SCHEDULING STATUS

S4

EVOREL® CONTI, 50 µg, 170 µg, Patches

Estradiol/norethisterone

EVOREL CONTI contains no sugar.

Read all of this leaflet carefully before you start using EVOREL CONTI patches

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- EVOREL CONTI has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

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

EVOREL CONTI patches contain estradiol and norethisterone.

EVOREL CONTI is used for hormone replacement therapy (HRT) in the treatment of symptoms of menopause, such as hot flushes and vaginal dryness in women who still have a womb.

In women who still have a womb, using estrogen regularly without using a progestogen may cause the lining of the womb to build up and thicken, which may lead to cancer of the womb. Adding a progestogen hormone to the estrogen treatment prevents this build-up of the lining of the womb. That is why the EVOREL CONTI patches also contain the progestogen, norethisterone acetate.

EVOREL CONTI does not cause a regular monthly period in the majority of women.

EVOREL CONTI should not be used by children.

EVOREL CONTI should not be used for contraception.

2. What you need to know before you use EVOREL CONTI

Do not use EVOREL CONTI if

- You are allergic (hypersensitive) to any of the ingredients in EVOREL CONTI patches (see section 6: "*What EVOREL CONTI contains*" below).
- You had, have or suspect that you have breast cancer.
- You have a family history of breast cancer.
- You have genital tract cancer or other cancers known to be sensitive to estrogens.
- You have undiagnosed vaginal bleeding.
- You are pregnant or breastfeeding.
- You have liver disease or a history of liver disease as long as liver function tests have not returned to normal.
- You have or have had blood clots (thrombosis) or inflammation of veins (thrombophlebitis) or have, a family history thereof.
- You have active or previous arterial thrombotic disease (e.g. stroke, heart attack).
- You have porphyria.
- You have depression, which is not well controlled with treatment.
- You have had depression with previous use of estrogen and/or progesterone/progestogen containing medicines.

Warnings and precautions

Medical check-ups

- It is important that you have a full and thorough physical and gynaecological examination and that your own family's medical histories regarding thrombosis (blood clots) are taken before you start EVOREL CONTI.
- You should receive regular full medical examinations whilst using EVOREL CONTI.

Before you use EVOREL CONTI, tell your doctor if:

- You are known to have inherited genetic changes called "BRCA1 and/or BRCA2 genes".
- You started your menstrual periods before the age of 12 years.
- You have a history of non-cancerous breast diseases such as atypical hyperplasia or lobular carcinoma *in situ*.
- You had any previous treatment using radiation therapy to the chest or breast.

- You have been treated or exposed while in your mother's womb to a medicine called diethylstilboestrol (DES).
- You are on treatment for depression.
- You have had depression with previous use of estrogen and/or progesterone/progestogen containing medicines.
- You have a substance abuse problem.
- You have underlying psychiatric disorder such as post-traumatic stress disorder or bipolar disorder.
- You have a family history of mental disorders.
- You have a history of physical or sexual abuse.

If you have any of the following, you may still be able to use EVOREL CONTI, but you should discuss this with your doctor first. He/she may need to see you more regularly for monitoring purposes whilst you are using EVOREL CONTI.

If any of the following conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, you should be closely supervised by your doctor as these conditions may recur or be aggravated during treatment with EVOREL CONTI.

- Leiomyoma (uterine fibroids) or endometriosis
- Risk factors for blood clots
- Risk factors for estrogen dependent tumours, e.g. first degree relative with breast cancer
- High blood pressure
- Liver disorders (including benign tumours of liver cells)
- Diabetes mellitus
- Gall stones
- Migraine or severe headache
- Systemic lupus erythematosus (lupus)
- A history of endometrial overgrowth (endometriosis)
- Epilepsy
- Breast disease

Your doctor will give you regular medical check-ups if you have any of the following conditions:

- Fluid retention (swelling) from estrogens, such as in EVOREL CONTI
- If you have heart or kidney dysfunction, it should be carefully monitored
- Disturbances of liver function
- History of yellow pigmentation of skin or eyes (jaundice)

- Pre-existing high cholesterol or triglycerides

If you develop any of the following conditions during whist using EVOREL CONTI, immediately inform your doctor and stop using EVOREL CONTI:

- Yellowing of the skin or eyes (jaundice) or deterioration of liver function
- Increase in blood pressure
- New migraine type of headaches
- You become pregnant

If you are not sure about any of the conditions mentioned above, please speak to your doctor.

EVOREL CONTI and breast cancer

Breast cancer has been diagnosed slightly more often in women who use the Pill than in women of the same age who do not use the Pill. This slight increase in the numbers of breast cancer diagnoses gradually disappears during the course of the 10 years after stopping use of the Pill.

When you are using EVOREL CONTI, you must perform monthly breast self-examinations. Your doctor will advise you on when to report for breast examinations and any appropriate investigations.

There is evidence that HRT, such as EVOREL CONTI may increase the risk of breast cancer in postmenopausal women receiving long- term HRT. You should not use EVOREL CONTI for more than 5 years.

Ovarian cancer

Long-term use of estrogen containing HRT products such as in EVOREL CONTI has been associated with an increased risk of ovarian cancer.

Venous thromboembolism (blood clots)

If you have had a blood clot in the leg or lung, a stroke or a heart attack or are bed-ridden for any reason, such as after an operation, you may still be able to use EVOREL CONTI, but your doctor should decide on this, and you should have a regular medical check-up with your doctor if you do use it. If, while using EVOREL CONTI, you develop symptoms of a blood clot such as unexplained pains in the chest, abdomen or legs, the patch should be removed, and your doctor contacted immediately.

Heart disease

Combined estrogen-progestogen therapy such as EVOREL CONTI: The relative risk of heart disease during use of combined estrogen-progestogen HRT is increased.

Stroke

There is an increased risk of stroke in healthy women during treatment with HRT such as EVOREL CONTI.

Depressed mood, depression and the risk of suicidality

Estrogen and/or progesterone/progestogen containing medicines including EVOREL CONTI, may cause mood changes and depression, which may be severe. Severe depression is associated with a higher risk of suicidal thoughts/behavior (e.g. talking about suicide, withdrawing from social contact, having mood swings, being preoccupied with death or violence, feeling hopeless about a situation, increasing use of alcohol/drugs, doing self-destructive things, personality changes) and suicide. If you experience mood changes and depression, contact your doctor for advice.

Mental impairment

There is some evidence of mental deterioration in women using continuous combined HRT, such as EVOREL CONTI.

EVOREL CONTI should not be used for contraception.

Children and adolescents

EVOREL CONTI should not be used by children.

Other medicines and EVOREL CONTI

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Some medicines can reduce the effect of EVOREL CONTI, such as, anti-epilepsy medicines (barbiturates, hydantoins, carbamazepine, meprobamate), phenylbutazone, rifampicin, rifabutin, bosentan, St. John's wort preparations (*Hypericum perforatum*) and certain medicines used for treatment of HIV infections and hepatitis, such as nevirapine, efavirenz, ritonavir and nelfinavir.

EVOREL CONTI use may result in a decreased therapeutic effects and spontaneous bleeding if you use these medicines.

Estrogen-containing oral contraceptives have been shown to significantly decrease plasma concentrations of the anti-epileptic medicine lamotrigine when co-administered. This may reduce seizure control.

Therefore, your doctor may adjust the dosage of lamotrigine if necessary.

If you are taking any of these medicines, tell your doctor. If you are taking other medicines on a regular basis, including medicines obtained without a prescription, the use of any of these medicines together with EVOREL CONTI can cause undesirable interactions. Please consult your doctor, pharmacist or health care provider for advice.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before using this medicine.

Tell your doctor if you are pregnant, or think you are pregnant. You should not use EVOREL CONTI during pregnancy. You should not breastfeed when using EVOREL CONTI.
Stop using EVOREL CONTI should you fall pregnant whilst on this medication.

Driving and using machines

There is no information about whether EVOREL CONTI affects your ability to drive or use machines.

It is not always possible to predict to what extent EVOREL CONTI may interfere with your daily activities. Do not engage in above activities until you are aware of the measure to which EVOREL CONTI affects you.

3. How to use EVOREL CONTI

Do not share medicines prescribed for you with any other person.
Always use EVOREL CONTI exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

EVOREL CONTI treatment should not be continued for longer than 5 years.

When to use the patch

There are enough hormones in each patch to last for several days but to ensure a steady supply to the body, the patches must be changed at 3 or 4-day intervals.

To make it easy to remember when this should be done, keep to the same two days every week. This will mean that one patch is on for three and the other for four days. For example, if you use your first patch on a Monday, it should be changed on Thursday and again on the following Monday.

You can work out the two days of your own schedule from the following table, starting from the first day of use:

If you put your first patch on:	**Change on:**	**Change again on:**
Monday	Thursday	Monday
Tuesday	Friday	Tuesday
Wednesday	Saturday	Wednesday
Thursday	Sunday	Thursday
Friday	Monday	Friday
Saturday	Tuesday	Saturday
Sunday	Wednesday	Sunday

To help you to remember your “two patch change” days, mark them as shown:

Mon Tues Wed Thur Fri Sat Sun

Thur Fri Sat Sun Mon Tues Wed

How to put the patch on

The patch should be applied to clean, dry skin but not on top of cuts, spots or other skin blemishes or on an area where you have just applied cream, moisturiser or talc.

The EVOREL CONTI patch should be applied to the skin as soon as it is removed from the wrapper and applied as described below:

(a) Tear open the wrapper, first between the “V’s” along one edge and then along the other edge. Take out the patch.

(b) With the backing foil facing you, bend the patch and peel off one half of the foil. **Do not touch the sticky side of the patch** otherwise it may not stick properly.

(c) Apply the open half of the patch to your skin, remove the other half of the foil and press down the rest of the patch.

(d) Press the patch with the palm of your hand to ensure it is firmly stuck to the skin.

(e) To remove, peel away an edge of the patch and pull smoothly away from the skin.

(f) You may use soap and water to help remove any gum/glue, which may remain on your skin after patch removal.

Where to place 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. **It should never be worn on or near the breasts.** Although it can be worn underneath clothing, it should not be placed under elasticized waistbands.
The patch should not be placed on the same area of skin twice in a row.

What if the patch falls off?

Just apply a new patch and keep to your original “patch change” days.

Can I wash, bath or shower as normal?

YES, but do not scrub too hard in case you loosen the edges of the patch. It is recommended, however, that the patch be removed prior to a sauna bath, and that a new patch is applied immediately thereafter.

Can I go swimming with the patch on?

YES, the patch will not be affected.

Can I exercise or play sports?

YES, but try to avoid wearing it under tight clothing or waistband.

Can I sunbathe with the patch on?

YES, but keep the patch covered to avoid direct sunlight.

What if I am allergic to the patch?

As with normal sticking plaster, allergic reactions to the patch are unlikely. However, should you have such a reaction, please consult your doctor.

Does the patch work as a contraceptive?

NO, the levels of hormone supplied by the EVOREL CONTI patch are too low for it to do this. Although menopausal women face an ever-decreasing risk of pregnancy, normal precautions should be taken during intercourse. If in doubt, talk to your doctor.

If you use more EVOREL CONTI than you should

Overdose with the patch is unlikely. Effects of too much EVOREL CONTI can be reversed simply by removal of the patch. The most common symptoms of EVOREL CONTI overdose are breast tenderness, nausea, irregular bleeding, stomach pain and/or bloating.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to use EVOREL CONTI

If you forget to change the patch, change it as soon as possible and then keep to your original "patch change" days.

Forgetting a dose may increase the likelihood of breakthrough bleeding and spotting.

4. Possible side effects

EVOREL CONTI can cause side effects.

Side effects include the following:

Frequent:

- Sudden swelling of the face or throat which may cause difficulty in swallowing or breathing. This may be a sign of an allergic reaction
- Depression
- Nervousness
- Anxiety
- Sleeplessness
- Headache
- Sensation of tingling, burning, pricking or numbness of the body
- Abnormal heart beat
- High blood pressure
- Widening of blood vessels
- Varicose veins

- Stomach pain
- Feeling sick
- Red rash
- Joint pain
- Back pain
- Menstrual disorder (Irregular, heavy or prolonged bleeding from the vagina)
- Breast pain
- Bleeding at irregular intervals
- Genital discharge
- Small, fingerlike growths of opening of vagina (cervical polyps)
- Painful periods
- Excessive proliferation of the cells of the inner lining of the womb
- Abnormally heavy and prolonged menstrual period at regular intervals
- Application site reaction – this includes sensitivity, redness, swelling and/or itchiness on the skin where the patch was placed
- Swelling may occur on the skin where the patch was placed
- Tiredness
- Pain
- Weight gain

Less frequent:

- Decreased sex drive
- Suicidal thoughts/behaviour and suicide
- Itching
- Swelling may occur on the skin where the patch is placed
- Genital/ vaginal fungal thrush
- Breast cancer
- Dizziness; epilepsy
- Formation of a blood clot inside a blood vessel,
- Frequent and loose watery stools with excessive gas in stomach or intestines
- Muscle pain
- Vaginal thrush
- Abnormal growth of breast tissue, endometrial cancer
- Mood swings
- Stroke, dizziness, migraine
- Deep vein blood clots

- Clots in the lungs
- Abdominal enlargement
- Gall stones
- Severe skin and mucous membrane rash (Stevens-Johnson Syndrome)
- Breast enlargement

If you develop skin rashes or irritation where you applied the patch, remove the patch and ask your doctor for advice.

Not all side effects reported for EVOREL CONTI are included in this leaflet. Should your general health worsen or if you experience any other untoward effects while using this medicine, please consult your health care provider for advice.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of EVOREL CONTI.

5. How to store EVOREL CONTI

Store all medicines out of reach of children.
Store at or below 25 °C. Do not freeze.
Return all unused medicine to your pharmacist.
Do not dispose unused medicine in drains or sewerage systems (e.g. toilets).

Other important information:

Do not use the patches:
⌦ After the expiry date shown on the label
⌦ If the protective sachet/pouch is open

6. Contents of the pack and other information

What EVOREL CONTI contains

The active substances are estradiol and norethisterone.

Each EVOREL CONTI patch contains 3,1 mg estradiol, formulated as 3,2 mg of estradiol hemihydrate and 9,82 mg norethisterone, formulated as 11,2 mg norethisterone acetate. Each patch delivers 50 micrograms of estradiol and 170 micrograms of norethisterone (a progestogen hormone) per 24 hours.

EVOREL CONTI patches contain the following inactive ingredients:
Acrylate-vinylacetate copolymer (adhesive), guar gum (absorbent) and polyethylene terephthalate foil (backing film).

What EVOREL CONTI looks like and contents of the pack

EVOREL CONTI patches are square shaped, transparent patches with a self-adhesive backing, which can be stuck to the skin. EVOREL CONTI is marked CEN1 and has a surface area of 16 cm^2.
In each patch the active ingredients are spread evenly in the adhesive and pass slowly through the skin into the body.

EVOREL CONTI comes in a carton pack containing eight patches in protective sealed foil-lined pouches.

Holder of Certificate of Registration

Adcock Ingram Limited
1 New Road
Erand Gardens
Midrand 1685
Customer Care: 0860 ADCOCK / 232625

This leaflet was last revised in

17 December 2021

Registration number

31/21.8.2/0537

Namibia: NS2 04/21.8.2/0244

adcock ingram