

**CORE PACKAGE LEAFLET FOR
HORMONAL REPLACEMENT THERAPY PRODUCTS
based on core SPC HRT revision 3, Dec 2009**

*Doc. Ref.: CMDh/240/2011, Rev0
July 2011*

General note:

Product specific package leaflets should comply with the QRD template. The proposed text refers throughout to 'taking X'. The wording 'taking X' may be replaced by 'using X' for non-oral routes of administration, in line with the QRD template.

1. WHAT X IS AND WHAT IT IS USED FOR

X is a Hormone Replacement Therapy (HRT). It contains <the female hormone oestrogen> <two types of female hormones, an oestrogen and a progestogen>. X is used in postmenopausal women with at least *x months (x year)* since their last natural period.

X is used for:

Relief of symptoms occurring after menopause

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

If indicated:

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 X to prevent osteoporosis after menopause.

2. BEFORE YOU TAKE X

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 X 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 X.

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

Do not take X

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 X,

Do not take X

- 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 oestrogens**, 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 are **allergic** (hypersensitive) to {**include active substance name(s)**} or any of the other ingredients of X (listed in section 6 Further information)
- <product specific contra-indications>

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

When to take special care with X

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 X. 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 a oestrogen-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
- gallstones
- migraine or severe headaches.
- 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)
- a very high level of fat in your blood (triglycerides)
- fluid retention due to cardiac or kidney problems

Stop taking X 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 X' 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: X 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 oestrogen-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).

For combination products: The progestogen in X protects you from this extra risk.

For oestrogen-only products:

Taking a progestogen in addition to the oestrogen for at least 12 days of each 28 day cycle protects you from this extra risk. So your doctor will prescribe a progestogen separately if you still have your womb. If you have had your womb removed (a hysterectomy), discuss with your doctor whether you can safely take this product without a progestogen.

In women who still have a womb 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 aged 50 to 65 who still have a womb and who take oestrogen-only HRT, between 10 and 60 women in 1000 will be diagnosed with endometrial cancer (i.e. between 5 and 55 extra cases), depending on the dose and for how long it is taken.

{Additional warning for oestrogen-only products which are tablets containing more than 2 mg per day of oestrogen, tablets with more than 0.625 mg conjugated oestrogen or patches releasing more

than 50 micrograms oestrogen per day } X contains a higher dose of oestrogens than other oestrogen-only HRT products. The risk of endometrium cancer when using X together with a progestogen is not known.

For continuous combined HRT:

Irregular bleeding

You may have irregular bleeding or drops of blood (spotting) during the first 3-6 months of taking X. However, if the irregular bleeding:

- carries on for more than the first 6 months
- starts after you have been taking X for more than 6 months
- carries on after you have stopped taking X

see your doctor as soon as possible.

For cyclic or sequential oestrogen-progestogen combinations (fixed preparations and oestrogen-only tablets or patches that are combined with progestogen tablets):

Unexpected bleeding

You will have a bleed once a month (so-called withdrawal bleed) while taking X. 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 X more than 6 months
- carries on after you have stopped taking X

see your doctor as soon as possible

Breast cancer

Evidence suggests that taking combined oestrogen-progestogen and possibly also oestrogen-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.

{Additional information for oestrogen-only products} For women who have had their womb removed and who are using oestrogen-only HRT for 5 years, little or no increase in breast cancer risk is shown.

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 oestrogen-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 is rare. A slightly increased risk of ovarian cancer has been reported in women taking HRT for 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).

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 an other organ
- you have systemic lupus erythematosus (SLE)
- you have cancer.

For signs of a blood clot, see “Stop taking X 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 oestrogen-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).

{Additional warning for oestrogen-only products} For women in their 50s who have had their womb removed and have been taking oestrogen-only HRT for over 5 years, there will be 5 to 8 cases in 1000 users (i.e. 1 extra case).

Heart disease (heart attack)

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

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

{Additional warning for oestrogen-only products} For women who have had their womb removed and are taking oestrogen-only therapy there is no increased risk of developing a 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.

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).

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.
- <other product specific conditions>

Using other medicines

Some medicines may interfere with the effect of X. This might lead to irregular bleeding. This applies to the following medicines:

- Medicines for **epilepsy** (such as phenobarbital, phenytoin and carbamazepin)
- 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*).

<other product specific interactions>

Please 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.

Laboratory tests

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

Pregnancy and breast-feeding

X is for use in postmenopausal women only. If you become pregnant, stop taking X and contact your doctor.

3. HOW TO <TAKE> <USE> X

- <product specific>
- *The section should include the statement:*
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.
- *For oestrogen-only products, cyclic or sequential: information on the bleeding pattern should be included*

If you need to have surgery

If you are going to have surgery, tell the surgeon that you are taking X. You may need to stop taking X 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 X again.

4. POSSIBLE 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.

<product specific side-effects with frequencies>

After product specific list of side effects, the following should be included (remove side effects already listed as product specific):

The following side effects have been reported with other HRTs:

- gall bladder disease
- 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)