrose, Titanium Dioxide, Edible Ink

In addition, the following ingredients are contained in specific strengths as indicated:

Erythrosine Aluminum Lake (0.625 mg), Methyl Parahydroxybenzoate (0.3mg), Povidone (0.3mg, 0.625 mg), Propyl parahydroxybenzoate (0.3mg), Sodium Benzoate (0.3 mg, 0.625 mg), FD&C Blue No. 2 (0.3 mg, 0.625 mg), FD&C Yellow No. 6 (0.625 mg, 1.25 mg), Iron Oxide Yellow (0.3 mg), Quinoline Yellow Lake (1.25 mg)

What dosage forms it comes in:

Premarin® is available as tablets, as follows:
0.3 mg (green) tablets in bottles of 100, 500;
0.625 mg (maroon) tablets in bottles of 100, 1000;
1.25 mg (yellow) tablets in bottles of 100.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

The Women's Health Initiative (WHI) 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 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 postmenopausal 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 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-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 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.

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® 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
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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® works. Premarin® may also affect how other medicines work.

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®.

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

Overdose:

Contact your physician or local Poison Control Center in case of accidental ingestion of high doses of Premarin®.

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, take 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 take 2 doses at the same time.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Possible side effects include:

Common
≥ 1% and < 10% Breast pain;
Breakthrough bleeding; spotting; joint pain;
hair loss; changes in weight (increase or
decrease)

Uncommon
≥ 0.1% and < 1% Change in menstrual flow; nausea; bloating;
abdominal pain; dizziness; headache
(including migraine); changes in libido;
mood disturbances; rash; itching;
inflammation of the vagina

Rare
≥ 0.01% and <
0.1%

A spontaneous flow of milk from the nipple;
Painful periods; vomiting; irritability; hives;
worsening of asthma

Very Rare
< 0.01%

Tender red nodules on the shins and legs;
increase in blood pressure

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	Breast lump, unusual discharge.		✓	
	Pain or swelling in the leg.			✓
	Unexpected vaginal bleeding.		✓	
Uncommon	Abdominal pain, nausea or vomiting	✓		
	Persistent sad mood		✓	

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	
Rare	Shortness of breath, weakness, unusual fatigue, cold sweat, dizziness, sleep disturbance, indigestion, anxiety		✓	
	Sharp pain in the chest, coughing blood or sudden shortness of breath			✓
	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	Sudden partial or complete loss of vision			✓
	Yellowing of the skin or eyes		✓	

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

REPORTING SUSPECTED SIDE EFFECTS

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

By toll-free telephone: 866-234-2345
 By toll-free fax: 866-678-6789
 On-line: www.healthcanada.gc.ca/medeffect
 By email: CanadaVigilance@hc-sc.gc.ca

By regular mail
 Canada Vigilance National Office
 Marketed Health Products Safety and Effectiveness Information Division
 Marketed Health Products Directorate
 Health Products and Food Branch
 Health Canada
 Tunney's Pasture, AL 0701C
 Ottawa ON KIA 0K9

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

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:
<http://www.wyeth.ca/en>.

or by contacting the sponsor, Wyeth Canada, at:

1-800-461-8844

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HOW TO STORE IT

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

Keep out of reach of children.