

Package leaflet: Information for the patient
Prempak[®]-C 0.625mg Coated Tablets
Prempak[®]-C 1.25mg Coated Tablets

(conjugated estrogens and norgestrel)

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

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Prempak-C is and what it is used for
2. What you need to know before you take Prempak-C
3. How to take Prempak-C
4. Possible side effects
5. How to store Prempak-C
6. Contents of the pack and other information

1. What Prempak-C is and what it is used for

Prempak-C is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an estrogen and a progestogen. Prempak-C is used to treat some of the symptoms and conditions associated with the menopause. Prempak-C is a sequential HRT (an HRT product where you have a monthly bleed).

Prempak-C 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.

You must talk to a doctor if you do not feel better or if you feel worse after taking this medicine.

2. What you need to know 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.

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

Warning and precautions

Talk to your doctor, pharmacist or nurse before taking 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 "Blood clots in a vein (thrombosis)")
- increased risk of getting an estrogen-sensitive cancer (such as having a mother, sister or grandmother who has had breast cancer)
- high blood pressure
- a liver disorder, such as a benign liver tumour

- diabetes
- gall bladder disease or gallstones
- migraine or severe headaches.
- fluid retention due to cardiac or kidney problems
- a disease of the immune system that affects many organs of the body (systemic lupus erythematosus, SLE)
- epilepsy
- asthma
- a disease affecting the eardrum and hearing (otosclerosis)
- hypocalcaemia (low blood calcium levels)
- thyroid deficiency
- hypertriglyceridemia (high levels of fatty substances in the blood)
- a very high level of fat in your 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
- 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.

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 have 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.

Unexpected bleeding

You will have a bleed once a month (so-called withdrawal bleed) while taking Prempak-C. But, if you have unexpected bleeding or drops of blood (spotting) besides your monthly bleeding, which:

- carries on for more than the first 6 months
 - starts after you have been taking Prempak-C more than 6 months
 - carries on after you have stopped taking Prempak-C
- see your doctor as soon as possible**

Breast cancer

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.

Compare

Women aged 50 to 79 who are not taking HRT, on average, 9 to 17 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 23 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 is rare- much rarer than breast cancer.

The use of estrogen-only or combined estrogen-progestogen HRT has been associated with a slightly increased risk of ovarian cancer.

The risk of ovarian cancer varies with age. For example, in women aged 50 to 54 who are not taking HRT, about 2 women in 2000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there will be about 3 cases per 2000 users (i.e. about 1 extra case).

Effect of HRT on heart and circulation

Blood clots in a vein (thrombosis)

The risk of **blood clots in the veins** is about 1.3 to 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, fainting or even death.

You are more likely to get a blood clot in your veins as you get older and if any of the following applies to you. Inform your doctor if any of these situations applies to you:

- you are unable to walk for a long time because of major surgery, injury or illness (see also section 3, If you need to have surgery)
- you are seriously overweight (BMI >30 kg/m²)
- you have any blood clotting problem that needs long-term treatment with a medicine used to prevent blood clots
- if any of your close relatives has ever had a blood clot in the leg, lung or another organ
- you have systemic lupus erythematosus (SLE)
- you have cancer
- you are pregnant or have recently had a baby.

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 have been taking estrogen-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).

Heart disease (heart attack)

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 years 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 getting 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:

- 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.

Compare

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

Other conditions

HRT will not 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. Speak to your doctor for advice.

Women with pre-existing hypertriglyceridemia (high levels of fat in the blood) might experience large increases of their plasma triglycerides, which can lead to inflammation of the pancreas (pancreatitis). Your doctor will monitor you closely if you have hypertriglyceridemia.

A two- to four-fold increase in the risk of gall bladder disease requiring surgery in women receiving HRT has been reported.

Other medicines and Prempak-C

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines including medicines obtained without a prescription, herbal medicines or other natural products. Some medicines may interfere with the effect of Prempak-C. This might lead to irregular bleeding.

This applies to the following medicines:

- Medicines for **epilepsy** (such as phenobarbital, phenytoin and carbamazepine).
- Medicines for **tuberculosis** (such as rifampicin, rifabutin).
- Medicines for **HIV infection** (such as nevirapine, efavirenz, ritonavir and nelfinavir).
- Herbal remedies containing **St John's wort** (*Hypericum perforatum*).
- Metyrapone (most commonly used in the treatment of Cushing's syndrome).

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.

Pregnancy, breast feeding and fertility

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.

Driving and using machines

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

Prempak-C contains lactose monohydrate, sucrose and E110

Prempak-C 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 medicinal product.

The colouring agent E110, which is present in the maroon and yellow tablets, may cause allergic reactions.

3. How to take Prempak-C

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

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.

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 or crush the tablets as this could affect the way Prempak-C works.

Dosage

The recommended 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. Swallow the tablet(s) with a drink of water. Take your tablet(s) at about the same time each day.

You may start your first pack at any convenient time. However, if you are transferring from another sequential HRT product (an HRT product that gives you a monthly bleed), treatment should begin the day following completion of the prior product unless instructed otherwise by your doctor.

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.

Duration of treatment

That really depends on why you and your doctor have decided on a course of treatment. If you are taking HRT to relieve your immediate menopausal symptoms, such as hot flushes and night sweats, you may be prescribed HRT for a relatively short period of time.

If, however, you or your doctor are worried about osteoporosis you may be prescribed HRT for longer.

If you take more Prempak-C than you should

If you take too many tablets do not worry as it is unlikely that serious problems will occur. If in any doubt, consult your doctor or pharmacist. You may feel some nausea (sickness), or experience a short period of vaginal bleeding if you take too many tablets.

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 missed take the tablet for the day that you remember and continue as normal. Do not take a double dose to make up for a forgotten tablet. Always finish your current pack before starting a new one.

Missed tablets may cause breakthrough bleeding in women with a uterus (womb).

If you need to have surgery

If you are going to have surgery, 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 (see section 2, Blood clots in a vein). Ask your doctor when you can start taking Prempak-C again.

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

4. Possible side effects

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

Stop taking Prempak-C and tell your doctor immediately if you experience:

- migraine-like headache
- shortness of breath
- sharp pains in the chest
- jaundice (yellowing of the skin or whites of the eyes)
- painful swelling of a leg.
- a large rise in your blood pressure (symptoms may be headache, tiredness, dizziness).

Do not take any more tablets unless your doctor tells you to.

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.

The following list of side effects have also been reported in women taking HRT, each event is categorised according to how frequently an event is likely to occur:

Very common: may affect more than 1 in 10 people

- breast pain

Common: may affect up to 1 in 10 people

- breakthrough bleeding or spotting, inflammation of the vagina resulting in discharge, dysmenorrhoea (lower back or abdominal pain associated with menstruation)
- 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: may affect up to 1 in 100 people

- changes in menstrual flow
- abnormal turning out of the cervix
- change in cervical mucus
- thrush
- nausea, bloating, abdominal pain
- headache, migraine
- dizziness
- changes in mood including irritability, nervousness/anxiety
- changes in your interest in sex (increased or decreased libido)
- visible swelling of the face or ankles
- itchiness, acne
- minor eye changes which may cause difficulties if you wear contact lenses
- gall bladder disease (e.g. gallstones)
- hair loss

Rare: may affect up to 1 in 1,000 people

- vomiting
- changes in breast tissue, milky secretion from the breasts
- allergic-like reactions
- irritability
- increase in hair growth
- a worsening of glucose tolerance
- a worsening of asthma
- increase the growth of existing benign meningioma (a tumour of the membranes around the brain or spinal cord)
- inflammation of the pancreas
- inflammation of the colon (part of the intestine) which may present as lower left sided abdominal pain and/or bloody diarrhoea
- inflammation of veins just under the skin
- heart attack
- worsening of epilepsy
- increased size of fibroids
- discoloration of the skin especially of the face or neck known as “pregnancy patches” (chloasma)

Very rare: may affect up to 1 in 10,000 people

- 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) in patients who already have a known risk of low levels of calcium in their blood
- enlargement of liver tumours
- worsening of porphyria (a rare inherited metabolic disorder)
- blood clots in the veins of the eye
- thickening of the lining of the uterus
- Increase in blood pressure
- painful reddish skin nodules (erythema nodosum)
- rash with target-shaped reddening or sores (erythema multiforme)

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

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRAs Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Prempak-C

Keep this medicine out of the sight and reach of children.

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

Do not store above 25°C.

If the pack has been opened or damaged return it to your pharmacist.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Prempak-C contains

The active substance in the maroon and yellow tablets is conjugated estrogen. Each maroon tablet contains 0.625 mg conjugated estrogens. Each yellow tablet contains 1.25 mg conjugated estrogens.

The active substance in the light brown tablets is norgestrel. Each light brown tablet contains 0.15 mg norgestrel.

The other ingredients in the conjugated estrogen tablets are: lactose monohydrate, sucrose (see section 2 this medicine contains lactose monohydrate and sucrose), methylcellulose, magnesium stearate, glyceryl mono-oleate, polyethylene glycol, carnauba wax, calcium sulfate anhydrous, microcrystalline cellulose, pharmaceutical glaze (shellac), titanium dioxide (E171), stearic acid, coating and edible ink.

The coating on the maroon tablets contains sucrose, sunset yellow (E110) (see section 2 this medicine contains lactose monohydrate, sucrose and E110), erythrosine (E127), titanium dioxide (E171), indigo carmine (E132), povidone and sodium benzoate. The edible white ink on the maroon tablet contains titanium dioxide (E171) and shellac (E904).

The coating on the yellow tablets contains sucrose, sunset yellow (E110) (see section 2 this medicine contains lactose monohydrate, sucrose and E110), quinoline yellow (E104). The edible black ink on the yellow tablet contains iron oxide black (E172) and shellac (E904).

The other ingredients in the norgestrel tablets are: lactose monohydrate, sucrose (see section 2 this medicine contains lactose monohydrate, sucrose and E110), starch, povidone, talc,

magnesium stearate,, polyethylene glycol, calcium carbonate, bleached wax, carnauba wax, titanium dioxide (E171) and iron oxide (E172).

The inks and dyes used to coat your tablets are approved for use as food colourings.

What Prempak-C looks like and contents of the pack

The Prempak-C carton contains a single calendar pack. The 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 colour of the estrogen tablets will depend upon which dose of estrogen your doctor has prescribed for you: the oval maroon tablets are marked with "0.625" in white ink and contain 0.625 mg conjugated estrogens, and the yellow tablets are marked with "1.25" in black ink and contain 1.25 mg conjugated estrogens.

The norgestrel tablets are round and light brown in colour.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder is

Pfizer Healthcare Ireland, 9 Riverwalk, National Digital Park, Citywest Business Campus, Dublin 24, Ireland.

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

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