Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT PREMARIN VAGINAL CREAM IS AND WHAT IT IS USED FOR

Premarin Vaginal Cream is an estrogen-only HRT. It contains a mixture of natural hormones called conjugated estrogens.

Premarin Vaginal Cream is one of a group of medicines known as Hormone Replacement Therapy (HRT). It is used to treat some of the symptoms and conditions associated with the menopause.

Estrogen is one of the main hormones responsible for helping to keep many of the tissues in the body healthy, such as the tissues of the urinary system and the lining of the vagina. During the menopause, the level of the estrogen in your body will decrease. By replacing the estrogen that your body no longer produces, Premarin Vaginal Cream can relieve some of the symptoms that you may experience at this time, such as vaginal itching and dryness.

2. BEFORE YOU USE PREMARIN VAGINAL CREAM

Do not use Premarin Vaginal Cream if:

- you are allergic (hypersensitive) to conjugated estrogens or any of the ingredients of Premarin Vaginal Cream; the ingredients are listed in Section 6 of this leaflet
- you have or have had breast cancer
• you have endometrial cancer (cancer of the lining of the womb) or have been told you have another type of estrogen dependent cancer
• you have been told you have a blood circulation disorder or have had a blood clot
• you have a heart condition such as angina or have had a heart attack
• you have porphyria (a rare inherited metabolic disorder).

If any of the following applies to you discuss this with your doctor before using Premarin Vaginal Cream, as it may not be suitable for you:
  • you have recently had unexpected or very heavy vaginal bleeding
  • you have been told that you have endometrial hyperplasia (abnormal growth of the lining of the womb)
  • you have or have previously had liver disease
  • you are pregnant, or you are breast-feeding.

Before you start using HRT, your doctor should ask about your own and your family’s medical history. Your doctor may decide to examine your breasts and/or your abdomen, and may do an internal examination — but only if these examinations are necessary for you, or if you have any special concerns.

Once you’ve started on HRT, you should see your doctor for regular check-ups (at least once a year). At these check-ups, your doctor may discuss with you the benefits and risks of continuing to take HRT.

You are advised to:
  • go for regular breast screening and cervical smear tests
  • regularly check your breasts for any changes such as dimpling of the skin, changes in the nipple, or any lumps you can see or feel.

Some diseases may be made worse by HRT. Therefore, if you have or have ever had any of the following remind your doctor as he or she may want to monitor you more closely:
  • uterine fibroids or endometriosis
  • risk factors for blood clots (see section titled Blood Clots below)
  • a close relative who has had breast cancer or an estrogen dependent cancer, such as cancer of the womb or ovaries
  • high blood pressure
  • heart disease
  • kidney disease
  • diabetes
  • gallbladder disease or gallstones
  • migraine
  • systemic lupus erythematosus (SLE – a rare chronic inflammatory disease)
  • epilepsy
  • asthma
  • otosclerosis (hearing loss due to a problem with the bones in your ear)
  • low blood calcium levels (hypocalcaemia)
  • high levels of fatty substances in the blood (hypertriglyceridaemia).
If there is a change in any of the above conditions whilst using Premarin Vaginal Cream tell your doctor.

**Effects on your heart or circulation:**

**Heart Disease**

HRT is not recommended for women who have heart disease, or have had heart disease recently. If you have ever had heart disease, talk to your doctor to see if you should be using HRT.

HRT will not help to prevent heart disease.

Studies with one type of HRT (containing conjugated estrogens plus the progestogen MPA) have shown that women may be slightly more likely to get heart disease during the first year of using the medication. For other types of HRT, the risk is likely to be similar, although this is not yet certain.

**If you get:**

- a pain in your chest that spreads to your arm or neck
  - See a doctor as soon as possible and do not take any more HRT until your doctor says you can. This pain could be a sign of heart disease.

**Stroke**

Recent research suggests that HRT slightly increases the risk of having a stroke. Other things that can increase the risk of stroke include:

- getting older
- high blood pressure
- smoking
- drinking too much alcohol
- an irregular heartbeat

**If you are worried about any of these things, or if you have had a stroke in the past,** talk to your doctor to see if you should take HRT.

Looking at women in their 50s who are not taking HRT — on average, over a 5-year period, 3 in 1000 would be expected to have a stroke.

For women in their 50s who are taking HRT, the figure would be 4 in 1000.

Looking at women in their 60s who are not taking HRT — on average, over a 5-year period, 11 in 1000 would be expected to have a stroke.

For women in their 60s who are taking HRT, the figure would be 15 in 1000.

**If you get:**

- unexplained migraine-type headaches, with or without disturbed vision
➤ See a doctor as soon as possible and do not take any more HRT until your doctor says you can. These headaches may be an early warning sign of a stroke.

**Blood Clots**

HRT may increase the risk of blood clots in the veins (also called deep vein thrombosis, or DVT), especially during the first year of taking it.

These blood clots are not always serious, **but if one travels to the lungs**, it can cause chest pain, breathlessness, collapse or even death. This condition is called pulmonary embolism, or PE.

DVT and PE are examples of a condition called venous thromboembolism, or VTE.

You are more likely to get a blood clot:

- if you are seriously overweight
- if you have had a blood clot before
- if any of your close family have had blood clots
- if you have had one or more miscarriages
- if you have any blood clotting problem that needs treatment with a medicine such as warfarin
- if you’re off your feet for a long time because of major surgery, injury or illness
- if you have a rare condition called SLE (systemic lupus erythematosus).

**If any of these things apply to you**, talk to your doctor to see if you should take HRT.

Looking at **women in their 50s** who are **not taking HRT** — on average, over a 5-year period, **3 in 1000** would be expected to get a blood clot.

For women in their 50s who are **taking HRT**, the figure would be **7 in 1000**.

Looking at **women in their 60s** who are **not taking HRT** — on average, over a 5-year period, **8 in 1000** would be expected to get a blood clot.

For women in their 60s who are **taking HRT**, the figure would be **17 in 1000**.

**If you get:**

- painful swelling in your leg
- sudden chest pain
- difficulty breathing
  ➤ See a doctor as soon as possible and do not take any more HRT until your doctor says you can. These may be signs of a blood clot.

**If you’re going to have surgery**, make sure your doctor knows about it. You may need to stop using HRT about 4 to 6 weeks before the operation, to reduce the risk of a blood clot. Your doctor will tell you when you can start using HRT again.

**Effects on your risk of developing cancer:**
Breast Cancer
Women who have breast cancer, or have had breast cancer in the past, should not take HRT.

Taking HRT slightly increases the risk of breast cancer; so does having a later menopause. The risk for a post-menopausal woman taking estrogen-only HRT for 5 years is about the same as for a woman the same age who’s still having periods over that time and not taking HRT.

For all kinds of HRT, the extra risk of breast cancer goes up the longer you take it, but returns to normal within about 5 years after stopping.

Your risk of breast cancer is also higher:
- if you have a close relative (mother, sister or grandmother) who has had breast cancer
- if you are seriously overweight.

Looking at women aged 50 who are not taking HRT – on average, 32 in 1000 will be diagnosed with breast cancer by the time they reach the age of 65.

For women who start taking estrogen-only HRT at age 50 and take it for 5 years, the figure will be between 33 and 34 in 1000 (i.e. an extra 1-2 cases).

If they take estrogen-only HRT for 10 years, the figure will be 37 in 1000 (i.e. an extra 5 cases).

If you notice any changes in your breast, such as:
- dimpling of the skin
- changes in the nipple
- any lumps you can see or feel
  ➢ Make an appointment to see your doctor as soon as possible.

Endometrial cancer (cancer of the lining of the womb)
Taking estrogen-only HRT for a long time can increase the risk of developing cancer of the womb lining (the endometrium). It is possible there may be a similar risk with estrogen cream used for repeated treatments or over a long time.

If you get breakthrough bleeding or spotting, it’s usually nothing to worry about, but you should,

➢ Make an appointment to see your doctor. It could be a sign that your endometrium has become thicker.

Ovarian cancer
Ovarian cancer (cancer of the ovaries) is very rare, but it is serious. It can be difficult to diagnose, because there are often no obvious signs of the disease.
Some studies have indicated that taking estrogen-only HRT for more than 5 years may increase the risk of ovarian cancer. It is not yet known whether other kinds of HRT increase the risk in the same way.

**Other conditions**
HRT will not help prevent memory loss. In one study of women who started using combined HRT after the age of 65, a small increase in the risk of dementia was observed.

Women with hypertriglyceridaemia may experience large increases of their plasma triglycerides, which can lead to inflammation of the pancreas (pancreatitis). Symptoms of pancreatitis include sudden sharp abdominal pains, abdominal swelling, fever and feeling or being sick.

If you are taking thyroid hormone replacement therapy (e.g. thyroxine), your doctor may monitor your thyroid function more often when you start treatment.

HRT may affect some medical tests. If you visit a hospital or clinic for any medical tests, you should tell the doctor concerned that you are using HRT.

**Taking other medicines**
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In particular tell your doctor if you are taking:
- an anticonvulsant (used in the treatment of epilepsy e.g. phenobarbital, phenytoin, carbamazepine)
- an anti-infective (e.g. rifampicin, rifabutin, nevirapine, efavirenz, erythromycin, ketoconazole, ritonavir, nelfinavir)
- a herbal preparation such as St. John’s wort (*Hypericum perforatum*)
- metyrapone (most commonly used in the treatment of Cushing’s syndrome).

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

**Pregnancy and breast-feeding**
You should stop taking Premarin Vaginal Cream and tell your doctor immediately if you know or suspect you are pregnant, or if you are breast-feeding.

Premarin Vaginal Cream is not a contraceptive. It is important that you use a reliable form of non-hormonal contraception if there is any possibility that you may still become pregnant. Premarin Vaginal Cream has been shown to weaken latex condoms. Therefore, you should not use condoms, diaphragms or cervical caps made of latex or rubber as a form of contraception while using Premarin Vaginal Cream. You should discuss alternative forms of contraception with your doctor.
Driving and using machinery
There is no evidence to suggest that Premarin Vaginal Cream will affect your ability to drive or to operate machinery.

Important information about some of the ingredients in Premarin Vaginal Cream
Premarin Vaginal Cream contains cetyl alcohol and propylene glycol monostearate. These may cause skin irritation.

3. HOW TO USE PREMARIN VAGINAL CREAM

Always use Premarin Vaginal Cream exactly as your doctor has told you. You should check with your doctor or pharmacist if you are unsure.

Your doctor will aim to give you the lowest dose for the shortest time to treat your symptoms.

The usual dose is 1g or 2g of the cream daily - the applicator has dosage markings showing how much of the cream is equivalent to 1g or 2g to help you to apply the correct amount of cream.

Instructions for proper use
If you are still having regular periods, you should start using Premarin Vaginal Cream on the fifth day of your monthly bleed. If you are no longer having periods, then you can start at any time.

You should apply the cream according to your doctor’s instructions, either on the outside of the vagina or into the vagina using the enclosed applicator.

To apply the cream into the vagina, the applicator should be used as follows:

1. Remove the cap from the aluminium tube of cream and screw the nozzle end of the applicator onto the tube.

2. Gently squeeze the tube to force the cream into the barrel of the applicator. Depending on the dose your doctor advised you to use, fill the applicator with cream up to the appropriate dosage marking.

3. Unscrew the filled applicator from the tube of cream and replace the cap on the tube.

4. To apply the cream, gently insert the applicator into your vagina and then press the plunger back to its original position.

5. After use, remove the empty applicator.
To clean the applicator after use, pull the plunger out from the barrel and wash both parts with mild soap and warm water. Do not boil or use hot water.

**Duration of treatment**
Premarin Vaginal Cream may be used for differing periods of time from a few days to several months. If you are using the cream for a month or more you should use the cream for a period of 3 weeks and then have a week without using the cream. After this week, you should use the cream for another 3 weeks and then have another week off. You should keep to this "3 weeks on, 1 week off" plan for as long as you are using Premarin Vaginal Cream.

**If you use more Premarin Vaginal Cream than you should**
If you apply too much cream don’t worry. It is unlikely that serious problems will occur with Premarin Vaginal Cream. If in any doubt consult your doctor or pharmacist.

You may feel some nausea (sickness), or experience a short period of vaginal bleeding (unless you have had a hysterectomy) if you apply too much medicine.

If an adult or a child swallows Premarin Vaginal Cream, it is unlikely that any serious problems will occur. However, you should consult your doctor or pharmacist.

**If you forget to use Premarin Vaginal Cream**
If you forget to apply the cream, do so as soon as you remember, then go on as before. If more than one dose has been missed, apply the cream on the day that you remember and continue as normal. Do not use double your usual dose to make up for the missed application.

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

4. **POSSIBLE SIDE EFFECTS**

Like all medicines, Premarin Vaginal Cream can cause side effects, although not everybody gets them.

**Stop using Premarin Vaginal Cream and tell your doctor immediately if you:**
- have an allergic reaction, signs of which include rash, itching, shortness of breath, difficulty breathing and a swollen face
- experience a migraine type headache (typically a throbbing headache and nausea preceded by visual disturbances) for the first time
- develop signs of jaundice (yellowing of the skin or the whites of the eyes)
- become pregnant
- experience a significant increase in your blood pressure
- develop a contraindication (see section titled Before you use Premarin Vaginal Cream)

Do not use any more Premarin Vaginal Cream until your doctor says you can.
HRT can increase the risk of heart disease, stroke, blood clots, breast cancer, endometrial cancer and ovarian cancer. Please see Section 2 (Before you use Premarin Vaginal Cream).

In addition to those discussed in section 2, the following side effects have been reported in women taking HRT:

- breakthrough bleeding or spotting, changes in menstrual flow, pelvic pain, vaginal inflammation and vaginal discharge
- vaginal discomfort including burning, itching and irritation at the site of application
- a tendency to get thrush
- breast pain, breast tenderness, swollen breasts, discharge from the nipples and changes in breast tissue
- feeling or being sick, a feeling of being bloated, abdominal pain
- headache or migraine
- dizziness
- changes in mood including anxiety, depression and irritability
- joint pain, leg cramps
- changes in your interest in sex (increased or decreased libido)
- visible swelling of the face or ankles
- rash, itchiness, acne and dark or red patches on the skin
- changes in hair growth (loss or increase)
- minor changes to the eye, difficulty wearing contact lenses
- changes in weight (increase or decrease)
- changes in your triglyceride levels (fatty substances in the blood)
- an intolerance to glucose
- memory loss
- a worsening of chorea (an existing neurological disorder characterised by involuntary spasmodic movements of the body)
- a worsening of otosclerosis (inherited deafness).
- induce or exacerbate symptoms of angioedema, which consists of generalized swelling of parts of the body, most frequently around the face, mouth, tongue and neck areas, particularly in women with hereditary angioedema.

These side effects are usually temporary and should get better over time.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE PREMARIN VAGINAL CREAM

Keep out of the reach and sight of children.

Do not use Premarin Vaginal Cream after the expiry date stated on the carton and tube. The expiry date refers to the last day of that month.
Do not store above 25°C.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help the environment.

6. FURTHER INFORMATION

What Premarin Vaginal Cream contains

- The active substance is conjugated estrogens. Each tube contains 42.5g of cream. Each gram contains 0.625mg of conjugated estrogens.

- The other ingredients in your cream are liquid paraffin, glycercyl monostearate, cetyl alcohol, cetyl esters, white wax, methyl stearate, sodium lauryl sulphate, phenylethyl alcohol, glycerin, purified water and propylene glycol monostearate.

What Premarin Vaginal Cream Looks like and contents of the pack

- Each tube of Premarin Vaginal Cream contains 42.5g of a white to off-white cream.
- Each carton contains an aluminium tube containing 42.5g of cream and an applicator.

The marketing authorisation holder is John Wyeth & Brother Ltd, trading as Wyeth Pharmaceuticals, Huntercombe Lane South, Taplow, Maidenhead, Berkshire SL6 0PH.

The manufacturer is Wyeth Pharmaceuticals, New Lane, Havant PO9 2NG, UK

This leaflet applies to Premarin Vaginal Cream only.

This leaflet was last approved in 07/2010

* Trade mark