PART III: CONSUMER INFORMATION

Premarin® Intravenous
Intravenous / Intramuscular
(Conjugated Estrogens for Injection, C.S.D.)

This leaflet is part III of a three-part "Product Monograph" published when Premarin Intravenous 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 Intravenous injected into a vein or a muscle. Contact your healthcare professional if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
Premarin Intravenous is used for the treatment of abnormal bleeding caused by hormonal imbalance when your healthcare professional has found no serious cause of the bleeding.

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

Premarin Intravenous should be used only under the supervision of a healthcare professional, 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 healthcare professional. Your healthcare professional may recommend some blood tests.

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

What it does:

When using Premarin Intravenous women are using a hormone, estrogen (i.e. conjugated estrogens for injection, C.S.D.). Premarin Intravenous replaces estrogens in your body, which naturally decrease 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 and abnormal bleeding. In some women the symptoms are mild; in others they can be severe. These symptoms may last a few months or longer. Premarin Intravenous can help treat abnormal bleeding caused by dropping levels of estrogens.

When it should not be used:
Before using Premarin Intravenous be sure to tell your healthcare professional if you have any of the following medical problems, as Premarin Intravenous should not be used under these conditions:

- Have a liver condition that has not returned to normal.
- Have a known, suspected or past history of breast cancer.
- Have a known or suspected hormone dependent cancer (e.g.endometrial cancer).
- Have unusual thickening of the lining of the womb (endometrial hyperplasia).
- You are or may be pregnant.
- You have unusual vaginal bleeding.
- Have or have had blood clot disorders, including blood clots in the legs or lungs, or inflammation of the veins (thrombophlebitis).
- Have active or past history of heart disease, heart attacks or stroke.
- Have partially or completely lost vision due to blood vessel disease of the eye.
- 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).
- Are allergic (hypersensitive) to conjugated estrogens or any of the other ingredients in Premarin Intravenous (including lactose).
- Have been diagnosed with a bleeding disorder.

What the medicinal ingredients are:
Conjugated Estrogens, CSD

What the nonmedicinal ingredients are:
Lactose, simethicone, and sodium citrate.

What dosage forms it comes in:
Premarin Intravenous is available in vials containing 25mg of powder.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

In postmenopausal women taking estrogen with progestin, there is an increased risk of:
- Heart attack
- Stroke (bleeding or blood 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 blood clot in the brain), and
- 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.

Breast Cancer

There is an increased risk of 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.

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

Talk to your healthcare professional 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

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

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

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 healthcare professional. You should also report any unexpected or unusual vaginal bleeding to your healthcare professional.
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 healthcare

professional 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 Intravenous 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 or liver tumors, 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 been diagnosed with otosclerosis (hearing loss due to a problem with the bones in your ear)
- have a history of high cholesterol or high triglycerides
- are pregnant or may be pregnant. If pregnancy occurs while taking Premarin Intravenous contact your healthcare professional immediately
- have had a hysterectomy (surgical removal of the uterus)
- smoke
- 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
- other existing conditions include very low calcium levels, thyroid problems, fluid retention and breastfeeding

INTERACTIONS WITH THIS MEDICATION

Tell your healthcare professional if you are taking any other medications, including prescription medications, over-the-counter medications, vitamins or herbal products. The following may interact with Premarin Intravenous:
- Blood thinners (drugs that prevent or reduce blood clots)
- Medicine to control your diabetes
- Medicine to control high blood pressure
- Barbiturates (class of sedatives)
- Hydantoins (anticonvulsants)
- Carbamazepine (anticonvulsant)
- Lamotrigine (anticonvulsant)
- Meprobamate (drug that treats tension, anxiety, and nervousness)
- Phenylbutazone (nonsteroidal anti-inflammatory drug)
- Rifampicin (antibiotic)
- St. John's Wort (Hyperticum perforatum)
- Phenobarbital (drug used to control seizures)
- Phenytoin (drug that can treat and prevent seizures)
- Dexamethasone (drug that can treat inflammation)
- Cimetadine (drug that can reduce acid in the stomach to treat ulcers and acid reflux)
- Erythromycin (antibiotic)
- Ketoconazole (drug that can treat fungal infection)
- Clarithromycin (antibiotic)
- Itraconazole (drug that can treat fungal infection)
- Ritonavir (drug used to treat HIV/AIDS)
- Grapefruit juice

Premarin Intravenous may interfere with laboratory testing.

PROPER USE OF THIS MEDICATION

Usual Adult Dose:
Your healthcare professional will inject Premarin Intravenous into a vein or a muscle.

You will receive one 25 mg dose. The dose may be repeated in 6 to 12 hours, if deemed necessary by your healthcare professional. Following this, your healthcare professional should begin treating you with lower doses of the medicine that you can take in pill form.

Overdose:

If you think you, or a person you are caring for, have taken too much Premarin Intravenous, contact a healthcare professional, hospital emergency department, regional poison control centre 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, dizziness, abdominal pain, drowsiness/fatigue or vaginal bleeding may occur in women.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects may include:

- Breast pain
- Vaginal bleeding or spotting
- Bloating, nausea, vomiting, abdominal pain
- Weight gain
- Dizziness
- Headache (including migraine)
- Nervousness
- Rash

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

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

Frequency	Symptom / possible side effect	Talk with your healthcare professional		Stop taking this drug and get immediate medical help
		Only if severe	In all cases	
Rare	**Inflammation of the Large Intestine (ischemic colitis):** abdominal pain, tenderness and/or cramping, blood in your stool, diarrhea, feeling of urgency to move your bowls, nausea			√

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

Frequency	Symptom / possible side effect	Talk with your healthcare professional		Stop taking this drug and get immediate medical help
		Only if severe	In all cases	
	Benign (non-cancerous) Brain Tumour: headache, seizures, blurred vision, weakness in arms or legs, numbness, trouble speaking			√
	Blood Clot in the Leg: pain, swelling, redness and tenderness in the leg			√
	Blood Clot in the Lung: sharp pain in the chest, coughing blood, sudden shortness of breath.			√
	Injection Site Reaction: pain, swelling, redness, tenderness		√	
	Edema: swelling of the hands, ankles and/or feet	√		
Very Rare	**Superficial Thrombophlebitis (blood clot in a vein just under the skin):** redness and inflammation along a vein, skin warm to the touch, pain, hardening of the vein			√

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

Frequency	Symptom / possible side effect	Talk with your healthcare professional		Stop taking this drug and get immediate medical help
		Only if severe	In all cases	
	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			√
	Low Blood Pressure: dizziness, fainting, lightheadedness May occur when you go from lying or sitting to standing up		√	
Unknown	**Breast Cancer:** breast lump, unusual discharge		√	
	Heart attack: crushing chest pain or chest heaviness, pain in the arm, back, neck or jaw, shortness of breath, cold sweat, nausea, light-headedness			√
	Persistent sad mood			√
	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 healthcare professional		Stop taking this drug and get immediate medical help
		Only if severe	In all cases	
	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			√
	Unexpected vaginal bleeding		√	
	Liver Disorder: yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite		√	
	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		√	

This is not a complete list of side effects. For any unexpected effects while taking Premarin Intravenous, contact your healthcare professional.

HOW TO STORE IT

Premarin Intravenous will be stored by your health care professional in the refrigerator between 2-8ºC.

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

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Consumer Information by visiting the Health Canada Drug Product Database website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (http//www.pfizer.ca); or by calling 1-800-463-6001.

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