

# ESTRADERM MX® 25, 50, 75 and 100 (estradiol hemihydrate)

## Patient Information Leaflet

These patches will usually be referred to as Estraderm MX in this leaflet.

## What you need to know about Estraderm MX

Your doctor has decided that you need this medicine to help treat your condition.

**Please read this leaflet carefully before you start to use the patches. It contains important information.** Keep the leaflet in a safe place because you may want to read it again.

If you have any other questions, or if there is something you don't understand, please ask your doctor or pharmacist.

This medicine has been prescribed for you. Never give it to someone else. It may not be the right medicine for them even if their symptoms seem to be 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 Estraderm MX patches are, and what they are used for
2. Things to consider before you start to use Estraderm MX patches
3. How to use Estraderm MX patches
4. Possible side effects
5. How to store the patches
6. Further information

## 1. What Estraderm MX patches are and what they are used for

Estraderm MX is a patch which you stick on your skin. The patch contains a supply of estradiol which is released from the patch and absorbed through the skin into your blood stream. This is called a transdermal patch.

The active ingredient in the patches is estradiol. This is one of a group of hormones called estrogens which are the natural female sex hormone produced in large amounts by the ovaries before the menopause. After the menopause the ovaries produce less estrogen.

Estraderm MX is used as hormone replacement therapy (HRT) to relieve the symptoms of the menopause. The menopause can occur naturally or as the result of surgery.

Estraderm MX 50 and 75 patches can also be used to prevent osteoporosis (thinning of the bones), when you have a high risk of future fractures, and if you are unable to take other medicines for this purpose.

- **To relieve the symptoms of the menopause:**

Estraderm MX is used to help relieve the uncomfortable symptoms which you sometimes get during and after the menopause (the time when menstrual periods stop). Menopause occurs naturally in all women, usually between the ages of 45 and 55. It also occurs in younger women who have had their ovaries removed by surgery. The reduced levels of estrogen can cause unpleasant symptoms such as hot face, neck and chest, hot flushes (sudden waves of heat and sweating all over), sleep problems, irritability and depression. Some women also have problems with urine control, or with a dry vagina which may cause discomfort during or after sexual intercourse. Taking estrogens can reduce or eliminate these symptoms.

- **To prevent osteoporosis:**

After the age of 40, and especially after the menopause, some women are at risk of developing osteoporosis. This is when the bones become thinner and weaker and more likely to break, especially the bones of the spine, hip and wrist. Lack of estrogens increases the risk of osteoporosis. Taking estrogens after the menopause slows down bone loss and can help to prevent it. The protective effects on the bone cease once treatment is stopped. You should discuss the benefits and risks of Estraderm MX and other therapies with your doctor.

## **2. Things to consider before you start to use Estraderm MX**

Read this section carefully because, there are some conditions your doctor should know about before you start your treatment.

### **Medical check-ups**

Before you start using HRT, your doctor should ask you 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 you have any special concerns. Once you have started 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 with HRT.

### **While you are using HRT make sure that you:**

- 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, a discharge from the nipple, or any lumps you can see or feel.

### **Some people MUST NOT use Estraderm MX. Talk to your doctor if:**

- you have ever had any unusual or allergic reaction to estrogens or to any other components of the patch, (These are listed at the end of the leaflet.)
- you have, or have ever had, breast cancer, (See the section below on breast cancer.)
- you have, or have ever had, cancer of the endometrium (lining of the womb) or any other cancer which is sensitive to estrogens, (See the sections below on endometrial and ovarian cancer.)
- you have a blood disease called porphyria,
- you have, or have ever had, a blood clot in a vein in your leg or anywhere else (a 'deep vein thrombosis') or a clot that has travelled to your lung or another part of your body (an 'embolus'), (See the section below on blood clots.)

- you have ever had a heart attack, stroke or angina, (See the sections below on heart disease and stroke.)
  - you have had any unexpected bleeding or very heavy bleeding from the vagina,
  - you have a history of liver disease,
  - you have a condition called endometrial hyperplasia (thickening of the lining of the womb),
  - you are pregnant or breastfeeding.
- Estraderm MX should not be used in children.

**You should also ask yourself these questions before using the patch. If the answer to any of these questions is YES, tell your doctor or pharmacist because Estraderm MX might not be the right medicine for you.**

- Has anyone in your immediate family had breast cancer?
- Do you have fibroids or any other growths in your womb?
- Have you had a hysterectomy?
- Do you have endometriosis (a condition which causes painful periods)?
- Do you have high blood pressure?
- Do you have any problems with your liver?
- Do you have diabetes, epilepsy or asthma?
- Do you get migraine or other bad headaches?
- Do you have a condition called lupus (SLE)?
- Do you have problems with your hearing?
- Do you have any of the conditions which put you at increased risk of blood clots (see below)?
- Do you have a high level of cholesterol or other fats in your blood?
- Do you have heart or kidney problems?
- Have you ever had problems with your gall bladder, such as gallstones?
- Do you have hypothyroidism, a condition in which your thyroid gland fails to produce enough thyroid hormone and for which you are treated with thyroid hormone replacement therapy?
- Do you have hereditary angioedema or if you have had episodes of rapid swelling of the hands, feet, face, lips, eyes, tongue, throat (airway blockage) or digestive tract?
- Are you over 65?

#### **Are you taking other medicines?**

Some medicines can interfere with your treatment. Tell your doctor or pharmacist if you are taking any of the following:

- medicines to treat epilepsy such as phenobarbital, phenytoin and carbamazepine,
- antibiotics and other medicines to treat infections (e.g. rifampicin, rifabutin, nevirapine, efavirenz, ritonavir, nelfinavir),
- the herbal medicine St John's Wort (also known as *Hypericum perforatum*).

Always tell your doctor or pharmacist about all the medicines you are taking. *This means medicines you have bought yourself as well as medicines on prescription from your doctor.*

**Before you have a blood test** remind your doctor that you are using Estraderm MX as it may affect the result. Some laboratory tests, such as tests for glucose tolerance or thyroid function, may be affected by Estraderm MX therapy.

**Will there be any problems with driving or using machinery?**

No problems have been reported.

**Using contraception whilst taking Estraderm MX**

Estraderm MX is not a contraceptive, nor a fertility treatment.

If you are using an oral or other hormone contraceptive, e.g. the pill or depot injection, you must change to a non-hormone contraceptive, for example, a diaphragm or condom, BEFORE starting Estraderm MX.

If you have been told that you don't need to use a contraceptive any longer, you won't need one while you are using Estraderm MX even if you have a monthly bleed.

**Other special warnings**

**HRT will not help to prevent heart disease.**

As well as benefits, HRT has some risks which you need to consider when you are deciding whether to use it, or whether to carry on using it. These are:

**Effects on your heart or circulation**

**i. 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.

Studies with one type of HRT (containing conjugated estrogen plus a progestogen) 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 use any more HRT until your doctor says you can.**

**This pain could be a sign of heart disease.**

**ii. 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 ought to be using HRT.**

**If you get:**

- Unexplained migraine-type headaches, with or without disturbed vision,

**See a doctor as soon as possible and do not use any more HRT until your doctor says you can.**

These headaches may be an early warning sign of a stroke.

### iii. Blood clots

Using HRT may increase the risk of blood clots in the veins (also called deep vein thrombosis, or DVT), especially during the first year. 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
- You have had a blood clot before
- Any of your close family have had blood clots
- You have had one or more miscarriages
- You have any blood clotting problem that needs treatment with a medicine such as warfarin
- You're off your feet for a long time because of major surgery, injury or illness
- You are going on a long journey and will be immobile for some time
- You have a rare condition called systemic lupus erythematosus (SLE – a connective tissue disease).

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

#### If you get:

- Painful swelling in your leg
- Sudden chest pain
- Difficulty breathing

See a doctor as soon as possible and do not use 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.

*A comparison – the approximate risk of stroke or blood clots in women not using, or using, HRT over a 5 year period*

|            | Women in their 50s |            | Women in their 60s |             |
|------------|--------------------|------------|--------------------|-------------|
|            | Not using HRT      | Using HRT  | Not using HRT      | Using HRT   |
| Stroke     | 3 in 1,000         | 4 in 1,000 | 11 in 1,000        | 15 in 1,000 |
| Blood clot | 3 in 1,000         | 7 in 1,000 | 8 in 1,000         | 17 in 1,000 |

#### Effects on your risk of developing cancer

##### i. Breast cancer

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

Using HRT slightly increases the risk of breast cancer; so does having a late menopause. The risk for a post-menopausal woman using estrogen-only HRT for 5 years is about the same as for a woman of the same age who's still having periods over that time and not using HRT. The risk for a woman who is using combined HRT (estrogen plus progestogen) is higher than for estrogen-

only HRT (but combined 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 use it, but returns to normal within about 5 years of stopping HRT.

Your risk of breast cancer is also higher if:

- You have a close relative (mother, sister or grandmother) who has had breast cancer
- You are seriously overweight.

If you notice any changes in your breast, such as:

- Dimpling of the skin
- Changes in the nipple or a discharge from the nipple
- Any lumps you can see or feel

**Make an appointment to see your doctor as soon as possible.**

*A comparison – the risk of developing breast cancer: the number of women aged 50 who will get breast cancer by the time they are 65.*

| Not using HRT | Using estrogen-only HRT            |                                | Using combined HRT             |                                 |
|---------------|------------------------------------|--------------------------------|--------------------------------|---------------------------------|
|               | For 5 years                        | For 10 years                   | For 5 years                    | For 10 years                    |
| 32 in 1,000   | 33.5 in 1,000<br>(1-2 cases extra) | 37 in 1,000<br>(5 cases extra) | 38 in 1,000<br>(6 cases extra) | 51 in 1,000<br>(19 cases extra) |

**ii. Endometrial cancer (cancer of the lining of the womb)**

Estraderm MX is an estrogen-only product.

**Using estrogen-only HRT for a long time can increase the risk of cancer of the lining of the womb.** 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. They can 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.

*A comparison – the risk of developing endometrial cancer*

**Women who still have their uterus and who do not use HRT**

About 5 in 1,000 women aged 50 will get endometrial cancer by the time they are 65.

**Women who have used estrogen-only HRT**

The number will be 2-12 times higher depending on the dose and length of use.

**Women who have used estrogen plus progestogen HRT**

The risk of endometrial cancer is substantially reduced.

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 using HRT

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

### iii. Ovarian cancer (cancer of the ovaries)

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 using 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.

### Effects on your risk of developing dementia

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

## 3. How to use Estraderm MX patches

The doctor will tell you how to use Estraderm MX and what dose you need. Always follow his/her instructions carefully. The information will be on the pharmacist's label. Check the label carefully. If you are not sure, ask your doctor or pharmacist. Do not change the dose or stop the treatment without talking to your doctor.

If you have not had a hysterectomy, your doctor will give you tablets containing another hormone called progesterone to offset the effects of estrogens on the lining of the womb. (See the section above on endometrial cancer.) Your doctor will explain to you how to take these tablets. Withdrawal bleeding may occur at the end of the progesterone treatment period. Tell your doctor if you get irregular and/or heavy bleeding (see endometrial cancer).

### Starting to use the patches

Estraderm MX patches are applied to the skin. You wear them all the time. You should apply a new patch twice a week i.e. every 3 or 4 days.

- If you are not currently using any form of HRT (patch or tablets), if you have had a hysterectomy or if you have been using a continuous combined HRT product (where estrogen and the progesterone are given every day without interruption), you can start to use Estraderm MX on any convenient day.
- If you are changing from a cyclic or sequential HRT treatment where the progesterone is added for 12-14 days of the cycle, start to use Estraderm MX the day after you complete the cycle.
- If you are still having periods you should start to use Estraderm MX within 5 days of starting your period, irrespective of how long you bleed.

## About the patch

### Where to apply the patch

Stick the patch on to a hairless area of skin below the waist. Most patients find that the buttock is the best place. Choose an area of the buttock where the skin is not inflamed, broken, or irritated. You could also try the lower back, hip or abdomen.

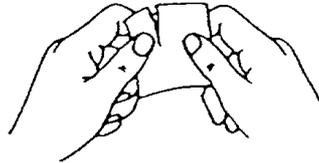
### Never put a patch on or near the breasts.

Choose a clean, dry area of skin. To help the patch stick, the skin should be clean, dry, and free of creams, lotions, oil, or powder. You should use a different area of skin each time. Wait a week before using the same area again. Avoid skin which is red or irritated.

Do not expose the patch to direct sunlight.

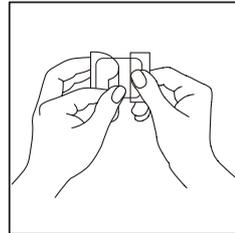
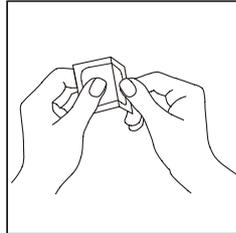
### Opening the sachets

Each Estraderm MX patch is sealed in an airtight sachet. Tear open one of the sachets at the notch (do not use scissors) and take out the patch. Don't take the patch out of the sachet until immediately before you intend to use it.



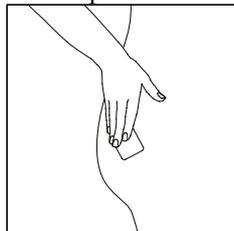
### Removing the lining

A stiff, transparent protective lining covers the sticky side of the patch, i.e. the side that will be placed against your skin. First remove the smaller piece of the transparent liner. Then peel off the larger piece. Try to avoid touching the adhesive and remember not to allow the patch to become folded so that the sticky surfaces come in contact with each other. Now apply the patch.



### Applying the patch

With the palm of your hand press the sticky side of the patch firmly onto the spot you have chosen. Hold it there for about 10-20 seconds. Make sure that it sticks well, especially around the edges, but once the patch is in place do not pull at it to test that it is sticking properly.



### **When and how to remove the patch**

The patches should be changed twice a week on the same two days of the week, e.g. Mondays and Thursdays. Choose two days which you are likely to remember.

You will find a table at the end of this leaflet for you to fill in to jog your memory. Tick the day of the week on which you are starting the treatment and keep this leaflet somewhere safe so that you can refer back to it if you need to.

When the time comes to change the patch, peel it off and fold it in half with the sticky side inside. Dispose of the patch carefully (see Section 5), making sure that it is kept out of the reach of children because it will still contain some medication. Stick a new patch onto a different area of skin.

### **What to do if a patch comes off**

If a patch falls off it will not stick to your skin again. Use another patch on a different area of your skin (see **Where to apply the patch**). Make sure you choose a clean, dry, lotion-free area of the skin. No matter what day this happens, go back to changing the patch on the same days as usual.

### **Other useful information**

- Bathing, swimming, showering or exercising should not affect the patch if it has been correctly applied. You may wear the patch under your swimming costume.
- Never apply a patch on a sweaty area or after a hot bath or shower. Wait until the skin is completely cool and dry.
- Do not remove the patch and try to put it somewhere else, it will not stick to your skin again. Instead apply a new patch in the usual way. Remember to apply your next patch at the normal time. If you have run out of patches, please contact your doctor straight away. (See also advice on “What to do if a patch comes off”.)
- Sunbathing: always make sure your patch is covered by clothing.
- Using a sunbed: cover up the patch
- The drug in your patch is contained in the adhesive and not in a special reservoir.
- The drug in your patch is a gel which is colourless. This does not mean that the patch does not contain any medication.

### **How long to use Estraderm MX**

Estraderm MX should be used only as long as needed, possibly for several months or more. This will help to control your symptoms.

While you are using Estraderm MX you should go to the doctor regularly to discuss the possible risks and benefits associated with HRT, and whether you still need the treatment. Your doctor will aim to give you the lowest possible dose for the shortest possible length of time to treat your symptoms.

### **If you forget to use Estraderm MX**

If you forget to apply a patch, apply a new patch as soon as you remember. No matter what day that happens, go back to changing this patch on the same day as you usually do. There is an increased chance of breakthrough bleeding or spotting if there is a break in treatment.

#### 4. Possible side effects

Estraderm MX is suitable for most people, but, like all medicines, there are sometimes side effects.

**Stop using Estraderm MX immediately and tell your doctor if you develop any of the following:**

- Signs of an allergic reaction (difficulty in breathing, tight chest, itching all over, generalised swelling or itching).
- Migraine or unusually severe headaches, or signs of stroke
- You become pregnant
- Signs of jaundice (yellowing of your skin or eyes).

**The side effects listed below have also been reported:**

**Up to 1 in 10 people have experienced:**

- Headache
- Feeling sick or bloated, stomach ache
- Redness, pain and itching where the patch has been applied
- Tender, painful or swollen breasts
- Breakthrough bleeding.

**Up to 1 in 100 people have experienced:**

- Breast cancer.

**Up to 1 in 1,000 people have experienced:**

- Dizziness
- Blood clots, bruising, worsening varicose veins, raised blood pressure
- Abnormal liver function test results, jaundice
- Rash and itching over large areas of the skin. This sensitivity reaction may become severe if you carry on using the patches without talking to your doctor.
- Changes in the pigmentation in your skin (lightening or darkening of your skin colour)
- Unusual weight changes, fluid retention (swelling or accumulation of fluid in the lower legs or ankles), leg pain.

**Other side effects include:**

- Estrogen-dependent conditions such as cancer of the endometrium, heart attack, stroke, dementia (these are discussed in Section 2) and gall bladder disease.
- Dry eyes.
- Contact lens discomfort.

**Tell your doctor or pharmacist as soon as possible if you do not feel well while you are using Estraderm MX. Ask your doctor or pharmacist to answer any questions you may have.**

#### 5. How to store the patches

Keep Estraderm MX out of the reach and sight of children both before and after use.

Store below 25°C, away from direct sunlight.

Do not use Estraderm MX after the expiry date shown on the pack.

Do not use a new Estraderm MX pack that is damaged or shows signs of tampering. If your doctor tells you to stop using Estraderm MX, please take any patches left back to your pharmacist to be destroyed. Only keep them if the doctor tells you to. Do not throw them away with your normal household water or waste. This will help to protect the environment.

## 6. Further information

The active substance in Estraderm MX is estradiol. The estradiol is derived from plants and is produced synthetically.

The other ingredients in Estraderm MX are isopropyl palmitate, acrylic adhesive (in solution in ethylacetate/hexane) and ethyl acetate. The backing film consists of ethylene vinyl acetate/polyester film laminate. The protective liner, which is removed before the patch is used, is a siliconized polyester film. The estradiol is released gradually while you are wearing the patch. Estraderm MX 25 contains 0.75 mg estradiol releasing about 25 micrograms of estradiol a day. Estraderm MX 50 contains 1.5 mg estradiol releasing about 50 micrograms of estradiol a day. Estraderm MX 75 contains 2.25 mg estradiol releasing about 75 micrograms of estradiol a day. Estraderm MX 100 contains 3.0 mg estradiol releasing about 100 micrograms of estradiol a day.

A one month pack contains 8 patches; a 3-month pack contains 24 patches of one size.

The product licence holder is Novartis Pharmaceuticals UK Limited, Frimley Business Park, Frimley, Camberley, Surrey, GU16 7SR, England.

Estraderm MX patches are made by Lohmann LTS, Lohmannstr. 2, P.O. Box 1525, 56605 Andernach, Germany.

**This leaflet was revised in December 2010.**

Fill this in to remind you when to change your patch. Please tick the box for the days of the week when you should change your patch.

- Monday + Thursday
- Tuesday + Friday
- Wednesday + Saturday
- Thursday + Sunday
- Friday + Monday
- Saturday + Tuesday
- Sunday + Wednesday

If you would like any more information, or would like the leaflet in a different format, please contact Medical Information at Novartis Pharmaceuticals UK Ltd, telephone number 01276 698370.

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