PATIENT INFORMATION

This leaflet summarizes the major risks and benefits of treatment with PREMPRO or PREMPHASE. Read this PATIENT INFORMATION before using the product and each time you get medicine because there may be new information. Talk with your healthcare provider if you have any questions about this medicine.

What is PREMPRO or PREMPHASE?

PREMPRO or PREMPHASE is a combination of two hormones, an estrogen and a progestin.

What is PREMPRO or PREMPHASE used for?

The use of PREMPRO or PREMPHASE may increase your risk of getting breast cancer, blood clots, heart attacks, and strokes. PREMPRO and PREMPHASE should be used only as long as needed. Periodically, you and your healthcare provider should discuss whether you still need treatment.

PREMPRO and PREMPHASE should not be used to prevent heart disease.

PREMPRO and PREMPHASE are used

- **To reduce moderate to severe menopausal symptoms.**
  Estrogens are hormones produced by a woman's ovaries. Between the ages of 45 and 55, the ovaries normally stop making estrogens. This drop in body estrogen level causes the "change of life" or menopause (the end of monthly menstrual periods). Sometimes both ovaries are removed during an operation before natural menopause takes place. The sudden drop in estrogen levels causes "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" or "hot flushes"). In some women the symptoms are mild; in others they can be severe. Taking PREMPRO or PREMPHASE can help reduce these symptoms.

  Every 3 to 6 months you and your healthcare provider should discuss whether you still need PREMPRO or PREMPHASE to control your hot flushes.

- **To treat itching, burning, and dryness in and around the vagina due to menopause.**
  Every 3 to 6 months you and your healthcare provider should discuss whether you still need PREMPRO or PREMPHASE to control your vaginal symptoms.

- **To help reduce your chance of getting osteoporosis (thin weak bones).**
  Osteoporosis is a thinning of the bones that makes them weaker and allows them to break more easily.

  If you use PREMPRO or PREMPHASE only to prevent osteoporosis, discuss with your healthcare provider whether a different treatment might be more appropriate for you.

Women who have menopause at an early age, are thin, smoke and/or have a family history of osteoporosis are more likely to develop osteoporosis.

PREMPRO or PREMPHASE may be used as part of a program which includes weight-bearing exercise, like walking or running, and taking calcium and vitamin D supplements to reduce your chances of getting osteoporosis. Before you change your exercise habits or calcium or vitamin D intake, it is important to discuss these lifestyle changes with your healthcare provider to find out if they are safe for you. Before you make any change in your use of PREMPRO or PREMPHASE, talk with your healthcare provider.

During menopause, some women develop nervous symptoms or depression. Estrogens do not relieve these symptoms. You may have heard that taking estrogens for years after menopause will keep your skin soft and supple and keep you feeling young. There is no evidence for this.

Who should not take PREMPRO or PREMPHASE?

Do not take PREMPRO or PREMPHASE

- **If you think you may be pregnant.**
  Taking PREMPRO or PREMPHASE while you are pregnant may harm your unborn child. Do not take PREMPRO or PREMPHASE to prevent miscarriage.

- **If you have unusual vaginal bleeding.**
  Unusual vaginal bleeding can be a warning sign of a serious condition, including cancer of the uterus, especially if it happens after menopause. If you develop vaginal bleeding while taking PREMPRO or PREMPHASE, you may need further evaluation. Your healthcare provider needs to find out the cause of the bleeding so you can receive proper treatment. If you develop vaginal bleeding while taking PREMPRO or PREMPHASE talk with your healthcare provider about proper treatment.

- **If you have or had certain cancers.**
  Estrogens may increase the risk of certain types of cancer, including cancer of the breast or uterus. If you have or have had cancer, talk with your healthcare provider about whether you should take PREMPRO or PREMPHASE.

- **If you have or had blood clots, a heart attack, or a stroke.**
  Talk with your healthcare provider if you have or had these conditions, or if you have abnormal blood clotting conditions.

- **If you have recently had a baby.**
  PREMPRO and PREMPHASE can be passed to the nursing baby in the breastmilk. The effect of this on the baby is not known. Do not take PREMPRO or PREMPHASE to stop your breasts from filling with milk after a baby is born.

- **If you had your uterus removed.**
  PREMPRO or PREMPHASE contain a progestin to decrease the risk of developing endometrial hyperplasia (an overgrowth of the lining of the uterus that may lead to cancer).

In general, if you do not have a uterus, you do not need a progestin, and you should not take PREMPRO or PREMPHASE.

- **If you have liver problems.**
  Talk with your healthcare provider about your condition.

- **If you are allergic to PREMPRO or PREMPHASE or any of their ingredients.**

How should I take PREMPRO or PREMPHASE?

- Take 1 PREMPRO or PREMPHASE tablet each day at the same time.

- If you miss a dose, take it as soon as possible. However, 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.

PREMPRO comes in two strengths. Check with your healthcare provider periodically to make sure you are using the appropriate dose.

PREMPRO or PREMPHASE use may increase your risk of getting breast cancer, blood clots, heart attacks, and strokes. PREMPRO and PREMPHASE should be used only as long as needed. Periodically, you and your healthcare provider should discuss whether you still need treatment.

What are the possible risks and side effects of PREMPRO or PREMPHASE?

1. **Heart disease, stroke and blood clots**
   The use of PREMPRO or PREMPHASE may increase your chance of having a heart attack, a stroke, blood clots, a pulmonary embolus (a blood clot formed in the legs or pelvis that breaks off and travels to the lungs), retinal thrombosis (a clot in a blood vessel of the eye), or other blood clotting problems. Any of these conditions may cause death or serious long-term disability. These conditions have been seen in healthy, postmenopausal women, as well as in women with a history of heart disease.

2. **Cancer of the breast**
   Long-term use of PREMPRO or PREMPHASE may increase your chance of having breast cancer. Regular breast exams by a health professional and monthly self-exams are recommended for all women. Mammography should be scheduled depending on your age and risk factors.

3. **Cancer of the uterus**
   Estrogens increase the risk of getting a condition (endometrial hyperplasia) that may lead to cancer of the lining of the uterus. The risk of cancer of the uterus increases when estrogens are used alone, the longer they are used, and when larger doses are taken. Taking progestins with estrogens lowers the risk of getting this condition. PREMPRO and PREMPHASE contain estrogen and progestin.

4. **Ovarian cancer**
   Some studies suggest that there is a greater risk of ovarian cancer in women who have used estrogen alone for a long period of time, especially 10 years or more. Other studies have not shown this risk. The risk with PREMPRO or PREMPHASE treatment is unclear.

5. **Vaginal bleeding**
   If you develop vaginal bleeding while taking PREMPRO or PREMPHASE, discuss your bleeding pattern with your healthcare provider. This is because vaginal bleeding after menopause may be a warning sign of a serious condition, including cancer of the uterus.

6. **Gallbladder disease**
   Women who use PREMPRO or PREMPHASE after menopause are more likely to develop gallbladder disease needing surgery than women who do not use estrogens.

7. **Blood pressure**
   Some women who are taking PREMPRO or PREMPHASE may have increases in blood pressure.

8. **Liver problems**
   If you had yellowing of your skin or eyes associated with pregnancy, or with taking estrogens (eg, oral contraceptives), this condition may occur again with PREMPRO or PREMPHASE treatment.

9. **Hypothyroidism**
   Women who are taking PREMPRO or PREMPHASE, and who use thyroid replacement therapy may require increased doses of their thyroid medication.

10. **Effects on blood sugar**
    Taking PREMPRO or PREMPHASE may affect blood sugar levels, which might make a diabetic condition worse.

11. **Other conditions**
    Fluid retention due to PREMPRO or PREMPHASE treatment may make some conditions worse, such as heart disease or kidney disease. Estrogen treatment may also worsen asthma, epilepsy, migraine, porphyria and endometriosis.

In addition to the risks listed above, the following common side effects have been reported with estrogen and/or progestin use:

- Nausea, vomiting, pain, cramps, swelling, or tenderness in the abdomen.
- Breast tenderness or enlargement, pain or discharge.
- Enlargement of benign tumors ("fibroids") of the uterus.
- Change in amount of cervical secretion.
- Vaginal yeast infections.

- A spotty darkening of the skin, particularly on the face; reddening of the skin; skin rashes.
- Retention of fluid (edema).
- Headache, migraines, dizziness, or changes in vision (including intolerance to contact lenses).
- Mental depression.
- Involuntary muscle spasms.
- Hair loss or abnormal hairiness.
- Increase or decrease in weight.
- Changes in sex drive.

What can I do to lower my chances of getting a serious side effect with PREMPRO or PREMPHASE?

If you take PREMPRO or PREMPHASE you can reduce your risks by doing these things:

· **See your healthcare provider regularly.**

Check with your healthcare provider to make sure you do not stay on treatment longer than needed. While you are taking PREMPRO or PREMPHASE, it is important to visit your healthcare provider at least once a year for a checkup. If you develop vaginal bleeding while taking PREMPRO or PREMPHASE, you may need further evaluation. Every 3 to 6 months you and your healthcare provider should discuss whether or not you still need PREMPRO or PREMPHASE to control your hot flushes and vaginal symptoms.

You should talk with your healthcare provider about stopping PREMPRO or PREMPHASE 4 to 6 weeks before surgery or during prolonged bedrest.

If members of your family have had breast cancer or if you have ever had breast lumps or an abnormal mammogram (breast X-ray), you may need to have more frequent breast examinations. Examine your breasts for changes every month.

· **Be alert to signs of trouble.**

If any of the following warning signals (or any other unusual symptoms) happen while you are using PREMPRO or PREMPHASE, call your healthcare provider immediately:

- Abnormal bleeding from the vagina (possible uterine abnormality/cancer).
- Pains in the calves or chest, a sudden shortness of breath or coughing blood (indicating possible clots in the legs, heart, or lungs).

- Severe headache or vomiting, dizziness, faintness, or changes in vision or speech, weakness or numbness of an arm or leg (indicating possible clots in the brain [stroke] or eye).

- Breast lumps (possible breast cancer). Ask your healthcare provider to show you how to examine your breasts.

- Yellowing of the skin and/or whites of the eyes (possible liver problems).

- Pain, swelling, or tenderness in the abdomen (possible gallbladder problem).

Other information

1. Your healthcare provider prescribed this drug for you and you alone. Do not give this drug to anyone else.

2. Keep this and all drugs out of reach of children. In case of overdose, call your doctor or healthcare provider, hospital, or poison control center right away.

HOW SUPPLIED
PREMPRO™ therapy consists of a single tablet to be taken once daily.

PREMPRO 0.625 mg/2.5 mg
Each carton includes 3 EZ DIAL™ dispensers containing 28 tablets. One EZ DIAL dispenser contains 28 oval, peach tablets containing 0.625 mg of the conjugated estrogens found in Premarin® tablets and 2.5 mg of medroxyprogesterone acetate for oral administration.

PREMPRO 0.625 mg/5 mg
Each carton includes 3 EZ DIAL dispensers containing 28 tablets. One EZ DIAL dispenser contains 28 oval, light-blue tablets containing 0.625 mg of the conjugated estrogens found in Premarin tablets and 5 mg of medroxyprogesterone acetate for oral administration.

PREMPHASE® therapy consists of two separate tablets; one maroon Premarin tablet taken daily on days 1 through 14 and one light-blue tablet taken on days 15 through 28.

Each carton includes 3 EZ DIAL dispensers containing 28 tablets. One EZ DIAL dispenser contains 14 oval, maroon Premarin tablets containing 0.625 mg of conjugated estrogens and 14 oval, light-blue tablets that contain 0.625 mg of the conjugated estrogens found in Premarin tablets and 5 mg of medroxyprogesterone acetate for oral administration.

The appearance of PREMPRO tablets is a trademark of Wyeth-Ayerst Laboratories.

The appearance of Premarin tablets is a trademark of Wyeth-Ayerst Laboratories. The appearance of the conjugated estrogens/medroxyprogesterone acetate combination tablets is a registered trademark.

Keep out of reach of children.

Store at controlled room temperature 20°C - 25°C (68°F - 77°F).

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® Ayerst Laboratories
A Wyeth-Ayerst Company
Philadelphia, PA 19101

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