PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

PREMARIN® 0,3 mg tablet

PREMARIN® 0,625 mg tablet

PREMARIN® 1,25 mg tablet

Conjugated estrogens

Contains sugar (lactose monohydrate and sucrose)

Each PREMARIN 0,3 mg tablet contains 61,7 mg lactose monohydrate and 45,0 mg sucrose

Each PREMARIN 0,625 mg tablet contains 54,1 mg lactose monohydrate and 45,0 mg sucrose

Each PREMARIN 1,25 mg tablet contains 120,3 mg lactose monohydrate and 115,0 mg sucrose

Read all of this leaflet carefully before you start taking PREMARIN

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- PREMARIN has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What PREMARIN is and what it is used for

PREMARIN is a Hormone Replacement Therapy (HRT) and contains the female hormone estrogen.

PREMARIN is used to treat some of the symptoms and conditions associated with the menopause, such as hot face, neck and chest ("hot flushes") and to treat the thinning, inflammation and/or decreased lubrication of the vaginal walls.

After the menopause some women may be at risk of developing fragile bones (osteoporosis). PREMARIN is used to manage and prevent osteoporosis in these women.

PREMARIN is also used

- to treat certain conditions in women before menopause if their ovaries do not make enough estrogen naturally
- to ease symptoms of certain cancers that have spread through the body, in men and women

2. What you need to know before you take PREMARIN

Do not take PREMARIN:

- if you are hypersensitive (allergic) to conjugated estrogens or any of the other ingredients of PREMARIN (listed in section 6)
- if you are pregnant or think you may be pregnant
- if you have undiagnosed abnormal genital bleeding
- if you have or have had breast cancer
- if you have a family history of breast cancer
- if you have a history of non-cancerous breast disease
- if you had any previous treatment using radiation therapy to the chest or breast
- if you have had a stroke or heart attack
- if you have had blood clots in your veins or lungs
- if you have an inherited disorder that affects your blood clotting
- if you have been diagnosed with a bleeding disorder
- if you have endometriosis, a problem with the lining of your womb (the endometrium), often causing pelvic pain

- if you have liver problems
- if you are known to have inherited genetic changes called “BRCA1 and/or BRCA2 genes”
- if you started your menstrual periods before the age of 12 years
- if you have been treated or exposed while in your mother’s womb to a medicine called diethylstilbestrol (DES)

Warnings and precautions

Take special care with PREMARIN:

- PREMARIN has been associated with an increased risk of stroke and blood clots. Should these occur or be suspected, you should stop taking PREMARIN and contact your doctor immediately.
- PREMARIN may increase the risk of certain types of cancers (e.g. breast cancer, endometrial cancer and ovarian cancer). If you have risk factors for developing any of these conditions, you doctor may keep you under careful observation.

PREMARIN and breast cancer

Breast cancer has been diagnosed slightly more often in women who use menopausal hormone therapy than in women of the same age who do not use menopausal hormone therapy. After stopping use of menopausal hormone therapy, some excess risk for breast cancer persisted after 10 years. When you are taking PREMARIN, you must perform monthly breast self-examinations. Your doctor will advise you on when to report for breast examinations and any appropriate investigations.

There is some evidence of a higher risk of getting dementia in women who start using PREMARIN after the age of 65, however it is unknown whether these findings apply to younger women.

Make sure your doctor knows:

- if you have problems with your gallbladder
- if you experience sudden unexplained changes in vision
- if you develop migraines or suffer from worsening migraine headaches
- if you have high levels of calcium in your blood

- if you have angioedema (swelling that occurs below the surface of the skin especially around the face, lips or tongue)
- if you suffer from water retention as this may affect other conditions you have
- if you have hypertriglyceridaemia (high levels of fatty substances in your blood), as this can lead to inflammation of the pancreas
- if you have problems with your liver
- if you have a history of jaundice (a yellowing of the skin and eyes) associated with past estrogen use or with pregnancy
- if you have excessive thickening of the lining of the womb (endometrial hyperplasia)
- if you have high blood pressure
- if you have asthma
- if you have epilepsy
- if you have diabetes mellitus
- if you have porphyria (a disorder that can cause nerve or skin problems)
- if you have lupus (an autoimmune disease that causes tiredness, joint pain, rash and fever)
- if you have a non-cancerous liver tumour
- if you have endometriosis (cells similar to the lining of the uterus growing outside the uterus, causing pain or bleeding)
- if you have low calcium levels in your blood (often causing muscle cramps)
- if you have an underactive thyroid gland
- if you develop abnormal uterine bleeding

You should stop taking PREMARIN at least 4 to 6 weeks before undergoing surgery or if you are unable to walk for a long time because of major surgery, injury or illness,

Hormonal contraceptives, including PREMARIN, may cause mood changes and depression, which may be severe. Severe depression is associated with a higher risk of suicidal thoughts/behaviour (e.g. talking about suicide, withdrawing from social contact, having mood swings, being preoccupied with death or violence, feeling hopeless about a situation, increasing use of alcohol/drugs, doing self-destructive

things, personality changes) and suicide. If you experience mood changes and depression contact your health care provider for advice.

Other medicines and PREMARIN

Always tell your health care provider if you are taking any other medicine. (This includes complementary or traditional medicines.) If you are taking medicines on a regular basis, concomitant use of the medicine may cause undesirable interactions.

PREMARIN may affect the action of other medicines and sometimes PREMARIN is affected by other medicines. These may include:

- St. John's Wort (*Hypericum perforatum)* used to treat depression
- Anti-epileptic medicines including phenobarbital, phenytoin or carbamazepine
- Immunosuppressive medicines such as dexamethasone
- Antibiotics, antifungal or antiviral medicines used to treat infection e.g. rifampicin, erythromycin, clarithromycin, ketoconazole, itraconazole, and ritonavir
- Medicines used to treat ulcers or other gastrointestinal disorders such as cimetidine

PREMARIN can affect some laboratory test results therefore please tell your doctor you are taking PREMARIN before any blood tests are taken.

PREMARIN with food and drink

You should not drink grapefruit juice while taking PREMARIN, as this may result in side effects. PREMARIN may also impair your tolerance to glucose, a type of sugar.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

PREMARIN should not be used during pregnancy or breastfeeding.

The estrogen hormones in PREMARIN can pass into your breast milk.

Driving and using machines

No studies on the effect of ability to drive or use machines have been performed.

It is not always possible to predict to what extent PREMARIN may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which PREMARIN affects them.

PREMARIN contains lactose monohydrate and sucrose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine. PREMARIN contains sucrose, this should be taken into account in patients with diabetes mellitus.

3. How to take PREMARIN

Do not share medicines prescribed for you with any other person.

Always take PREMARIN exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Your prescription of PREMARIN may be continuous (i.e. without a break in therapy) or cyclic (e.g. three weeks on and one week off). Continuous daily administration of PREMARIN is generally recommended.

Usual dosage ranges

For treatment of moderate to severe symptoms associated with the menopause

Vasomotor symptoms (e.g., hot face, neck and chest, “hot flushes”) and atrophic vaginitis (thinning, inflammation and decreased lubrication of the vaginal walls): 0,3 mg to 1,25 mg daily depending on your response to the medicine.

Prevention and management of osteoporosis

0,625 mg to 1,25 mg daily, depending on your response to the medicine.

Lower than normal level of estrogen due to:

Female hypogonadism (below normal development of genital organs): 1,25 mg to 7,5 mg daily, administered cyclically (e.g., three weeks on and one week off).

Female castration or primary ovarian failure (certain conditions in women before menopause if their ovaries do not make enough estrogen naturally or ovaries have been removed): 1,25 mg daily, cyclically.

Advanced hormone-dependent cancers

Easing the symptoms of prostatic cancer: 1,25 mg to 2,5 mg PREMARIN three times daily.

Easing the symptoms of breast cancer: up to 10 mg PREMARIN three times daily for a period of at least three months.

Children

PREMARIN should not be used in children.

Your doctor will tell you how long your treatment with PREMARIN will last. Do not stop treatment early. If you have the impression that the effect of PREMARIN is too strong or too weak, tell your doctor or pharmacist.

If you take more PREMARIN than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

Symptoms of overdosage may include nausea, vomiting, breast tenderness, dizziness, abdominal pain, drowsiness/fatigue; withdrawal bleeding may occur in females.

If you forget to take a dose of PREMARIN

Do not take a double dose to make up for forgotten individual doses.

4. Possible side effects

PREMARIN can have side effects.

Not all side effects reported for PREMARIN are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking PREMARIN, please consult your health care provider for advice.

If any of the following happens, stop using PREMARIN and tell your doctor immediately or go to the casualty department at your nearest hospital:

- severe allergic reaction including swelling of the hands, feet, ankles, face, lips, mouth or throat which may cause difficulty in swallowing or breathing
- stroke (symptoms of which may be facial drooping, weakness on side of the body, speech difficulties)
- heart attack (symptoms of which may be tightness or pain in the chest, neck, back or arms, tiredness, sweating)

Tell your doctor if you notice any of the following:

Frequent side effects

- hair loss
- joint pain
- leg cramps
- irregular vaginal bleeding or spotting
- breast pain
- breast tenderness

- breast enlargement
- discharge from the breast
- vaginal discharge
- changes in weight (increase or decrease)
- increased triglycerides (fatty substances in the blood)

Less frequent side effects

- vaginal inflammation, burning, irritation and itching
- vaginal yeast infections
- breast cancer
- cancer of the ovary
- painful lumps in the breasts
- increased risk of growth of a tumour of the membranes around the brain or spinal cord
- cancer of the lining of the uterus (womb)
- enlargement of a non-cancerous tumour in the liver
- red itchy bumps on the skin
- high blood sugar
- worsening of porphyria (often causing dark urine, mental disturbances and extreme sensitivity of the skin to light)
- low calcium levels in the blood
- changes in sex drive
- mood changes
- depression
- memory loss (dementia)
- irritability
- dizziness
- headache
- migraine
- nervousness

- worsening of epilepsy
- worsening of chorea (a disorder characterised by jerky involuntary movements)
- discomfort wearing contact lenses
- blockage of the small veins in the eye causing blurred or loss of vision
- blood clot in the lungs
- blood clot in the deep veins of the leg, groin or arm
- inflammation of the veins
- worsening of asthma
- nausea
- bloating
- stomach pain
- vomiting
- inflammation of the pancreas
- inflammation of the large intestine
- gallbladder disease
- jaundice (yellowing of the skin and eyes)
- dark, discoloured patches on the skin, often on the face
- male-pattern hair growth in women
- skin rash
- tender, red bumps, particularly on the shins
- change in menstrual flow
- change in vaginal secretion (caused by changes in the cervix)
- painful menstruation/pelvic pain
- excessive or inappropriate production of milk
- enlargement of benign tumours of the uterus (fibroids)
- a thickening of the lining of your womb
- enlargement of breasts in males
- fluid retention
- increase in blood pressure

- suicidal thoughts/behaviour and suicide

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting side effects

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of PREMARIN.

5. How to store PREMARIN

- Store all medicines out of the of children.
- Store in a cool, dry place at or below 25 °C.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g., toilets).

6. Contents of the pack and other information

WHAT PREMARIN CONTAINS:

- The active substance is conjugated estrogens. Each PREMARIN tablet contains 0,3 mg, 0,625 mg and 1,25 mg of conjugated estrogen respectively.
- The other ingredients in the tablets are hypromellose, lactose monohydrate, magnesium stearate and microcrystalline cellulose.

The tablet coating contains hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, Opadry green 15B21511 (0,3 mg tablet), Opadry maroon 03B16083 (0,625 mg tablet), Opadry yellow 15B32143 (1,25 mg tablet), polyethylene glycol and sucrose.

The polish and printing ink contains: carnauba wax, hypromellose, Opacode WB NS-78-18011 white ink (0,3 mg and 0,625 mg tablet) and Opacode NS-78-17821 black ink (1,25 mg tablet).

What PREMARIN looks like and contents of the pack

PREMARIN tablets are sugar coated.

PREMARIN 0,3 are oval, green and biconvex, coated tablets branded “0,3” in white ink.

PREMARIN 0,625 are oval, maroon and biconvex, coated tablets branded “0,625” in white ink.

PREMARIN 1,25 are oval, yellow and biconvex, coated tablets branded “1,25” in black ink.

PREMARIN 0,3: Blister packs (clear or opaque PVC/Aclar/PVC/Al) of 28’s.

PREMARIN 0,625: Blister packs (clear or opaque PVC/Aclar/PVC/Al) of 28’s.

PREMARIN 1,25: Blister packs (clear or opaque PVC/Aclar/PVC/Al) of 28’s.

Holder of Certificate of Registration

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9. REGISTRATION NUMBERS:

PREMARIN 0,3: G/21.8.1/3016

PREMARIN 0,625: G/21.8.1/3015

PREMARIN 1,25: G/21.8.1/3014