



Media Statement:  
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**Pfizer Response to Results from the  
Kronos Early Estrogen Prevention Study**

NEW YORK, N.Y., Oct. 3, 2012 - Findings from the Kronos Early Estrogen Prevention Study (KEEPS), presented today at The North American Menopause Society (NAMS) Annual Meeting in Orlando, Fla., show that among early menopausal women, neither PREMARIN® (conjugated estrogen tablets USP) nor an estrogen patch (Climara® estradiol transdermal system), both given with a progestogen, changed the rate of progression of atherosclerotic cardiovascular disease, as measured by carotid intima media thickness (CIMT). The Kronos Early Estrogen Prevention Study was sponsored by the Kronos Longevity Research Institute.

Heart disease risk increases with age, and, for women, the risk may increase more rapidly after menopause. The Kronos Early Estrogen Prevention Study was initiated in September 2005 to determine whether women who begin hormone therapy in the early years of menopause may derive a cardiovascular benefit.

The study followed 727 nonhysterectomized, postmenopausal women between the ages of 42 and 59 for four years. Women were randomly assigned Premarin (0.45 mg daily), Climara (50 mcg daily) or placebo. Women receiving Premarin or Climara also received Prometrium® (progesterone, USP, capsules 200 mg cyclically). The overall incidence of adverse events was low, and similar, among the three arms of the study.

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Pfizer applauds the efforts of the Kronos Longevity Research Institute and those of the broader scientific community to investigate the potential effects of hormone therapy on younger postmenopausal women. Studies like KEEPS generate new hypotheses that help inform the scientific community's exploration of women's health.

The Kronos Early Estrogen Prevention Study was designed to look for potential cardiovascular benefits of hormone therapy in women treated early after menopause; however, the study was not large enough to assess health outcomes such as heart attack, and focused rather on a marker of atherosclerotic cardiovascular disease, the rate of change in CIMT. In addition, KEEPS was not designed to test the efficacy or safety of hormone therapy in the treatment of menopausal symptoms. The results of KEEPS support that the benefit-risk profiles of oral and patch (transdermal) hormone therapy may be similar. The labeling of all hormone therapy products includes a boxed warning against the use of hormone therapy for the prevention of cardiovascular disease.

Hormone therapy has been described by the U.S. Food and Drug Administration (FDA) as the most effective FDA-approved medicine for the relief of hot flashes, night sweats or vaginal dryness associated with menopause. Estrogen-alone therapy can increase the chance of getting cancer of the uterus in nonhysterectomized women. Adding a progestogen reduces this risk. The benefit-risk profile of hormone therapy is well established for the treatment of vasomotor symptoms. There is an increased risk of pulmonary embolism, deep vein thrombosis, stroke, breast cancer and myocardial infarction with estrogen-plus-progestogen therapy.

As with any prescription medication, the decision to initiate hormone therapy - and the route of administration - should be made in close collaboration with a healthcare provider, carefully weighing the patient's risk factors, including lifestyle and

family medical history. The science-based guidance in the package inserts of all hormone therapy products advises healthcare providers to prescribe the medicine at the lowest effective dose and for the shortest duration, consistent with treatment goals and risks for the individual woman.

Premarin® is the most-prescribed branded estrogen therapy in the United States. Premarin is used to reduce moderate-to-severe hot flashes; treat moderate-to-severe dryness, itching and burning in and around the vagina; and to help reduce the chances of getting osteoporosis, associated with menopause. When prescribed for women with a uterus, the addition of a progestogen is generally recommended to reduce the risk of endometrial hyperplasia, a precursor to endometrial cancer.

#### **IMPORTANT SAFETY INFORMATION**

**Using estrogen-alone may increase your chance of getting cancer of the uterus (womb). Report any unusual vaginal bleeding right away while you are using PREMARIN. Vaginal bleeding after menopause may be a warning sign of cancer of the uterus (womb). Your healthcare provider should check any unusual vaginal bleeding to find out the cause.**

**Do not use estrogens, with or without progestins, to prevent heart disease, heart attacks, strokes or dementia (decline in brain function). Using estrogens, with or without progestins, may increase your chance of getting dementia, based on a study of women 65 years of age or older.**

**Using estrogen-alone may increase your chances of getting strokes or blood clots. Using estrogens with progestins may increase your chances of getting heart attacks, strokes, breast cancer, or blood clots.**

**You and your healthcare provider should talk regularly about whether you still need treatment with PREMARIN.**

PREMARIN should not be used if you have unusual vaginal bleeding; have or had cancer; had a stroke or heart attack; have or had blood clots or liver problems; have a bleeding disorder; are allergic to any of its ingredients; or think you may be pregnant. In general, the addition of a progestin is recommended for women with a uterus to reduce the chance of getting cancer of the uterus.

In a clinical trial, the most commonly reported ( $\geq 5\%$ ) side effects that occurred more frequently with PREMARIN than with placebo were vaginitis due to yeast or other causes, vaginal bleeding, painful menstruation, and leg cramps.

#### INDICATIONS

PREMARIN is used after menopause to reduce moderate to severe hot flashes; to treat moderate to severe dryness, itching, and burning, in and around the vagina; and to help reduce the chances of getting osteoporosis (thin weak bones).

If you are using or are considering using PREMARIN only to treat symptoms of vaginal dryness, consider topical therapies first. If you are using or are considering using PREMARIN only to prevent osteoporosis due to menopause, talk with your health care professional about whether a different treatment or medicine without estrogens might be better for you. PREMARIN should be used at the lowest effective dose and for the shortest duration consistent with your treatment goals and risks.

Please see Full Prescribing Information including Boxed Warning and Patient Information on [www.premarin.com](http://www.premarin.com).

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