

PACKAGE LEAFLET

Package leaflet: Information for the user

Evorel® Conti 50/170 micrograms per 24 hours Transdermal Patch 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 Conti is and what it is used for
2. What you need to know before you use Evorel Conti
3. How to use Evorel Conti
4. Possible side effects
5. How to store Evorel Conti
6. Contents of the pack and other information

1. What Evorel Conti is and what it is used for

The name of your medicine is Evorel Conti 50/170 micrograms per 24 hours Transdermal patch. It is called Evorel Conti in this leaflet. Evorel Conti is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an oestrogen and a progestogen. Evorel Conti is used in postmenopausal women with at least 18 months since their last natural period.

Evorel Conti comes in a pack that helps you to remember when to change your patches (see section 3 'How to use Evorel Conti'). Each pack contains eight patches.

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

What Evorel Conti is used for

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 Conti alleviates these symptoms after menopause. You will only be prescribed Evorel Conti if your symptoms seriously hinder your daily life. It is suitable for women who have been post-menopausal for 6 months. This is usually taken to be 18 months after the last period (menstrual bleed), but your doctor will advise you.

How Evorel Conti works

Evorel Conti is known as 'continuous combined' HRT. This is because both hormones in the patch are released all the time.

Evorel Conti patches replace the oestrogen that is normally released by the ovaries. However, in women who still have a womb, 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
- This is why Evorel Conti patches also contain a progestogen.

Most women do not have a regular monthly period with Evorel Conti. However, bleeding or spotting does often occur in the first few months until treatment settles down.

Evorel Conti 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 Conti

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

Do not use Evorel Conti

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 Evorel Conti,

Do not take Evorel Conti:

- You have or have ever had **breast cancer**, or if you are suspected of having it;
- You have **cancer which is sensitive to oestrogens**, such as cancer of the womb lining (endometrium), or if you are suspected of having it;
- You have **unexplained vaginal bleeding**;
- You have **excessive thickening of the womb lining** (endometrial hyperplasia) that is not being treated;
- You have or 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 **heart attack, stroke or angina**
- 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 Estradiol (as hemihydrate), norethisterone acetate or any of the other ingredients of Evorel Conti (listed in section 6 Further information);

Stop using Evorel Conti at once if any of the above appears for the first time and talk to your doctor immediately.

When to take special care with Evorel Conti

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 Conti. 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 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 levels of fat in your blood (triglycerides)
- Fluid retention due to cardiac or kidney problems;
- hereditary and acquired angioedema.

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

Stop using Evorel Conti and see a doctor immediately

If you notice any of the following when using Evorel Conti

- any of the conditions mentioned in the ‘DO NOT use Evorel Conti’ 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)

Safety of HRT

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

Effect of HRT on heart and circulation 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 have any more HRT** until your doctor says you can This pain may 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.

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 have any more HRT** until your doctor says you can These headaches may be an early warning sign of a stroke.

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 using 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

For signs of a blood clot, see “Stop taking Evorel Conti and see a doctor immediately”

How likely is a blood clot?

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

- In women in their 50s **not taking HRT – between 4 and 7 in 1000** would be expected to get a blood clot
- In women in their 50s **taking oestrogen-progestogen HRT – between 9 and 12 in 1000** would be expected to get a blood clot (an **extra 5 cases**)

HRT and Cancer

Breast cancer

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

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 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.

How likely is breast cancer?

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).

If you notice any **changes in your breast**, 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 mammogram 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.

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

HRT is **not recommended** for women who have ever had cancer of the lining of the womb.

Using 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 Conti protects you from this extra risk.

How likely is endometrial cancer?

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.

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

Irregular bleeding

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

- Carries on for more than the first 6 months
- Starts after you have been on Evorel Coti for more than 6 months

- Carries on even after you've stopped using HRT
see your doctor as soon as possible.

Ovarian cancer

Ovarian cancer 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).

Dementia

Evorel Conti and medicines like it will not stop memory loss (dementia). Women who start using medicines like Evorel Conti after the age of 65 may have a small increase in the risk of dementia.

Using other medicines

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

- Medicines to help you sleep (called barbiturates)
- A medicine for pain and inflammation called phenylbutazone
- A medicine for anxiety called meprobamate
- Medicines for **epilepsy** (such as phenobarbital, phenytoin or carbamazepine);
- Medicines for **tuberculosis** (such as rifampicin or rifabutin);
- Medicines used to treat **HIV infection** (such as nevirapine, efavirenz, ritonavir and nelfinavir);
- Herbal remedies containing **St John's Wort** (*Hypericum perforatum*);
- Medicine for Hepatitis C infection, telaprevir
- A medicine for high blood pressure in the blood vessels of the lungs called bosentan

HRT can affect the way some other medicines work:

- A medicine for epilepsy (lamotrigine), as this could increase frequency of seizures
- Medicines for Hepatitis C virus (HCV) (such as combination regimens ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin; glecaprevir/pibrentasvir or sofosbuvir/velpatasvir/voxilaprevir) may cause increases in liver function blood test results (increase in ALT liver enzyme) in women using CHCs containing ethinylestradiol. Evorel Conti contains estradiol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Evorel Conti with this HCV combination regimen.

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. Your doctor will advise you.

Operations or tests

Tell your doctor if you are going to have surgery. 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.

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

Pregnancy and breast-feeding

Evorel Conti is for postmenopausal women only. If you become pregnant, contact your doctor straight away and remove the patch.

Driving and using machines

There is no information about whether Evorel Conti 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 Conti

Always use this medicine Evorel Conti 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 Conti

Put an Evorel Conti patch on at the end of a treatment cycle or two weeks 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.

You may put an Evorel Conti patch on at any time if:

- You have not been using another type of HRT

Using the patches

The patches need to be changed twice a week.

Start a new pack of Evorel Conti 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

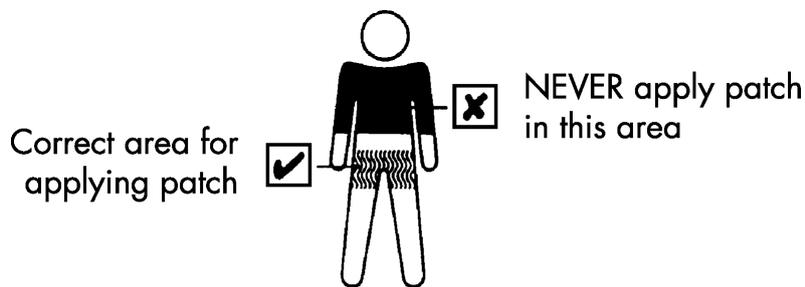
Sat
Tue

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

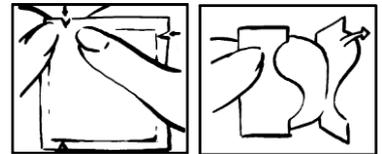


Putting a patch on

Do not use a patch if its protective pouch is 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 a shower, wait until your skin cools before applying the new patch.

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 Conti than you should

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

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

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

Contraception while using Evorel Conti

The levels of hormone from the patches are too low to act as a contraceptive. Talk to your doctor for advice on contraception.

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.

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. This may be a sign of an allergic reaction. This only happens in a small number of people
- Blood clots (thrombosis) (affects less than 1 in 1000 people)
- Stroke (frequency not known)

- Breast cancer or ovarian cancer
- Endometrial cancer or hyperplasia (long, heavy or irregular vaginal bleeding)
- 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 100 people)
- An increase in blood pressure (affects less than 1 in 10 people)
- Widespread rash with peeling skin and blistering in the mouth, eyes and genitals (Stevens-Johnson syndrome) (frequency not known)
- Convulsions or fits (affects less than 1 in 1,000 people)

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

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)

- Allergic reaction (hypersensitivity)
- Feeling depressed, nervous or anxious
- Being unable to sleep
- Headache
- Being aware of your heartbeat (palpitations)
- Varicose veins
- Flushing, skin reddening
- Breast pain
- Numb or tingling hands or feet
- Feeling sick (nausea)
- Diarrhoea
- Stomach ache
- Pain including pain in the back or joints
- Painful periods or thick white discharge from the vagina
- Discharge from the vagina
- Irregular, heavy or prolonged bleeding from the vagina, including after sex
- Water retention or build-up of fluid under the skin (oedema)
- Feeling tired
- Weight gain

Uncommon (affects less than 1 in 100 people)

- Vaginal infections such as thrush
- Less interested in sex than usual
- Wind
- Itchy skin
- Rash
- Swelling of hands and feet (peripheral oedema)
- Muscle pain

Frequency not known

- Mood swings
- Feeling dizzy
- Bloating feeling
- Gallstones
- Fuller breasts

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)

- Mood changes

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

Uncommon (affects less than 1 in 100 people)

- Dizziness
- Being sick
- Skin discolouration
- 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

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 oestrogen/progestogen treatment

- Gall bladder disease
- Brown patches on your face or body (chloasma)
- Rash with painful reddish skin nodules (erythema nodosum)
- Rash with target shaped reddening or sores (erythema multiforme)
- Bruising on the legs
- 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 Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Evorel Conti

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

Do not use Evorel Conti after the expiry date which is stated on the carton and pouch (after 'EXP'). The expiry date refers to the last day of that month.

Do not store above 25°C. Keep in the original pouch and carton. Do not use a patch if its protective pouch is open.

Refer to Section 3, 'Removing a patch', for disposal instructions for used patches.

Ask your pharmacist how to dispose of unused patches.

6. Contents of the pack and other information

What Evorel Conti contains

The active substances in Evorel Conti are estradiol hemihydrate and norethisterone acetate. 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 acetate over 24 hours.

The other ingredients are polyethylene terephthalate layer with guar gum and acrylate-vinyl acetate copolymer (that makes the patches sticky). The protective backing that is removed before applying the patch is made of siliconised polyethylene terephthalate.

What Evorel Conti looks like and contents of the pack

Evorel Conti comes in a pack containing eight patches (marked CEN1).

The clear sticky patches are square with rounded corners. They are protected with a clear removable plastic backing. Each patch has a surface area of 16 sq cm and comes in a protective sealed pouch.

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