

Package leaflet: Information for the user

ESTRAMONconti® 30/95 micrograms/24 h Transdermal Patch

Active substances: Estradiol/Norethisterone acetate

Read the entire package leaflet carefully before you start using this medicine because it contains important information.

- Keep the package leaflet. You may want to read it again later.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you personally. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you notice any side effects, contact your doctor or pharmacist. This also applies to side effects not listed in this package leaflet. See section 4.

What is in this package leaflet

1. What is ESTRAMON conti and what is it used for?
2. What should you consider before using ESTRAMON conti?
3. How to use ESTRAMON conti?
4. What side effects are possible?
5. How to store ESTRAMON conti?
6. Contents of the pack and other information

1. What is ESTRAMON conti and what is it used for?

ESTRAMON conti is a preparation for hormone replacement therapy (HRT). It contains 2 different female sex hormones, an estrogen and a progestogen. ESTRAMON conti is used in women after menopause, whose last menstrual period (menopause) was at least 1 year ago.

ESTRAMON conti is used for:

Relief of symptoms after menopause During menopause, the body's production of estrogen decreases. This can cause symptoms such as hot flashes in the face, neck, and chest (so-called hot flashes). ESTRAMON conti alleviates these post-menopausal symptoms. ESTRAMON conti is only prescribed to you if your symptoms significantly affect your daily life.

2. What should you consider before using ESTRAMON conti?

Medical history and regular check-ups

Hormone replacement therapy is associated with risks that must be considered before deciding to start or continue treatment.

Experience in treating women with premature menopause (due to ovarian failure or surgical removal) is limited. If you have premature menopause, the risks of hormone replacement therapy may differ from those of other women. Please consult your doctor.

Before you start (or resume) hormone replacement therapy, your doctor will take your personal and family medical history. Your doctor will decide on the necessity of a physical examination. This may include a breast examination and/or a pelvic examination if necessary.

After you have started hormone replacement therapy, you should see your doctor regularly (at least once a year) for check-ups. During these examinations, please discuss with your doctor the benefits and risks associated with continuing treatment with ESTRAMON conti.

Please attend regular breast screenings as recommended by your doctor.

ESTRAMON conti must not be used if any of the following apply to you. If you are unsure, please consult your doctor before using ESTRAMON conti.

You must not use ESTRAMON conti if

- you have or have had breast cancer, or if there is a suspected case
- you have a form of cancer that is estrogen-dependent, such as cancer of the uterine lining (endometrium), or if there is a suspected case
- you experience unexplained vaginal bleeding
- you have untreated excessive thickening of the uterine lining (endometrial hyperplasia)
- you have or have had a blood clot in a vein (thrombosis), such as in the legs (deep vein thrombosis) or in the lungs (pulmonary embolism)
- you have a blood clotting disorder (e.g., protein C, protein S, or antithrombin deficiency)
- you have or have had a disease caused by blood clots in the arteries, such as a heart attack, stroke, or angina pectoris
- you have or have had a liver disease and your liver function tests have not returned to normal
- you have a rare, inherited blood disorder called porphyria
- you are allergic to estradiol, norethisterone acetate, soy, peanut, or any of the other ingredients listed in section 6 of this medication

If any of the above conditions occur for the first time while using ESTRAMON conti, please stop the treatment immediately and consult your doctor.

Warnings and Precautions

Please consult your doctor before starting treatment if you have ever had any of the health problems listed below, as these may recur or worsen during treatment with ESTRAMON conti. In this case, you should visit your doctor more frequently for check-ups:

- benign tumors in the uterus (myomas)
- growth of uterine lining outside the uterus (endometriosis) or previously occurred excessive growth of the uterine lining (endometrial hyperplasia)
- increased risk of blood clot formation
- (see under "Venous Blood Clots (Thrombosis)")
- increased risk of estrogen-dependent cancer (e.g., if your mother, sister, or grandmother had breast cancer)
- high blood pressure
- liver disease, e.g., a benign liver tumor
- diabetes
- gallstones
- migraine or severe headaches

- immune system disorder affecting many body organ functions (Systemic Lupus Erythematosus [SLE])
- epilepsy
- asthma
- condition affecting the eardrum and hearing (otosclerosis)
- very high blood fat levels (triglycerides)
- fluid retention due to heart or kidney diseases
- a condition called hypothyroidism (your thyroid does not produce enough thyroid hormones and you are receiving thyroid hormone replacement therapy)
- a condition called hereditary angioedema or if you have episodes of rapid swelling of hands, feet, face, lips, eyes, tongue, throat (airway blockage), or digestive tract

You must stop the treatment immediately and consult a doctor, if any of the following diseases or situations occur during the use of hormone replacement therapy:

- Diseases mentioned in the section "ESTRAMON conti must not be used"
- Yellowing of your skin or the whites of your eyes (jaundice). This may indicate a liver disease.
- significant increase in your blood pressure (symptoms may include headaches, fatigue, and dizziness)
- migraine-like headaches that occur for the first time
- if you become pregnant
- if you notice signs of blood clots, such as
 - painful swelling and redness of the legs
 - sudden chest pain
 - shortness of breath

For more information, see "Venous blood clots (thrombosis)".

Note: ESTRAMON conti is not a contraceptive. If less than 12 months have passed since your last menstrual period or if you are under 50 years old, additional use of contraceptive methods may be necessary. Consult your doctor for advice.

Hormone replacement therapy and cancer

Excessive thickening of the uterine lining (endometrial hyperplasia) and cancer of the uterine lining (endometrial carcinoma)

During estrogen monotherapy, the risk of excessive thickening of the uterine lining (endometrial hyperplasia) and cancer of the uterine lining (endometrial carcinoma) increases.

The progestogen contained in ESTRAMON conti protects you from this additional risk.

Irregular bleeding

During the first 3-6 months of using ESTRAMON conti, irregular bleeding or spotting may occur. However, if the irregular bleeding

- persist beyond the first 6 months of treatment
- start after you have been using ESTRAMON conti for more than 6 months
- persist after discontinuation of treatment,

please consult your doctor as soon as possible.

Breast cancer

There is evidence of an increased risk of breast cancer with combined hormone replacement therapy with estrogen and progestogen, and possibly also with estrogen-only therapy. The additional risk depends on the duration of hormone replacement therapy and becomes apparent within a few years. However, after stopping the treatment, the risk returns to the level of non-users within a few years (usually 5 years).

For comparison

Among women aged 50-79 who do not use hormone replacement therapy, an average of 9-17 breast cancer cases per 1,000 women are diagnosed over a period of 5 years. Among women aged 50-79 who use combined hormone replacement therapy with estrogen and progestogen for 5 years, the number is 13-23 cases per 1,000 women (i.e., 4-6 additional cases).

Regularly examine your breasts. Consult your doctor if you notice changes in your breasts, such as

- indentations (dimpling) in the skin
- changes in the nipples
- lumps that you can see or feel

Ovarian cancer

Ovarian cancer is rare. A slightly increased risk of developing ovarian cancer has been reported for women who have used hormone replacement therapy for a period of at least 5-10 years.

Among women aged 50 to 69 who do not use hormone replacement therapy, an average of 2 cases of ovarian cancer per 1,000 women are diagnosed over a 5-year period. Among women who use hormone replacement therapy for 5 years, about 2-3 cases occur per 1,000 users (i.e., up to 1 additional case).

Cardiovascular effects of hormone replacement therapy

Venous blood clots (thrombosis)

The risk of developing blood clots in the veins (thrombosis) is increased by about 1.3 to 3 times in women who use hormone replacement therapy compared to non-users. An increased risk is particularly present during the first year of use.

Blood clots can have serious consequences. If a blood clot travels to the lungs, it can cause chest tightness, shortness of breath, or fainting, or even lead to death.

A higher probability

that the risk of a blood clot forming increases with age and if any of the following conditions apply to you. Please talk to your doctor if any of the following situations apply to you:

- if you are unable to walk for a long time due to major surgery, injury or illness (see also section 3 under "If you are scheduled for surgery")
- if you are severely overweight (BMI > 30 kg/m²)
- if you have a clotting disorder that requires long-term medication to prevent blood clots
- if a close relative has ever had a blood clot in the leg, lung, or another organ
- if you suffer from systemic lupus erythematosus (SLE)

- if you have cancer

For signs of blood clots, see "You must stop treatment immediately and see a doctor".

For comparison

Looking at women in their 50s who do not use hormone replacement therapy, an average of 4-7 out of 1,000 women are expected to have a venous blood clot over a 5-year period.

In women in their 50s who have used hormone replacement therapy with estrogen and progestogen for 5 years, 9-12 cases of thrombosis occur per 1,000 users (i.e., 5 additional cases).
Heart disease (heart attack)

There is no evidence that hormone replacement therapy prevents heart attacks.

In women over 60 who use combined hormone replacement therapy with estrogen and progestogen, there is a slightly increased likelihood of developing heart disease compared to women who do not use hormone replacement therapy.

Stroke

The risk of stroke is about 1.5 times higher in users of hormone replacement therapy than in non-users. The number of additional strokes due to hormone replacement therapy increases with age.

For comparison

Looking at women in their 50s who do not use hormone replacement therapy, 8 strokes per 1,000 women are expected over a 5-year period. In women in their 50s who have used hormone replacement therapy for 5 years, there are 11 cases per users (i.e., 3 additional cases).

Other diseases

Hormone replacement therapy does not prevent memory disorders. There is some evidence of an increased risk of memory disorders in women who were over 65 years old at the start of hormone replacement therapy. Consult your doctor for advice.

Use of ESTRAMON conti with other medicines

Certain medicines can affect the action of ESTRAMON conti. This can lead to irregular bleeding. These include the following medicines:

- Medicines for epilepsy, which contain, for example, phenobarbital, phenytoin, and carbamazepine
- Medicines for tuberculosis, which contain, for example, rifampicin or rifabutin
- Medicines for the treatment of HIV infections, which contain, for example, nevirapine, efavirenz, ritonavir, telaprevir, or nelfinavir
- Herbal medicines that contain St. John's wort (*Hypericum perforatum*).

Inform your doctor or pharmacist if you are taking/using, have recently taken/used, or intend to take/use other medicines, even if they are non-prescription medicines, herbal preparations, or natural remedies.

Laboratory tests

If you need a blood test, inform your doctor or the laboratory staff that you are using ESTRAMON conti, as this medicine can affect the results of some laboratory tests.

Pregnancy and breastfeeding

Pregnancy

The use of ESTRAMON conti is intended only for women after menopause. If you become pregnant, stop using ESTRAMON conti and consult your doctor.

Breastfeeding

Do not use ESTRAMON conti if you are breastfeeding.

Consult your doctor or pharmacist before taking/using any medicines.

Driving and using machines

ESTRAMON conti has no or negligible influence on the ability to drive and use machines.

3. How to use ESTRAMON conti?

Always use this medicine exactly as agreed with your doctor. Ask your doctor or pharmacist if you are not sure.

Your doctor has prescribed how much ESTRAMON conti you need to use. ESTRAMON conti is to be used twice a week, which means you need to apply a new transdermal patch every 3 or 4 days.

The recommended dose is:

Continuous therapy

Apply the ESTRAMON conti patches continuously (without interruption).

	Week 1	Week 2	Week 3	Week 4
Apply ESTRAMON conti	Day 1 Day 4	Day 1 Day 4	Day 1 Day 4	Day 1 Day 4

Method of application

Where to apply the patch

- Apply the patch to an area of skin that does not fold much with movement, e.g., on the side of the thigh. These patches **MUST NOT** be applied to the chest!
- The skin must not be reddened or injured.
- The area of skin should be hairless.
- Avoid areas of skin where clothing fits tightly or under a seam.
- Clean the skin thoroughly before applying the patch. Do not use body lotion, body oil, shower gel, sunscreen, or other greasy products. The skin must be dry and grease-free.

Opening the pouch

- Tear open the pouch carefully along the perforation at one of the two corners immediately before use.
- Hold the patch by the edge and remove it from the pouch.
- Note: The desiccant inside the pouch is only for ensuring product quality and must not be applied to the skin.

Removing the protective film

- Hold the protective film with both hands.
- Carefully bend the patch up and down along the perforated curved line.
- Carefully peel off the majority of the transparent protective film from the patch.
- Do not touch the adhesive layer of the patch.

Applying the patch

- Smoothly apply the adhesive side of the patch to the skin, ensuring no air bubbles are trapped under the patch.
- Remove the remaining protective film and apply the patch completely to the skin.
- Press the patch firmly with the palm of your hand for 1 minute. Now the estradiol patch is correctly applied.

Application of the patch

- You can bathe or shower while wearing the patch. In very hot bath water or in a sauna, the patch may come off.
- Avoid applying oily creams, lotions, and powders at the application site of the patch.
- The effectiveness of the patch may be impaired if it is exposed to sunlight or artificial sunlight (e.g., in a solarium).

When applied correctly, the estradiol/norethisterone acetate patch adheres well and usually stays on the skin for at least 4 days. If the patch is not properly applied or comes off during wear, you should not reuse it. In this case, apply a new patch. Change the patch on the usual day. If you forget to apply a patch, this may increase the risk of breakthrough or spotting bleeding.

Patch change

- Remove the patch after use, fold it with the adhesive side inwards, and dispose of it.
- Apply a new patch to a different skin site.

Start of treatment

- For women who have never received hormone replacement therapy before, or for women switching from continuous-combined hormone replacement therapy, treatment can be started on any day.
- For women switching from a cyclic or continuous-sequential hormone replacement therapy, treatment should begin directly on the day after the end of the previous treatment cycle.

Duration of treatment

Your doctor has told you how long to continue the treatment. Please strictly follow these instructions. Please talk to your doctor beforehand if you want to stop the treatment earlier. Your doctor will regularly reassess the need for estrogen treatment with you. This should be done at least once a year.

If you have applied a larger amount of ESTRAMON
containing more than you should

If you have applied more than the prescribed number of transdermal patches or if an overdose is suspected, you should remove the patch(es) and immediately consult a doctor or pharmacist.

Symptoms of an overdose may include breast tenderness, abdominal pain or bloating, anxiety, irritability, water retention, and bloating.

If you have forgotten to apply ESTRAMON conti

In such a case, please apply a new transdermal patch as soon as possible, unless it is almost time to apply the next patch according to your usual schedule. In this case, you should wait and simply stick to your usual plan. Never apply two patches at the same time. If you have forgotten a patch, the risk of breakthrough bleeding may be increased.

If you have a planned surgery If you have a planned surgery, inform the operating doctor that you are using ESTRAMON conti. It may be necessary to discontinue ESTRAMON conti 4-6 weeks before the planned surgery. must, to reduce the risk of thrombosis (see section 2 under "Venous blood clots (thrombosis)"). Ask your doctor when you can continue using ESTRAMON conti.

Your doctor will try to prescribe you the lowest dose necessary to treat your symptoms for the shortest time needed. Please talk to your doctor if you feel that the effect of ESTRAMON conti is too strong or too weak.

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

4. What side effects are possible?

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following diseases have been reported more frequently in women using hormone replacement therapy compared to non-users:

- Breast cancer
- Excessive 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
- Memory loss (dementia), if hormone replacement therapy was started over the age of 65

For more information on these side effects, see section 2 "What should you consider before using ESTRAMON conti?".

The following side effects have been reported with the use of ESTRAMON conti:

Very common (may affect more than 1 in 10 people treated)

- Headaches
- Skin reactions at the site where the patch is applied
- Breast tenderness and pain
- Painful menstruation (dysmenorrhea)
- Menstrual disorders

Common (may affect up to 1 in 10 people treated)

- Depression
- Nervousness
- Uncontrollable emotions
- Mood swings
- Dizziness
- Insomnia
- Nausea
- Feeling of bloating
- Diarrhea
- Stomach discomfort (dyspepsia)
- Flatulence
- Abdominal pain
- Acne
- Rash
- Itching
- Dry skin
- Skin redness (erythema)
- Back pain
- Pain in the hands or feet
- Breast enlargement
- Heavy menstrual bleeding
- Vaginal discharge
- Irregular vaginal bleeding
- Abdominal cramps
- Vaginitis
- Abnormal growth of the endometrium
- Pain
- Lack or loss of physical strength (asthenia)
- Swollen hands, ankles, or feet (edema)
- Weight gain

Occasionally (may affect up to 1 in 100 people treated)

- Migraine
- Dizziness
- Increase in blood pressure
- Varicose veins
- Vomiting
- Skin discoloration
- Breast cancer
- Increase in certain liver enzymes (transaminases)

Rare (may affect up to 1 in 1,000 people treated)

- Allergic reactions
- Changes in sexual desire (libido changes)
- Tingling, itching, or numbness without a recognizable cause
- Blood clot in a blood vessel (venous thromboembolism)

- Gallbladder diseases
- Gallstones
- Muscle weakness (myasthenia)
- Benign tumors in the uterus
- Cysts near the ovaries
- Polyps in the cervix

Very rare (may affect up to 1 in 10,000 people treated)

- Jaundice due to bile stasis

Frequency not known (frequency cannot be estimated from the available data)

- Severe allergic reaction (anaphylactic reaction)
- Hair loss

The following side effects have been reported during the use of other hormone replacement therapy preparations:

- Gallbladder diseases
- Various skin disorders
 - Skin discolorations, especially on the face and neck, so-called pregnancy spots (chloasma)
 - Painful, reddish skin nodules (erythema nodosum)
 - Rash with target-like or circular reddish spots or inflammations (erythema multiforme)
- Possible dementia in those over 65 years of age
- Dry eyes
- Changes in the composition of tear fluid

Soybean oil can very rarely cause allergic reactions.

Other serious side effects, diseases, and risks associated with HRT are listed in section 2 under 'Warnings and Precautions'.

Reporting of side effects

If you notice any side effects, contact your doctor or pharmacist. This also applies to side effects not listed in this leaflet. You can also report side effects directly to the

Federal Institute for Drugs and Medical Devices Dept. Pharmacovigilance

Kurt-Georg-Kiesinger-Allee 3 D-53175 Bonn

Website: www.bfarm.de

display.

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

5. How to store ESTRAMON conti?

Keep this medicine out of the reach of children.

Do not use this medicine after the expiry date stated on the pouch and carton after 'use by'. The expiry date refers to the last day of that month.

Store in the original package.

Do not store above 25 °C.

Disposal of used and unused patches Used patches must be disposed of carefully. The patch still contains considerable amounts of active ingredients after use. The hormones remaining in the patches can harm the environment if they enter the groundwater. Therefore, used patches must be folded with the adhesive side inwards. All used or unused patches must be kept out of reach of children and disposed of according to local requirements or returned to the pharmacy. To protect the environment, used patches must not be flushed down the toilet or disposed of in sewage systems.

6. Contents of the package and further information

What ESTRAMON conti contains

The active substances are estradiol and norethisterone acetate.

1 patch contains 3.2 mg estradiol (as estradiol hemihydrate) and 16 mg norethisterone acetate per 20 cm² (matrix system). It releases an average of 30 micrograms of estradiol and 95 micrograms of norethisterone acetate per day (24 hours).

The other ingredients are:

Self-adhesive matrix layer: Poly[(2-ethylhexyl)acrylate-co-methylacrylate-co-acrylic acid-co-(2,3-epoxypropyl)methacrylate], Vitamin E preparation (consisting of: RRR-alpha-tocopherol, partially hydrogenated or non-hydrogenated vegetable oils [main component soybean oil])

Backing film: Polyester without additives.

Removable protective film: Polyester, siliconized

What ESTRAMON conti looks like and contents of the package

ESTRAMON conti patches are rectangular, transparent transdermal matrix patches with rounded corners, applied to a larger removable protective film.

The original packages contain 8 and 24 transdermal patches, each individually heat-sealed in protective pouches.

Each pouch consists of the following four layers from outside to inside: paper, polyethylene film, aluminum foil, polyethylene film, and an attached polypropylene layer with moisture and oxygen-absorbing properties.

Pharmaceutical entrepreneur and manufacturer

Hexal AG Industriestraße 25

83607 Holzkirchen

Phone: (08024) 908-0

Fax: (08024) 908-1290

Email: service@hexal.com

This package leaflet was last revised in January 2014.

Transtoyou