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Package Leaflet: Information for the user

Conjugated Estrogens Vaginal Cream

0.625 mg Cream

Premarin® Vaginal Cream

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- If you have any further questions, ask your doctor.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Premarin (Conjugated Estrogens) vaginal cream is and what it is used for
2. What you need to know before you use Premarin (Conjugated Estrogens) vaginal cream
3. How to use Premarin (Conjugated Estrogens) vaginal cream
4. Possible side effects
5. How to store Premarin (Conjugated Estrogens) vaginal cream
6. Contents of the pack and other information

1. What Premarin (Conjugated Estrogens) vaginal cream is and what it is used for

What Premarin (Conjugated Estrogens) vaginal cream is

Conjugated estrogen vaginal cream contains a mixture of conjugated equine estrogens obtained exclusively from natural sources, occurring as the sodium salts of water-soluble estrogen sulfates blended to represent the average composition of material derived from pregnant mares' urine. It is a mixture of sodium estrone sulfate and sodium equilin sulfate. It contains as concomitant components, as sodium sulfate conjugates, 17 α -dihydroequilin, 17 α -estradiol, and 17 β -dihydroequilin.

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What Premarin (Conjugated Estrogens) vaginal cream is used for

Conjugated estrogen vaginal cream is used in the treatment of atrophic vaginitis, dyspareunia and kraurosis vulvae (associated with the menopause).

2. What you need to know before you use Premarin (Conjugated Estrogens) vaginal cream

Do not use Premarin (Conjugated Estrogens) vaginal cream

- If you are allergic to conjugated estrogens or any of the other ingredients of this medicine (listed in section 6).
- If you have liver dysfunction or disease as long as liver function tests have failed to return to normal.
- If you have known or suspected pregnancy.
- If you have any unexplained uterine bleeding.
- If you have known, suspected or past breast cancer.
- If you have known or suspected estrogen dependent malignant neoplasia (e.g., endometrial cancer)
- If you have endometrial hyperplasia.
- If you have active or history of arterial thromboembolic disease. (e.g., stroke, myocardial infarction) or venous thromboembolism (such as deep venous thrombosis, pulmonary embolism).
- If you have partial or complete loss of vision due to ophthalmic vascular disease.
- If you have known thrombophilic disorders (e.g., protein C, protein S OR antithrombin deficiency); prothrombin mutation or anticardiolipin antibodies).
- If you have migraine with or without aura.

If any of the above conditions appear for the first time while using Premarin vaginal cream, stop using it at once and consult your doctor immediately.

Warnings and precautions

Tell your doctor before using Premarin (Conjugated Estrogens) vaginal cream if you have ever had any of the following problems:

- If you have risk factors for thrombotic disorders
- If you have risk factors for heart (cardiovascular) disease [e.g., hypertension (high blood pressure), diabetes mellitus, tobacco use, hypercholesterolemia (increased cholesterol), and obesity]. The use of *estrogen plus progestin* is associated with an increased risk of coronary heart disease (CHD) in postmenopausal women

- If you are at risk of developing migraines with aura may be at risk of ischemic stroke and should be kept under careful observation.
- If you have had a history or are prone to Venous Thromboembolism (a condition that occurs when a blood clot forms in a vein) and Pulmonary Embolism (a blockage in one of the pulmonary arteries in your lungs); and stroke
- If there is an increased risk of getting an estrogen-sensitive cancer (endometrial, breast or ovarian cancer)
- If you have or have had gallbladder disease or gallstones
- If you have a risk of developing probable dementia (a group of symptoms affecting memory, thinking and social abilities severely enough to interfere with your daily life)
- If you have a risk of developing retinal vascular thrombosis (happens when a blood clot blocks the retinal vein in the eye)
- If you have or have had a history of cholestatic jaundice (retention of the constituents of bile in blood)
- If you feel an exacerbation of asthma (the airways become swollen and inflamed), epilepsy (fits), migraine, diabetes mellitus, systemic lupus erythematosus and hepatic hemangiomas (non-cancerous mass in the liver made up of a tangle of blood vessels)
- If you face hypocalcemia (decreased calcium) and hypothyroidism (decreased thyroid levels)
- May lead to weaken latex condoms, and lead to condom and diaphragm failure

Stop using Premarin (Conjugated Estrogens) vaginal cream and see a doctor immediately:

If you notice any of the following when using Premarin (Conjugated estrogens) vaginal cream:

- Any of the conditions mentioned in the “Do not use Premarin” section
- Yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease
- A large rise in your blood pressure (symptoms may be headache, tiredness, dizziness)
- Migraine-like headaches which happen for the first time
- If you become pregnant
- Have an allergic reaction, signs of which include a rash, itching, shortness of breath, difficulty in breathing and a swollen face
- If you notice signs of a blood clot, such as:
 - painful swelling and redness of the legs
 - sudden chest pain
 - difficulty in breathing

Other medicines and Premarin (Conjugated Estrogens) vaginal cream

Some medicines may interfere with the effect of Premarin. This might lead to irregular bleeding. Tell your doctor or pharmacist if you are taking, have recently taken or might take any other

medicines, including medicines obtained without a prescription, herbal remedies or other natural products.

- Medicines for **epilepsy** (such as phenobarbital, phenytoin, carbamazepine).
- Medicines for **tuberculosis** (such as rifampicin, rifabutin).
- Medicines for **HIV infection** (such as ritonavir).
- Other antibiotics or antifungal medicines (e.g. erythromycin, clarithromycin, ketoconazole, itraconazole).
- Herbal remedies containing **St. John's wort** (*Hypericum perforatum*).
- Cimetidine (used to treat stomach ulcers and reduce stomach acid).
- Dexamethasone (a corticosteroid).

The way that Premarin vaginal cream works may be altered if other medicines are used at the same time.

Premarin (Conjugated Estrogens) vaginal cream with food and drink and alcohol

Drinking grapefruit juice may affect the way that your medicine works.

Laboratory tests

If you need a blood test, tell your doctor or the laboratory staff that you are using Premarin vaginal cream, because this medicine can affect the results of some tests.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Driving and using machines

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

3. How to use Premarin (Conjugated Estrogens) vaginal cream

Instructions for proper use

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Dosage

Your doctor will aim to prescribe the lowest dose to treat your symptom for as short as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.

Given cyclically for short-term use only:

For treatment of atrophic vaginitis, dyspareunia and kraurosis vulvae, the lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Administration should be cyclic (e.g., 3 weeks on and 1 week off).

Usual Dosage Range:

½ to 2 g daily, intravaginally, depending on the severity of the condition.

Instructions for Use of Gentle Measure™ Applicator:

1. Remove cap from tube.
2. Screw nozzle end of applicator onto tube.
3. Gently squeeze tube from the bottom to force sufficient cream into the barrel to provide the prescribed dose. Use the marked stopping points on the applicator as a guideline to measure the correct dose.
4. Unscrew applicator from tube.
5. Lie on back with knees drawn up. To deliver medication, gently insert applicator deeply into vagina and press plunger downward to its original position.

To Cleanse: Pull plunger to remove it from barrel. Wash with mild soap and warm water.
DO NOT BOIL OR USE HOT WATER.

Use in the Elderly

The estrogen-alone substudy of the Women's Health Initiative (WHI) reported an increased risk of stroke compared with placebo in post-menopausal women 65 years of age or older.

A substudy of the Women's Health Initiative Memory Study (WHIMS), an ancillary study of WHI conducted in women aged 65-79, reported an increased risk of developing probable dementia when compared with placebo.

Use in children and adolescents

Safety and effectiveness in paediatric patients have not been established.

Duration of treatment

That really depends on why you and your doctor have decided on a course of treatment.

If you use more Premarin (Conjugated Estrogens) vaginal cream than you should

If you use too much Premarin (Conjugated Estrogens) vaginal cream, consult your doctor or pharmacist, in case of any doubt.

You may feel some nausea (sickness), vomiting, breast tenderness, dizziness, abdominal pain, drowsiness/fatigue or experience a short period of vaginal bleeding, if you use too much Premarin (Conjugated Estrogens) vaginal cream. There is no specific antidote and further treatment if necessary, should be symptomatic.

If you forget to use Premarin (Conjugated Estrogens) vaginal cream

If you forget a dose, use it as soon as you remember, then go on as before. If more than one dose has been missed, apply the cream for the day that you remember and continue as normal. Do not use a double dose to make up for a forgotten dose.

If you need to have surgery

If you are going to have surgery, make sure your doctor and/or your surgeon knows that you are using Premarin (Conjugated Estrogens) vaginal cream.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following adverse reactions have either been reported with Conjugated estrogen vaginal cream or are undesirable effects associated with estrogens.

- Breakthrough bleeding/spotting, dysmenorrhea (severe and frequent menstrual cramps and pain during your period)/pelvic pain, breast pain, tenderness, enlargement, discharge, application site reactions of vulvovaginal discomfort including burning, irritation, and genital pruritus (an itch localized to the anus and genital skin); vaginal discharge; leukorrhea (a whitish or yellowish discharge of mucus from the vagina); increased size of uterine leiomyomata (an extremely common benign neoplasm in women of reproductive age), endometrial hyperplasia (the lining of the uterus (endometrium) becomes unusually thick because of having too many cells (hyperplasia))
- Nausea; vomiting; bloating (a condition where your belly feels full and tight, often due to gas); abdominal (stomach) pain, pancreatitis (inflammation of the pancreas); ischemic colitis (when blood flow to part of the large intestine is temporarily reduced)
- Dizziness (feeling faint or unsteady); headache; migraine; nervousness, cerebrovascular accident/stroke (a loss of blood flow to part of the brain, which damages brain tissue.); exacerbation of chorea (an increase in Chorea, a movement disorder that causes involuntary, unpredictable body movements), neuritis (inflammation of nerves)
- Arthralgias (pain in joints); leg cramps
- Changes in libido (sex drive); mood disturbances; irritability; depression, dementia (memory loss)

- Pulmonary embolism (a blockage in one of the pulmonary arteries in your lungs); venous thrombosis (a condition that occurs when a blood clot forms in a vein)
- Edema (swelling caused by excess fluid trapped in your body's tissues)
- Alopecia (severe/uncontrollable hair fall), chloasma/melasma (a skin condition that causes patches and spots, usually on the face, which are darker than your natural skin tone); hirsutism (a condition in women that results in excessive growth of dark or coarse hair); pruritus (an uncomfortable, irritating sensation that makes you want to scratch); rash, erythema multiforme (skin infection); erythema nodosum (inflammatory condition characterized by inflammation of the fat cells under the skin)
- Gallbladder disease, cholestatic jaundice (retention of the constituents of bile in blood), asymptomatic impaired liver function
- Vaginitis (an inflammation of the vagina that can result in discharge, itching and pain), including vaginal candidiasis (yeast infection), cystitis-like syndrome (inflammation of the urinary bladder. It is often caused by infection and is usually accompanied by frequent painful urination)
- Breast cancer, ovarian cancer, fibrocystic breast changes (fluid-filled round or oval sacs (cysts) and more prominent scar-like (fibrous) tissue), endometrial cancer, enlargement of hepatic hemangiomas (a noncancerous mass in the liver made up of a tangle of blood vessels), growth potentiation of benign meningioma (a noncancerous tumor that arises from the meninges - the membranes that surround the brain and spinal cord)
- Urticaria (rash), angioedema (swelling underneath the skin), hypersensitivity, anaphylactic/anaphylactoid reactions (blood pressure drops suddenly and the airways narrow, blocking breathing)
- Glucose intolerance (abnormal blood sugar levels), hypocalcemia (in patients with pre-existing conditions of hypocalcemia (reduced calcium))
- Intolerance to contact lenses, retinal vascular thrombosis (happens when a blood clot blocks the retinal vein in the eye)
- Myocardial infarction (lack of blood flow to heart muscle)
- Changes in weight (increase or decrease), increased triglycerides, increases in blood pressure

These side effects are usually temporary and should get better over time. If you get any side effects, talk to your doctor or pharmacist. This includes any side effects not listed in this leaflet.

5. How to store Premarin (Conjugated Estrogens) vaginal creams

Store below 25°C.

Keep out of reach of children. For external (intravaginal) use only.

6. Contents of the pack and other information

List of Excipients

Conjugated Estrogens 0.625 mg Vaginal cream:

Cetyl esters wax, cetyl alcohol, white wax, glyceryl monostearate, propylene glycol monostearate, methyl stearate, phenylethyl alcohol, sodium lauryl sulfate, glycerin, purified water, nitrogen and mineral oil.

Contents of the pack

Conjugated estrogen vaginal cream is available in tubes of 14 g, each gram containing 0.625 mg of conjugated estrogen. Each tube is accompanied with a calibrated plastic applicator.

All strengths/presentations mentioned in this document might not be available in the market.

Manufactured By:

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