

PACKAGE LEAFLET: INFORMATION FOR THE USER

PREMIQUE® 0.625mg/5mg Coated Tablets Conjugated Estrogens and Medroxyprogesterone Acetate

Read all of this leaflet carefully before you start taking 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 Premique is and what it is used for
2. Before you take Premique
3. How to take Premique
4. Possible side effects
5. How to store Premique
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1. WHAT PREMIQUE IS AND WHAT IT IS USED FOR

Premique 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. Premique is a period-free HRT (an HRT product where you do not have a monthly bleed).

Your periods will stop once menopause is reached. This change is due to lowered levels of the hormones estrogen and progesterone. You may experience a number of unpleasant symptoms, including hot flushes, night sweats and vaginal dryness, around the time of menopause. Premique can relieve some of these symptoms by replacing some of the lost estrogen.

After the menopause some women may develop bone thinning (osteoporosis). If you are at an increased risk of fractures due to osteoporosis but are unable to take other treatments or if other therapies prove to be ineffective, Premique may also be used for this purpose. Your doctor should discuss all the available options with you.

2. BEFORE YOU TAKE PREMIQUE

2.1 Do not take Premique if:

- you are allergic (hypersensitive) to conjugated estrogens or medroxyprogesterone acetate or any of the other ingredients of Premique; 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 blood clotting disorder (*thrombophilic disorder, such as protein C, protein S, or antithrombin deficiency*)
- you have a heart condition such as angina or have had a heart attack
- you have porphyria (a rare inherited metabolic disorder)
- 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 taking 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 **2.2 - Blood Clots** for more detail)
- a close relative who has had breast cancer or an estrogen dependent cancer, such as cancer of the womb or ovaries (see section **2.3 – Effects on your risk of developing cancer** for more detail)
- high blood pressure
- heart disease (see section **2.2 – Heart Disease** for more detail)
- liver disease (e.g. liver adenoma)
- 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 taking Premique tell your doctor.

As well as benefits, HRT has some risks which you need to consider when you're deciding whether to take it, or whether to carry on taking it.

2.2 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 taking 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 taking 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 taking 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 taking HRT again.

2.3 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. The risk for a woman who is taking estrogen plus progestogen HRT is higher than for estrogen-only HRT (but estrogen plus progestogen HRT is beneficial for the endometrium, see ***Endometrial Cancer*** below).

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)**.

For women who start taking **estrogen plus progestogen HRT** at age 50 and take it for **5 years**, the figure will be **38 in 1000 (i.e. an extra 6 cases)**.

If they take estrogen plus progestogen HRT for **10 years**, the figure will be **51 in 1000 (i.e. an extra 19 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 cancer of the lining of the womb (the endometrium). Taking a **progestogen** as well as the estrogen helps to lower the extra risk.

If you still have your womb, your doctor may prescribe a progestogen as well as estrogen. If so, these may be prescribed separately, or as a combined HRT product.

If you have had your womb removed (a hysterectomy), your doctor will discuss with you whether you can safely take estrogen without a progestogen.

If you've had your womb removed because of endometriosis, any endometrium left in your body may be at risk. So your doctor may prescribe HRT that includes a progestogen as well as an estrogen.

Your product, Premique, contains a progestogen.

Looking at women who still have a uterus and who are **not taking HRT** – on average **5 in 1000** will be diagnosed with endometrial cancer between the ages of 50 and 65.

For women who take **estrogen-only HRT**, the number will be **2 to 12 times higher**, depending on the dose and how long they take it.

The addition of a progestogen to estrogen-only HRT substantially reduces the risk of endometrial cancer.

If you get breakthrough bleeding or spotting, it's usually nothing to worry about, especially during the first few months of taking HRT.

But if the bleeding or spotting:

- carries on for more than the first few months
- starts after you've been on HRT for a while
- carries on even after you've stopped taking HRT
- **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.

2.4 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 (high levels of fatty substances in the blood) 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 taking HRT.

2.5 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 to treat 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)
- aminoglutethimide (most commonly used in the treatment of breast cancer and Cushing's syndrome).

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

2.6 Pregnancy and breast-feeding

You should stop taking Premique and tell your doctor immediately if you know or suspect you are pregnant, or if you are breast-feeding.

Premique is not a contraceptive. It is important that you use a reliable form of non-hormonal contraception (e.g. condom or diaphragm) if there is any possibility that you may still become pregnant. You should discuss this with your doctor.

2.7 Driving and using machines

There is no evidence to suggest that Premique will affect your ability to drive or to operate machinery.

2.8 Important information about some of the ingredients in Premique

Premique contains lactose and sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW TO TAKE PREMIQUE

3.1 Instructions for proper use

Always take Premique exactly as your doctor has told you. You should check with your doctor or pharmacist if you are unsure.

The usual dose is one tablet every day.

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

Take your tablet at the same time each day as this will help to remind you to take your medicine.

If you are not currently taking HRT or you are taking another period-free HRT, you may start your first pack of Premique at any convenient time.

If you are changing from an HRT product that gives you a monthly bleed, start Premique the day after you finish the course of the previous product, unless instructed otherwise by your doctor.

Begin your pack of Premique by taking the first tablet marked for that day of the week. Continue to take one tablet each day following the arrows until all 28 tablets have been taken.

While you are taking Premique you will have no tablet-free days. You should start your next pack the day after you finish the previous one.

Premique does not cause periods. However, you may experience some irregular bleeding or light bleeding (spotting) during your first few months of taking Premique. If the bleeding is troublesome, or continues beyond the first 3 months of treatment you should discuss this with your doctor (see section titled *Endometrial Cancer* above).

Do not try to take off the coating, divide or crush the tablets as this could affect the way Premique works.

3.2 If you take more Premique than you should

If you take too many tablets don't worry. You may feel some nausea (sickness), breast tenderness, dizziness, abdominal pain, drowsiness, fatigue or experience a short period of vaginal bleeding, but it is unlikely that serious problems will result. If you are concerned talk to your doctor or pharmacist.

3.3 If you forget to take Premique

If you forget to take a tablet don't worry. Take it as soon as you remember and then carry on taking the remaining tablets at the usual time.

If more than one tablet has been forgotten, do not take extra to try to make up for the missed tablets.

Missed tablets may cause a short period of light bleeding in women who have not had a hysterectomy.

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

4. POSSIBLE SIDE EFFECTS

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

4.1 Serious side effects

Stop taking Premique 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 i.e. circumstances which make treatment inadvisable (see Section 2 - **Before you take Premique**).

Do not take any more tablets until your doctor says you can.

HRT can also increase the risk of heart disease, stroke, blood clots, breast cancer, endometrial cancer and ovarian cancer. Please see Section 2 - **Before you take Premique**.

4.2 Other side effects

Very common (affect more than 1 in 10 women)

- breast pain

Common (affect less than 1 in 10 women)

- breakthrough bleeding or spotting, vaginal inflammation, period pain
- breast tenderness, swollen breasts, nipple discharge
- depression
- muscle and joint aches, leg cramps
- weight change (increase or decrease)
- changes in your triglyceride levels (fatty substances in the blood)

Uncommon (affect less than 1 in 100 women)

- changes in menstrual flow, vaginal discharge
- thrush
- nausea, bloating, abdominal pain
- headache, migraine
- blood clots in the veins
- dizziness
- changes in mood including anxiety
- changes in your interest in sex (increased or decreased libido)
- visible swelling of the face or ankles
- itchiness, acne
- difficulty wearing contact lenses
- gallbladder disease (e.g. gallstones)
- hair loss

Rare (affect less than 1 in 1000 women)

- vomiting
- changes in breast tissue, milky secretion from the breasts
- irritability
- allergic reactions including swelling, rash or red patches on the skin
- increase in hair growth
- an intolerance to glucose
- a worsening of asthma
- increased size of fibroids
- ovarian cancer
- worsening of epilepsy
- heart attack, stroke
- inflammation of veins just under the skin
- inflammation of the pancreas
- irregular dark spots (usually on the face)

Very rare (affect less than 1 in 10000 women)

- jaundice (e.g. yellowing of the skin)
- a worsening of chorea (an existing neurological disorder characterised by involuntary spasmodic movements of the body)
- a worsening of hypocalcaemia (low blood levels of calcium)
- blurred vision or loss of vision
- worsening of porphyria (a rare inherited metabolic disorder)
- growth of benign liver tumours

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

Other side effects that may occur while taking an estrogen-progesterone combined HRT are:

- memory loss (dementia)

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 PREMIQUE

Keep out of the reach and sight of children.

Do not use this medicine after the expiry date stated on the carton and blister. The expiry date refers to the last day of the month.

Do not store above 25°C. Keep the blister in the outer carton to protect from light.

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 to protect the environment.

6. FURTHER INFORMATION

6.1 What Premique contains

- The active ingredients are an estrogen (conjugated estrogens) and a progestogen (medroxyprogesterone acetate).

Each blister pack contains 28 oval coated tablets, each tablet contains 0.625mg of conjugated estrogens and 5mg of medroxyprogesterone acetate (MPA). The tablets are light blue coloured and marked with “0.625/5”.

- The other ingredients are calcium phosphate tribasic, calcium sulphate, microcrystalline cellulose, carnauba wax, glyceryl mono-oleates, lactose, magnesium stearate, methylcellulose, macrogol, pharmaceutical glaze, povidone, sucrose, titanium dioxide (E171), stearic acid and colour (E132, indigo carmine) and edible ink containing iron oxide black (E172), shellac, N-Butyl alcohol, propylene glycol and ethyl acetate.
- The inks and dyes used to coat your tablets are approved for use as food colourings.

6.2 What Premique looks like and contents of the pack

Your Premique carton contains either one or three blisters, each containing 28 tablets. Not all pack sizes may be marketed.

The marketing authorisation holder is

Pfizer Limited
Ramsgate Road
Sandwich
Kent
CT13 9NJ
United Kingdom

The manufacturer is Pfizer Ireland Pharmaceuticals, Little Connell, Newbridge, County Kildare, Republic of Ireland.

This leaflet applies to Premique tablets only.

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* Trade mark

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