

**PACKAGE LEAFLET**

## **Package leaflet: Information for the user**

### **Evorel Sequi®**

Estradiol (as hemihydrate), norethisterone acetate

Evorel is a registered trademark

#### **Read all of this leaflet carefully before you start using 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 Evorel Sequi is and what it is used for
2. What you need to know before you use Evorel Sequi
3. How to use Evorel Sequi
4. Possible side effects
5. How to store Evorel Sequi
6. Contents of the pack and other information

#### **1. What Evorel Sequi is and what it is used for**

The name of your medicine is Evorel Sequi. It belongs to a group of medicines called hormone replacement therapy (HRT).

Evorel Sequi contains two medicines:

- An oestrogen (estradiol)
- A progestogen (norethisterone)

They are both female hormones.

Evorel Sequi comes in a 'memory pack'. This can be used to help you remember when to change your patches. Each pack contains eight patches.

- Four 'Evorel 50' patches marked CE50 (containing estradiol only)
- Four 'Evorel Conti' patches marked CEN1 (containing estradiol and norethisterone)

The hormones are spread evenly in each patch. They pass slowly into your body through the skin.

#### **Evorel Sequi is used for**

- The symptoms of the menopause (see 'What is the menopause?'). It is only used in women who still have a womb. It is suitable for women who have had the menopause (postmenopausal) or who are around the time of the menopause (perimenopausal)
- Prevent osteoporosis (fragile bones) in women who have had the menopause and are most likely to have bone problems. Evorel Sequi is only used if other medicines for osteoporosis have been tried first and they have not worked.

## **What is the menopause?**

Women produce oestrogen hormones from their ovaries throughout their adult life. These hormones are important in sexual development and control of the menstrual cycle.

The menopause happens when the level of hormones produced by the ovaries goes down. This is a gradual process. During this time the levels of oestrogen can go up and down. This can cause:

- Hot flushes, night sweats or moodswings
- Vaginal problems such as dryness or itching
- Uncomfortable or painful sexual intercourse

You may get the same symptoms if you have had your ovaries taken out in an operation.

## **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"). Evorel Sequi alleviates these symptoms after menopause. You will only be prescribed Evorel Sequi 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 Evorel Sequi to prevent osteoporosis after menopause.

## **How Evorel Sequi works**

Evorel Sequi is known as 'continuous sequential' HRT. This is because two hormones are used one after another:

- Estradiol is used by itself for two weeks
- Then estradiol and norethisterone are used together for the next two weeks.

Evorel Sequi patches replace the oestrogen that is normally released by the ovaries. However, taking an oestrogen hormone regularly may cause the lining of your womb to build up and get thicker.

- This means it is necessary to add a progestogen hormone to the oestrogen
- This helps shed the lining of the womb and stop any problems happening. Evorel Conti patches used during weeks 3 and 4 contain this progestogen

The shedding of the lining of the womb will probably give a 'withdrawal bleed'. This will be like having a period each month. The withdrawal bleed will start during week 4, before you finish an Evorel Sequi pack.

Evorel Sequi 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. What you need to know before you use Evorel Sequi**

### **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 Evorel Sequi 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 Evorel Sequi.

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

#### **Do not use Evorel Sequi 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**;
- You have a **thickening of the of the womb lining** (endometrial hyperplasia) that is not being treated;
- You have ever had a **blood clots in a vein** (thrombosis) such as in the legs (deep vein thrombosis) or the lungs (pulmonary embolism);
- You have a **blood clotting disorder** (such as protein C, protein S, or antithrombin deficiency);
- You have or recently have had a disease caused by blood clots in the arteries such as **a heart attack, asthma or angina**
- You have or have ever had a **liver disease** and your liver function tests have not returned to normal;
- You have a rare blood problem called "porphyria" which is passed down in families (inherited);

You are allergic to estradiol hemihydrate norethisterone acetate or any of the other ingredients of this medicine (listed in section 6).

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

#### **When to take special care with Evorel Sequi**

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 Evorel Sequi. 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 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;
- hereditary and acquired angioedema;
- history of sudden swelling of the face or throat, which may cause difficulty in swallowing or breathing, rapid swelling of the hands and feet and stomach cramps;

- thyroid problems.

You may still be able to use Evorel Sequi, but you should discuss this with your doctor first. Also tell your doctor if these illnesses return or get worse while you are using Evorel Sequi.

If you have had a premature menopause the risk of using HRT may be different. Talk to your doctor about the risks.

Make sure that you:

- Go for regular breast screening and cervical smears
- Regularly check your breasts for any changes such as dimpling of the skin, changes in the nipple or any lumps you can see or feel.

### **Stop using Evorel Sequi and see a doctor immediately**

If you notice any of the following when using Evorel Sequi

- any of the conditions mentioned in the ‘DO NOT use Evorel Sequi’ section;
- yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease;
- swollen face, tongue and/or throat and/or difficulty swallowing or hives, together with difficulty breathing which are suggestive of an angioedema;
- 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:** Evorel Sequi 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.

As well as benefits, HRT has some risks. Consider the following when deciding to take or continue HRT.

### **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).

The progestogen in Evorel Sequi protects you from this extra risk.

### **Unexpected bleeding**

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

**see your doctor as soon as possible**

**If you still have your womb**, your doctor will usually prescribe a progestogen as well as oestrogen. 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 oestrogen without a progestogen.

**If you have had your womb removed because of endometriosis**, any endometrium left in your body may be at risk of cancer. This means your doctor may prescribe HRT that includes a progestogen as well as an oestrogen.

Your product, Evorel Sequi, contains a progestogen. Evorel Sequi is only used in women who still have a womb (see Section 1 'What Evorel Sequi is used for').

#### *Compare*

Looking at women aged 50 to 65 who still have a womb, on average:

- In women **not taking HRT - 5 in 1000** will get endometrial cancer
- In women **taking oestrogen-only HRT- between 10 and 60 in 1000** will get endometrial cancer, (i.e. between **5 and 55 extra cases**) depending on the dose and how long you take it for.

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

### **Breast cancer**

Evidence shows that taking combined oestrogen-progestogen or oestrogen-only hormone replacement therapy (HRT) increases the risk of breast cancer. The extra risk depends on how long you use HRT. The additional risk becomes clear within a 3 years of use. After stopping HRT the extra risk will decrease with time, but the risk may persist for 10 years or more if you have used HRT for more than 5 years.

#### *Compare*

Women aged 50 to 54 who are not taking HRT, on average 13 to 17 in 1000 will be diagnosed with breast cancer over a 5-year period. For women aged 50 who start taking oestrogen-only HRT for 5 years, there will be 16-17 cases in 1000 users (i.e. an extra 0 to 3 cases).

For women aged 50 who start **taking oestrogen-progestogen HRT for 5 years**, there will be **21 cases in 1000 users** (i.e. an extra **4-8 cases**).

Women aged 50 to 59 who are not taking HRT, on average, 27 in 1000 will be diagnosed with breast cancer over a 10-year period.

For women aged 50 who start taking oestrogen-only HRT for 10 years, there will be 34 cases in 1000 users (i.e. an extra 7 cases)

For women aged 50 who start taking oestrogen-progestogen HRT for 10 years, there will be 48 cases in 1000 users (i.e. an extra 21 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

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

Additionally, you are advised to join mammography screening programs when offered to you. For mammography screening, it is important that you inform the nurse/healthcare professional who is actually taking the x-ray that you use HRT, as this medication may increase the density of your breasts which may affect the outcome of the mammogram. Where the density of the breast is increased, mammography may not detect all lumps.

### **Ovarian cancer**

Ovarian cancer (cancer of the ovaries) is rare, much rarer than breast cancer. The use of oestrogen-only or combined oestrogen-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.

These blood clots can be serious, and if a clot travels to the lungs, it can cause chest pain, breathlessness, collapse or even death. This is called pulmonary embolism, or PE.

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 very overweight (BMI above 30 kg/m<sup>2</sup>);
- You have any blood clotting problem that needs treatment with a medicine used to prevent blood clots such as warfarin;
- Any of your close relatives has ever had a blood clot in the leg, lung or another organ;
- You have a rare illness called SLE (Systemic lupus erythematosus);
- You have cancer;
- You have had one or more miscarriages;
- You are off your feet for a long time because of major surgery, injury or illness;
- You are taking medicine containing an oestrogen;
- You are going on a long journey and will not be moving about for some time.

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

#### *Compare*

Looking at women in their **50s**, on average, over 5 years:

- In women **not taking HRT** – between 4 and 7 **in 1000** would be expected to get a blood clot
- In women **taking** oestrogen-progestogen HRT - 9 and 12 in 1000
- would be expected to get a blood clot (an **extra 5 cases**)

If you get painful swelling in your leg, sudden chest pain or have difficulty breathing

- **See a doctor as soon as possible**
- **Do not take any more HRT** until your doctor says you can

These may be signs of a blood clot.

#### **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.

If you get a **pain in your chest** that spreads to your arm and neck

- **See a doctor as soon as possible**
- **Do not take any more HRT** until your doctor says you can

This pain may be a sign of heart disease.

## Stroke

Research suggests that HRT slightly increases the risk of having a stroke. Other things that can increase the risk of stroke include:

- Getting older
- High blood pressure
- Smoking
- Drinking too much alcohol
- An irregular heartbeat

If you are worried about any of these things, or if you have had a stroke in the past, talk to your doctor to see if you should take HRT.

## Compare

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.

Looking at women in their **50s**, on average, over 5 years:

- In women **not taking HRT - 8 in 1000** would be expected to have a stroke
- In women **taking HRT - 11 in 1000** would be expected to have a stroke (an **extra 3 cases**)

If you get **migraine-type headaches** which you cannot explain

- **See a doctor as soon as possible**
- **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;
- If you have brown patches on your face or body (chloasma) or have a history of them, you may need to keep out of the sun or away from sunbeds (these patches may not completely disappear again)

## Other medicines and Evorel Sequi

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines that you buy without a prescription or herbal medicines.

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

- Medicines for **epilepsy** (such as phenobarbital, phenytoin or carbamazepine);
- Certain medicines for **tuberculosis** (such as rifampicin, rifabutin);
- Medicines used to treat **HIV infection** (such as nevirapine, efavirenz, ritonavir or nelfinavir);
- Herbal remedies containing **St John's Wort** (*Hypericum perforatum*);
- Medicines for Hepatitis C virus (HCV) (such as combination regimen ombitasvir/paritaprevir/ritonavir with or without dasabuvir as well as a regimen with glecaprevir/pibrentasvir) may cause increases in liver function blood test results (increase in ALT liver enzyme) in women using CHCs containing ethinylestradiol. Evorel sequi contains estradiol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Evorel sequi with this HCV combination regimen. Your doctor will advise you.



- Medicine for Hepatitis C infection, telaprevir
- Bosentan - for high blood pressure in the blood vessels of the lungs

Taking these medicines with Evorel Sequi can stop it from working as well. Because of this you may get some bleeding, like a period, when you are not expecting it.

- A medicine for epilepsy called lamotrigine. Using Evorel Sequi with lamotrigine could affect control of your epilepsy.

### **Operations or tests**

Tell your doctor if you are going to have surgery. You may need to stop taking HRT about 4 to 6 weeks before the operation to reduce the risk of a blood clot. Your doctor will tell you when you can start taking HRT again.

If you visit a hospital or your family doctor for a blood or urine test, tell them that you are taking Evorel Sequi. This is because this medicine may affect the results of the tests.

### **Children and adolescents**

Evorel Sequi should not be used by children.

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

Do not use this medicine if you are pregnant, think you may be pregnant or might become pregnant. This is because it may affect the baby.

Evorel Sequi is for use in postmenopausal women only. If you become pregnant, remove the patch and contact your doctor.

Do not use this medicine if you are breast-feeding.

Ask your doctor or pharmacist for advice before taking any medicine if you are pregnant or breast-feeding.

### **Driving and using machines**

There is no information about whether Evorel Sequi affects your ability to drive or use machines. See how this medicine affects you before you drive or use any tools or machines.

## **3. How to use Evorel Sequi**

Always use this medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. Your doctor will aim to reduce your symptoms with the lowest possible dose for the shortest amount of time.

### **When to start using Evorel Sequi**

#### **You may put an Evorel Sequi patch on at any time if:**

- You have not used HRT before your menopause and no longer have menstrual periods
- Your menstrual cycles are not regular and you are not pregnant
- You are changing from HRT that does not give you a withdrawal bleed

#### **Put an Evorel 50 patch on within 5 days of the start of bleeding if:**

- You are not currently using HRT and still having regular periods

#### **Put an Evorel 50 patch on at the end of a treatment cycle or one week after you finish using another HRT product if:**

- You are changing from an HRT medicine that gives you a withdrawal bleed

### If you are using another type of HRT:

- The day you start will depend on the type of HRT you have been using  
Talk to your doctor if you are not sure which type of HRT you are using.

### Using the patches

The patches need to be changed twice a week. You must use the patches in the right order.

### Weeks 1 and 2

Use the four Evorel 50 patches one at a time.

### Weeks 3 and 4

Use the four Evorel Conti patches one at a time. As soon as you remove your fourth Evorel 50 patch, replace it with the first Evorel Conti patch.

Start a new pack of Evorel Sequi as soon as you finish one. Do not leave a break between packs.

### Changing your patches

- You must change the patches twice a week to give your body a steady supply of hormones. There is enough hormone in each patch to last for several days
- Change your patch on the same two days every week. This will mean that one patch is on for three days and the next patch for four days
- For example, if you apply your first patch on a Monday, change it on Thursday and again on the following Monday. You can work out your two days from the following table, starting from the first day of use:

#### If you put your

#### first patch on:

Monday

→

#### Change on:

Thursday

&

#### Change again on:

Monday

Tuesday

→

Friday

&

Tuesday

Wednesday

→

Saturday

&

Wednesday

Thursday

→

Sunday

&

Thursday

Friday

→

Monday

&

Friday

Saturday

→

Tuesday

&

Saturday

Sunday

→

Wednesday

&

Sunday

To help you remember your two "patch change" days, mark them here or on the pack. They are written on the pack like this:

Mon  
Thur

Tue  
Fri

Wed  
Sat

Thur  
Sun

Fri  
Mon

Sat  
Tue

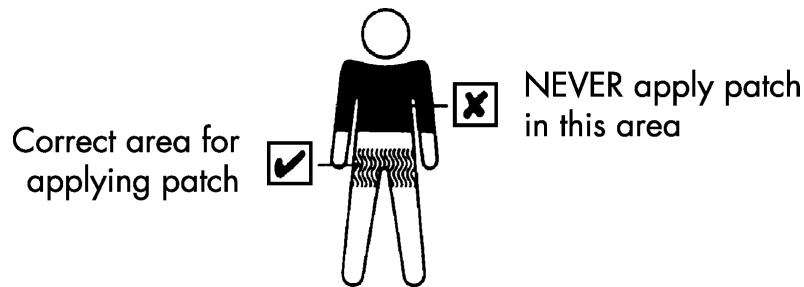
Sun  
Wed

### Where to apply the patch

Stick the patch onto a hairless area of skin below the waist. Most women prefer to wear the patch on the thigh or bottom.

- Do not apply on or near the breasts
- Do not put it on top of cuts, spots or anywhere the skin is irritated

- Do not use cream, moisturiser or talc before applying the patch
- Do not apply the patch on the same area of skin twice in a row
- It can be worn under loose areas of clothing.
- Do not wear a patch under elasticated areas or a tight waistband
- Apply the patch to clean, dry, cool skin as soon as you open the protective pouch

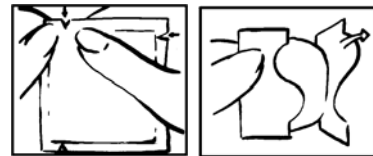


### Putting a patch on

Do not use a patch if its protective pouch is already open.

#### Step 1: Open and Peel

- Using the notches as a guide, tear along two



edges of the pouch. Remove the patch

- With the protective backing facing you, bend and peel off half the backing. Don't touch the sticky side - it may not stick properly if you do

#### Step 2: Apply and Press

- Apply the open half of the patch to your skin
- Remove the remaining backing and press down the rest of the patch
- Press the patch with the palm of your hand to make sure it is firmly stuck



### Removing a patch

- Peel an edge of the patch smoothly away from the skin
- Fold the patch in half, so that the sticky side sticks to itself
- Put it in with the household rubbish, safely out of the reach of children and pets
- Do not flush used patches down the toilet



When you remove the patch some glue may remain on your skin. It will disappear with time, or you can use baby oil to remove it.

### If a patch falls off

Apply a new patch but keep to your original 'patch change' days. If you have just had a bath or shower, wait until your skin cools before applying the new patch.

It is always useful to keep a spare pack that you can use to replace patches that have fallen off. Talk to your doctor if you need more patches.

### **If you forget to change the patch**

Change it as soon as you remember and then keep to your original 'patch change' days. You may get some bleeding and spotting like a period during this time.

### **If you use more Evorel Sequi than you should**

It is unlikely that you will have too much of the hormones in Evorel Sequi. The most common symptoms of having too much oestrogen or progesterone in your body are:

- Tender breasts
- Feeling sick (nausea) or being sick
- Unexpected vaginal bleeding
- Feeling depressed
- Tiredness
- Acne
- Growth of body or facial hair

Removing the patch can reverse the effects of too much oestrogen. Talk to your doctor or pharmacist before using any more patches.

### **Contraception while using Evorel Sequi**

The levels of hormone from the patches are too low to act as a contraceptive. Use non-hormonal contraceptive methods (such as a condom, diaphragm or coil) until your periods have completely stopped.

### **Everyday activities**

Everyday activities

- You can have a bath or shower as normal. Do not scrub too hard as this can loosen the edges of the patch
- You can go swimming. The patch will not be affected
- You can exercise and play sports. However, do not wear the patch under tight clothing or waist bands
- You can sunbathe. However, keep the patch covered, out of direct sunlight

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

### **If you need to have surgery**

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

### **If you stop using Evorel Sequi**

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.

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.

**Take off the patch and tell your doctor straight away if you notice or suspect any of the following. You may need urgent medical treatment.**

- Sudden swelling of the face or throat which may cause difficulty in swallowing or breathing, rapid swelling of the hands and feet and stomach cramps
- Blood clots (thrombosis) (affects less than 1 in 1000 people) or stroke (frequency not known)
- Yellowing of the skin or whites of the eyes (jaundice), or other liver problems
- Migraine-type headaches for the first time or more frequent (affects less than 1 in 10 people)
- An increase in blood pressure (affects less than 1 in 10 people)
- Breast or ovarian cancer, endometrial cancer or hyperplasia (long, heavy or irregular vaginal bleeding)
- Widespread rash with peeling skin and blistering in the mouth, eyes and genitals (Stevens-Johnson syndrome) (frequency not known)
- Convulsions or fits (frequency not known)

**Tell your doctor if you notice any of the following side effects while using Evorel Sequi:**

**Very common** (affects more than 1 in 10 people)

- Irritated, itchy, red skin and rash where the patch is applied

**Common** (affects less than 1 in 10 people)

- Feeling depressed or nervous
- Inappropriate signs of emotion
- Being unable to sleep
- Headache
- Itchy skin or red rash
- Feeling sick (nausea), or having stomach pain wind or other stomach upsets
- Diarrhea
- Pain including pain in the back, muscles, joints
- Breast pain
- Feeling generally unwell
- Weight gain
- Heavy vaginal bleeding, painful periods
- Water retention or build-up of fluid under the skin (oedema)

**Uncommon** (affects less than 1 in 100 people)

- Concentration problems
- Feeling dizzy
- More or less interest in sex than usual
- Allergic reaction (hypersensitivity)
- A fungal infection called thrush
- Feeling tired
- Being aware of your heartbeat (palpitations)
- Numb or tingling hands or feet, less skin sensitivity

- Breast lumps (non-cancerous)
- Fuller breasts
- Irregular vaginal bleeding
- Thickening of the lining of the womb

**Frequency not known**

- Mood swings
- Bloating feeling
- Gallstones
- Swelling of the hands and feet (peripheral oedema)
- Puffy skin where the patch is applied

**The following side effects have been reported with other combined HRTs:**

**Very common** (affects more than 1 in 10 people)

- Tender breasts

**Common** (affects less than 1 in 10 people)

- Indigestion
- Acne
- Dry skin
- Pain in extremity (e.g. back pain, arms, legs, wrists, ankles)
- Severe contractions of the uterus
- Vaginal infection or discharge (white or yellowish discharge from the vagina)

**Uncommon** (affects less than 1 in 100 people)

- Dizziness
- Varicose veins
- Being sick
- Skin discoloration
- Abnormal liver function tests

**Rare** (affects less than 1 in 1,000 people)

- Gallstones
- Muscle weakness
- Benign growths in the uterus smooth muscle
- Cysts close to the Fallopian tube
- Cervical polyps

**Very Rare** (affects less than 1 in 10,000 people)

- Yellowing of the skin, itching, dark coloured urine

**Frequency not known**

- Hair loss

**The following side effects have been reported in association with estrogen/progestogen treatment**

- Gall bladder disease
- Various skin disorders:
  - Brown patches on your face or body, discoloration of the skin especially of the face or neck known as “pregnancy patches” (chloasma)
  - Rash with painful reddish skin nodules (erythema nodosum)

- Rash with target shaped reddening or sores (erythema multiforme)
- Rash with red or purple coloured spots (vascular purpura)
- Loss of memory (Dementia) (see section 2)
- Dry eyes
- Change to composition of tears

### **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 the Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard).

By reporting side effects you can help provide more information on the safety of this medicine.

## **5. How to store Evorel Sequi**

Keep this medicine out of the sight and reach of children. It should be stored at room temperature (do not store above 25°C).

Do not use Evorel Sequi after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

Do not use a patch if the protective pouch is open.

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 Evorel Sequi contains**

**The active substances** in Evorel Sequi are estradiol hemihydrate and norethisterone acetate.

Each Evorel 50 patch contains 3.2 mg of estradiol hemihydrate. Each Evorel 50 patch delivers 50 micrograms of estradiol a day.

Each Evorel Conti patch contains 3.2 mg of estradiol hemihydrate and 11.2 mg of norethisterone acetate. Each Evorel Conti patch delivers 50 micrograms of estradiol and 170 micrograms of norethisterone a day.

**The other ingredients** are Duro-Tak 387-2287 (this makes the patches sticky), guar gum and Hostaphan MN19 (backing film).

### **What Evorel Sequi looks like and contents of the pack**

Evorel Sequi comes in a memory pack containing four Evorel 50 patches (marked CE50) and four Evorel Conti patches (marked CEN1).

Both types of patch are square with rounded corners. They are clear with a sticky backing that can be stuck to the skin. Each patch comes in a protective sealed pouch and has a surface area of 16 sq cm.

### **Marketing Authorisation Holder:**

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### **Manufacturer:**

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