

## **PACKAGE LEAFLET: INFORMATION FOR THE USER**

### **PREMPAK-C® 0.625 mg/0.15 mg & 1.25 mg/0.15 mg Coated Tablets** Conjugated Estrogens and Norgestrel

#### **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 if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

#### **In this leaflet:**

1. What Prempak-C is and what it is used for
2. Before you take Prempak-C
3. How to take Prempak-C
4. Possible side effects
5. How to store Prempak-C
6. Further information

## **1. WHAT PREMPAK-C IS AND WHAT IT IS USED FOR**

Prempak-C is a Hormone Replacement Therapy (HRT) preparation containing two types of female hormones, an estrogen and a progestogen (norgestrel). Prempak C is used in menopausal and postmenopausal women.

It is used for:

#### **Relief of symptoms occurring after menopause**

During the menopause, the amount of the estrogen produced by a woman's body drops. This can cause symptoms such as hot face, neck and chest ("hot flushes"). Prempak-C alleviates these symptoms after menopause. You will only be prescribed Prempak-C if your symptoms seriously hinder your daily life.

#### **Prevention of osteoporosis**

After the menopause some women may develop fragile bones (osteoporosis). You should discuss all available options with your doctor.

If you are at an increased risk of fractures due to osteoporosis and other medicines are not suitable for you, you can use Prempak-C to prevent osteoporosis after menopause.

## **2. BEFORE YOU TAKE PREMPAK-C**

#### **Medical history and regular check-ups**

The use of HRT carries risks which need to be considered when deciding whether to start taking it, or whether to carry on taking it.

The experience in treating women with a premature menopause (due to ovarian failure or surgery) is limited. If you have a premature menopause the risks of using HRT may be different. Please talk to your doctor.

Before you start (or restart) HRT, your doctor will ask about your own and your family's medical history. Your doctor may decide to perform a physical examination. This may include an examination of your breasts and/or an internal examination, if necessary.

Once you have started on Prempak-C you should see your doctor for regular check-ups (at least once a year). At these check-ups, discuss with your doctor the benefits and risks of continuing with Prempak C.

Go for regular breast screening, as recommended by your doctor.

### **2.1 Do not take Prempak-C**

If any of the following applies to you. If you are not sure about any of the points below, **talk to your doctor** before taking Prempak-C,

#### **Do not take Prempak C if:**

- you are allergic (hypersensitive) to conjugated estrogens or norgestrel or any of the other ingredients of Prempak-C; the ingredients are listed in Section 6 of this leaflet
- you have or have ever had breast cancer, or if you are suspected of having it
- you have cancer which is sensitive to estrogens, such as cancer of the lining of the womb (endometrium) or if you are suspected of having it.
- you have ever had a blood clot in a vein (thrombosis), such as in the legs (deep venous thrombosis) or the lungs (pulmonary embolism)
- you have a blood clotting disorder (*such as protein C, protein S, or antithrombin deficiency*)
- you have recently had a disease caused by blood clots in the arteries, such as a heart attack, stroke or angina
- you have a rare blood problem called "porphyria" which is passed down in families (inherited)
- you have any unexplained vaginal bleeding
- you have excessive thickening of the womb lining (endometrial hyperplasia) that is not being treated
- you have or have previously had liver disease
- you are pregnant, or you are breast-feeding.

If any of the above conditions appear for the first time while taking Prempak-C, stop taking it at once and consult your doctor immediately.

### **When to take special care with Prempak-C**

Tell your doctor if you have ever had any of the following problems, before you start the treatment, as these may return or become worse during treatment with Prempak-C. If so, you should see your doctor more often for check-ups:

- fibroids inside your womb

- growth of womb lining outside your womb (endometriosis) or a history of excessive growth of the womb lining (endometrial hyperplasia)
- increased risk of developing blood clots (see section 2.3 - “*Blood Clots in a vein (thrombosis)*” for more detail)
- increased risk of getting an estrogen-sensitive cancer (such as having a mother, sister or grandmother who has had breast cancer) (see section 2.2 – **HRT and cancer** for more detail)
- high blood pressure
- heart disease (see section 2.3 – *Heart Disease* for more detail)
- a liver disorder (e.g. a benign liver tumour)
- kidney disease
- fluid retention due to cardiac or kidney problems
- diabetes
- gallbladder disease or gallstones
- migraine or severe headaches
- a disease of the immune system that effects many organs of the body (systemic lupus erythematosus, SLE)
- epilepsy
- asthma
- a disease affecting the eardrum and hearing (otosclerosis) low blood calcium levels (hypocalcaemia)
- a very high level of fat in the blood (triglycerides).

**Stop taking Prempak-C and see a doctor immediately**

If you notice any of the following when taking HRT:

- any of the conditions mentioned in the ‘DO NOT take Prempak-C’ 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 rash, itching, shortness of breath, difficulty 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
 For more information, see ‘Blood clots in a vein (thrombosis)’

**Note:** Prempak-C is not a contraceptive. If it is less than 12 months since your last menstrual period or you are under 50 years old, you may still need to use additional contraception to prevent pregnancy. Speak to your doctor for advice.

**2.2 HRT and cancer**

***Excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)***

Taking **estrogen-only** HRT will increase the risk of excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the womb lining (endometrial cancer). The **progestogen** in Prempak-C protects you from this 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, Prempak-C, 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. After stopping treatment risk may remain elevated for at least 10 years. In women with a uterus, use of estrogen-only HRT is not recommended because it increases the risk of endometrial cancer

*The addition of a progestogen to estrogen-only HRT for at least 12 days per cycle can prevent this increased risk.*

**Irregular bleeding**

**If you get breakthrough bleeding or spotting**, it's usually nothing to worry about, especially during the first 3-6 months of taking HRT.

**But if the bleeding or spotting:**

- carries on for more than the first 6 months
- starts after you've been on HRT for more than 6 months.
- 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.

***Breast Cancer***

**Women who have breast cancer, or have had breast cancer in the past, should not take HRT.**

Evidence suggests that taking combined estrogen-progestogen and possibly also estrogen-only HRT increases the risk of breast cancer. The extra risk depends on how long you take HRT.

The additional risk becomes clear within a few years. However, it returns to normal within a few years (at most 5) after stopping treatment.

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.

### *Compare*

Women aged 50 to 79 who are not taking HRT, on average, 9 to 14 in 1000 will be diagnosed with breast cancer over a 5-year period. For women aged 50 to 79 who are taking estrogen-progestogen HRT over 5 years, there will be 13 to 20 cases in 1000 users (i.e. an extra 4 to 6 cases).

**Regularly check your breasts. See your doctor if you notice any changes, such as:**

- dimpling of the skin
- changes in the nipple
- any lumps you can see or feel

### ***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.

A slightly increased risk of ovarian cancer has been reported in women taking HRT at least 5 to 10 years. Women aged 50 to 69 who are not taking HRT, on average about 2 women in 1000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there will be between 2 and 3 cases per 1000 users (i.e. up to 1 extra case).

## **2.3 Effects of HRT on your heart or circulation:**

### ***Blood Clots in a vein (thrombosis)***

The risk of **blood clots in the veins** (also called **deep vein thrombosis**, or **DVT**) is about 1.3 – 3 times higher in HRT users than in non-users, especially during the first year of taking it.

Blood clots can be serious, **and 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 in your veins as you get older or if any of the following applies to you. Inform your doctor if any of these situations applies to you:

- you are seriously overweight (BMI >30 kg/m<sup>2</sup>)
- you have had a blood clot before

- if any of your close family has ever had a blood clot in the leg, lung or an other organ.
- you are pregnant or in your postpartum period
- you have any blood clotting problem that needs treatment with a medicine used to prevent blood clots
- you are unable to walk for a long time because of major surgery, injury or illness (see also ‘**if you’re going to have surgery**’ below)
- you have a rare condition called SLE (systemic lupus erythematosus).
- you have cancer

For signs of a blood clot, see “Stop taking Prempak-C and see a doctor immediately”.

### *Compare*

Looking at women in their 50s who are not taking HRT — on average, over a 5-year period, 4 to 7 in 1000 would be expected to get a blood clot in a vein.

For women in their 50s who are taking estrogen-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).

**If you’re going to have surgery**, make sure your doctor knows about it, or tell the surgeon that you are taking Prempak-C. You may need to stop taking Prempak-C 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 Prempak-C again.

### *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.

**There is no evidence that HRT will prevent a heart attack.**

Women over the age of 60 who use estrogen-progestogen HRT are slightly more likely to develop heart disease than those not taking any HRT.

### **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*

The risk of having a stroke is about 1.5 times higher in HRT users than in non-users. The number of extra cases of stroke due to use of HRT will increase with age.

Other things that can increase the risk of stroke include:

- 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.

### *Compare*

Looking at women in their 50s who are not taking HRT — on average, over a 5-year period, 8 in 1000 would be expected to have a stroke.

For women in their 50s who are taking HRT, the figure would be 11 cases in 1000 users, over 5 years (i.e. an extra 3 cases).

### **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.

## **2.4 Other Conditions**

HRT will not help prevent memory loss. There is some evidence of a higher risk of memory loss in women who start using HRT after the age of 65.

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**

Some medicines may interfere with the effect of Prempak-C. This might lead to irregular bleeding.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription, herbal remedies or other natural products.

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. used to treat **tuberculosis** (rifampicin, rifabutin) or **HIV** (nevirapine, efavirenz, ritonavir and 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 Prempak-C works may be altered if other medicines are used at the same time.

## **2.6 Laboratory tests**

If you need a blood test, tell your doctor or the laboratory staff that you are taking Prempak-C, because this medicine can affect the results of some tests.

## **2.7 Pregnancy and breast-feeding**

Prempak-C is for use in postmenopausal women only. You should stop taking Prempak-C and tell your doctor immediately if you know or suspect you are pregnant, or if you are breast-feeding.

## **2.8 Driving and using machines**

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

## **2.9 Important information about some of the ingredients in Prempak-C**

Prempak-C 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.

The colouring agent E110 (sunset yellow), that is used in the maroon and yellow tablets, may cause allergic reactions.

## **3. HOW TO TAKE PREMPAK-C**

Always take Prempak-C 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 for as short as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.

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

You may start your first pack at any convenient time. However, if you are still having periods you should start on the first day of your next period. If you are transferring from another sequential HRT product, treatment should begin the day following completion of the prior product, unless instructed otherwise by your doctor.



The usual dose is one estrogen tablet every day until Day 16. You should then take one estrogen tablet every day plus one norgestrel tablet every day from days 17-28 as marked on the pack.

Do not leave a break between packs unless your doctor tells you to. Do not stop taking Prempak-C without first discussing it with your doctor.

### **3.1 Instructions for proper use**

Start your pack with the tablet marked "Day 1". You will see that the days of the week have been printed on the top of your pack. Make a hole through the day of the week on which you take your first pill. Pills 8, 15 and 22 will also be taken on this day of the week, so if you are not sure if you have taken your pill(s) you can count backwards, as a reminder.

When you take HRT you will probably have a regular "period" or "withdrawal bleed" each month. This is caused by the hormones, and is perfectly normal. Some women on HRT do not bleed. This is also quite normal. If you have a bleed at any other time, or bleeding is excessively heavy, please inform your doctor.

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

### **3.2 If you take more Prempak-C 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 Prempak-C**

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, Prempak-C can cause side effects, although not everybody gets them.

### **4.1 Serious side effects**

The following diseases are reported more often in women using HRT compared to women not using HRT:

- breast cancer

- abnormal growth or cancer of the lining of the womb (endometrial hyperplasia or cancer)
- ovarian cancer
- blood clots in the veins of the legs or lungs (venous thromboembolism)
- heart disease
- stroke
- probable memory loss if HRT is started over the age of 65

For more information about these side effects, see Section 2.

## **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
- 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
- various skin disorders:
  - discoloration of the skin especially of the face or neck known as “pregnancy patches” (chloasma)
  - painful reddish skin nodules (erythema nodosum)
  - rash with target-shaped reddening or sores (erythema multiforme)

**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 become serious or if you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

## **5. HOW TO STORE PREMPAK-C**

Keep out of the reach and sight of children.

Do not use Prempak-C 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 Prempak-C contains**

- The active substances are conjugated estrogens and norgestrel.

Prempak-C contains two types of tablets: the set of 28 maroon or yellow tablets each contain conjugated estrogens, and the set of 12 light brown tablets each contain 0.15mg of the progestogen norgestrel.

The colour of the 28 estrogen tablets will depend upon which dose of estrogen your doctor has prescribed for you: the maroon tablets marked with '0.625' contain 0.625mg conjugated estrogens, and the yellow tablets marked with '1.25' contain 1.25mg of conjugated estrogens.

The other ingredients in the estrogen tablets are: lactose, methylcellulose, magnesium stearate, sucrose, glyceryl mono-oleate, macrogol, carnauba wax, calcium sulphate anhydrous, microcrystalline cellulose, pharmaceutical glaze (shellac), titanium dioxide (E171) stearic acid, edible ink and coating.

The edible ink on the maroon tablets contains titanium dioxide (E171), purified water, shellac (E904), ethanol, N-Butyl alcohol, propylene glycol (E1520), ammonia solution and ethyl acetate.

- The edible ink on the yellow tablets contains iron oxide black (E172), purified water, shellac (E904), ethanol, n-butyl alcohol, propylene glycol (E1520), ammonia solution and ethyl acetate.

The coating on the maroon tablets contains sucrose, purified water, erythrosine (E127), titanium dioxide (E171), sunset yellow (E110), indigo carmine (E132), povidone and sodium benzoate.

The coating on the yellow tablets contains quinoline yellow (E104) and sunset yellow (E110).

The other ingredients in the norgestrel tablets are: lactose, starch, povidone, talc, magnesium stearate, sucrose, macrogol, calcium carbonate, bleached wax, carnauba wax, titanium dioxide (E171) and colour (E172).

## **6.2 What Prempak-C looks like and contents of the pack**

Your Prempak-C carton contains three calendar packs. Each calendar pack contains 28 days' treatment: 28 estrogen tablets with 12 norgestrel tablets to take with the last 12 estrogen tablets in each pack. The calendar pack has days 1 to 28 printed on it to help you keep track of your tablets.

### **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 Prempak-C tablets only.

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