

Package leaflet: Information for the patient

ESTRAMON conti® 40/130 micrograms/24 h Transdermal Patch

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, please 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 production of the body's own estrogen in women decreases. This can cause symptoms that manifest as hot flashes in the face, neck, and chest area (so-called hot flashes). ESTRAMON conti alleviates these symptoms occurring after menopause. ESTRAMON conti will only be prescribed to you if your symptoms significantly affect your daily life.

There is only limited experience in treating women over 65 years with ESTRAMON conti.

2. What should you consider before using ESTRAMON conti?

Medical history and regular check-ups

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

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

Before you start (or resume) HRT, your doctor will record 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 HRT, you should see your doctor regularly (at least once a year) for check-ups. Please discuss with your doctor the benefits and risks associated with continuing HRT during these examinations.

Please go for 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 dependent on estrogens, such as cancer of the uterine lining (endometrium), or if there is a suspected case
- you experience unexplained vaginal bleeding
- there is untreated excessive thickening of the uterine lining (endometrial hyperplasia)
- you have or have had a blood clot in a vein (thrombosis),
- e.g., 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,
- e.g., heart attack, stroke, or angina pectoris (chest pain with tightness)
- You have or have had liver disease and your liver function values have not yet normalized
- You suffer from a rare, hereditary blood disorder called porphyria
- You are allergic to estradiol, norethisterone acetate, soy, peanut, or any of the other ingredients of this medicine listed in section 6.

If any of the above-mentioned conditions occur for the first time while using ESTRAMON conti, please stop the treatment immediately and consult your doctor without delay.

**Warnings and precautions** Please talk to your doctor or pharmacist before using ESTRAMON conti.

Talk to your doctor if you have ever had any of the health problems listed below, as they may recur or worsen during treatment with ESTRAMON conti. In this case, you should see 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 diseases, e.g., benign liver tumors
- 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 gland does not produce enough thyroid hormones) and you are receiving thyroid hormone replacement therapy.
- A condition called hereditary or acquired angioedema, or if you have episodes of rapid swelling of the 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 HRT:

- 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 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
- Swelling of the face, tongue and/or throat and/or difficulty swallowing, or hives associated with breathing problems, indicating angioedema
- 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.

#### HRT 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 and spotting may occur.

However, if the irregular bleeding

- persists beyond the first 6 months of treatment
- starts after you have been using ESTRAMON conti for more than 6 months
- persists after stopping the treatment,  
please see your doctor as soon as possible.

### Breast cancer

The available data show that the use of hormone replacement therapy (HRT) with a combination of estrogen and progestogen or the use of estrogen alone for HRT increases the risk of breast cancer. The additional risk depends on the duration of HRT and becomes apparent within 3 years of use. After stopping HRT, the additional risk decreases over time, but the risk may persist for 10 years or longer if you have used HRT for more than 5 years.

### For comparison

In women aged 50 to 54 who do not use HRT, an average of 13 to 17 cases of breast cancer are diagnosed over a 5-year period per 1,000 women.

In women aged 50 who start using HRT with estrogen alone for a period of 5 years, 16 to 17 cases occur per 1,000 users (i.e., 0 to 3 additional cases). In women aged 50 who start using HRT with estrogen and progestogen for a period of 5 years, 21 cases occur per 1,000 users (i.e., 4 to 8 additional cases).

In women aged 50 to 59 who do not use HRT, an average of about 27 cases of breast cancer are diagnosed over a 10-year period per 1,000 women diagnosed.

In women aged 50 years who start using estrogen-only HRT for a period of 10 years, 34 cases occur per 1,000 users (i.e., 7 additional cases).

In women aged 50 years who start using combined estrogen and progestogen HRT for a period of 10 years, 48 cases occur per 1,000 users (i.e., 21 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

If you have the opportunity to participate in a breast cancer screening program (mammography screening program), you should take advantage of this offer. Inform the professional conducting the mammography that you are using a medication for HRT. Medications used for HRT can make breast tissue denser and thus affect the result of the mammography. If the density of the breast tissue is increased, not all changes may be detected.

### Ovarian cancer

Ovarian cancer is rare - much rarer than breast cancer. The use of estrogen-only or combined estrogen-progestogen medications for HRT is associated with a slightly increased risk of developing ovarian cancer.

The risk of developing ovarian cancer changes with age. For example, in women aged between 50 and 54 years who do not use hormone replacement therapy, about 2 cases of ovarian cancer are diagnosed per 2,000 women over a 5-year period. In women who use hormone replacement therapy for 5 years, about 3 cases occur per 2,000 users (i.e., about 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 using HRT 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.

You are more likely to develop a blood clot as you get older and if 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 planning an operation")
- if you are severely overweight (BMI > 30 kg/m<sup>2</sup>)
- Pregnancy/postpartum
- if you suffer from a coagulation 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 consult a doctor".

For comparison

Considering women in their 50s who do not use HRT, over a 5-year period, 4-7 out of 1,000 women are expected to have a venous blood clot.

In women in their 50s who have used HRT 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 HRT prevents a heart attack.

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

Stroke

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

### For comparison

Considering women in their 50s who do not use HRT, 8 strokes per 1,000 women are expected over a 5-year period. In women in their 50s who use HRT, the corresponding number is 11 cases per 1,000 users (i.e., 3 additional cases).

### Other conditions

HRT does not prevent memory loss. There is some evidence of an increased risk of memory loss in women who were over 65 years old at the start of HRT use. Consult your doctor for advice.

All medications applied to the skin (such as patches) can cause allergic reactions. Although this is very rare, you should inform your doctor if you have or have ever had severe allergic reactions to any of the ingredients in the patches.

### Use of ESTRAMON conti together with other medicines

Inform your doctor or pharmacist if you are taking/using other medicines, have recently taken/used other medicines, or intend to take/use 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 containing, for example, phenobarbital, phenytoin, and carbamazepine
- Medicines for tuberculosis containing, for example, rifampicin or rifabutin
- Certain medicines for the treatment of HIV infections containing, for example, nevirapine, efavirenz, ritonavir, or nelfinavir
- Certain medicines for the treatment of hepatitis C infections containing, for example, telaprevir
- The combination treatment ombitasvir/paritaprevir/ritonavir with or without dasabuvir and also the treatment glecaprevir/pibrentasvir against the hepatitis C virus (HCV) can cause elevated liver values in blood tests (increase in liver enzyme ALT) in women using CHC containing ethinylestradiol. ESTRAMON conti contains estradiol instead of ethinylestradiol. It is not known whether an increase in liver enzyme ALT can occur when using ESTRAMON conti together with this combination treatment against HCV. Your doctor will be happy to advise you.
- Other anti-infective medicines (such as ketoconazole, erythromycin)
- Herbal medicines containing St. John's wort (*Hypericum perforatum*).

ESTRAMON conti can affect the metabolism of ciclosporin.

### Laboratory tests

If you require 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.

If you are pregnant or breastfeeding, or if you suspect you are pregnant or intend to become pregnant, ask your doctor or pharmacist for advice before using this medicine.

### Driving and using machines

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

ESTRAMON conti contains soybean oil

If you are allergic to peanut or soybean, you must not use this medicine.

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

ESTRAMON conti is to be used twice a week, which means you need to apply a new transdermal patch every 3 or 4 days.

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

### Start of treatment

- For women who have never received hormone replacement therapy before, or for women switching from a 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 be started directly on the day after the end of the previous treatment cycle.

### 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 breast!
- The skin must not be reddened or injured.
- The area of skin should be hairless.
- Avoid areas 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 firmly with both hands.
- Carefully bend the patch along the perforated curved line up and down.
- 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 there are no air bubbles 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 properly applied.

### Using 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 using 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 ESTRAMON conti patch adheres well and usually stays on the skin for at least 4 days. If the patch is not applied correctly 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, the risk of breakthrough or spotting bleeding may be increased.

### Patch change

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

### Duration of treatment

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

### Children and adolescents

Estradiol/Norethisterone is not indicated for use in children and adolescents.

If you have applied more ESTRA- MON conti than you should If you have applied more than the prescribed number of transdermal patches or if there is suspicion of an overdose, you should

remove the patch(es) and immediately consult a doctor or pharmacist seek medical advice. Symptoms of an overdose may include breast tenderness, metrorrhagia, nausea, vomiting, abdominal pain or bloating, anxiety, irritability, and water retention. Bloating, depressive mood, fatigue, acne, and hirsutism may also occur as symptoms of an overdose. These symptoms disappear when you remove the patch.

If you have forgotten to use ESTRAMON conti  
forgotten

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 adhere to your usual schedule. Never apply two patches at the same time. If you forget a patch, the risk of breakthrough bleeding may be increased.

If you have a planned surgery

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

If you have further questions about 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 uterine lining (endometrial hyperplasia or cancer)
- Ovarian cancer
- Blood clots in the veins of the legs or lungs (venous thromboembolism)
- Heart disease
- Stroke
- Memory loss (probable dementia), if HRT was started over the age of 65

For more information about these side effects, see section 2.

Hypersensitivity

Allergic reactions may occur. Signs of a hypersensitivity/allergic reaction may include one or more of the following symptoms: hives, itching, swelling, difficulty breathing, low blood pressure (paleness and coldness of the skin, rapid heartbeat), dizziness, sweating, which may also be signs of an anaphylactic reaction/shock. If any of the mentioned symptoms occur, stop using ESTRAMON conti and contact your doctor immediately.

Other serious side effects:

- Benign tumors of the uterus, cysts near the ovaries, polyps in the cervix
- Cholestatic jaundice

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

The following side effects have been reported with the use of estradiol/norethisterone acetate:

Very common may affect more than 1 in 10 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 treated

- Depression, nervousness, uncontrollable feelings, 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
- Vaginal infection, abnormal growth of the uterine lining
- Pain, lack or absence of physical strength (asthenia), swollen hands, ankles, or feet (edema), weight gain

Occasionally may affect up to 1 in 100 treated

- Migraine, dizziness
- Increased blood pressure, varicose veins
- Vomiting
- Skin discoloration
- Increase in certain liver enzymes (transaminases)

Rarely may affect up to 1 in 1,000 treated

- Allergic reactions
- Changes in sexual desire (libido changes)
- Tingling, itching, or numbness without a recognizable cause
- Gallbladder diseases, gallstones
- Muscle weakness (myasthenia)

Unknown (frequency cannot be estimated from the available data)

- Hair loss

Other possible side effects:

Partially hydrogenated soybean oil (DAB) can very rarely cause allergic reactions.

The following side effects have been reported during the use of other preparations for HRT:

- 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 disc-shaped redness or inflammation (erythema multiforme)
- Small-scale skin hemorrhages (vascular purpura)
- Possible dementia in those over 65 years of age
- dry eyes
- changes in the composition of the tear fluid

#### Reporting 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](http://www.bfarm.de)

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' or 'exp. by'. The expiry date refers to the last day of that month.

Do not store above 25 °C.

Store in the original package.

Disposal of used and unused patches Used patches must be disposed of carefully. The patch still contains significant amounts of active ingredients after use. The hormones remaining in the patches can harm the environment if they enter groundwater. Therefore, used patches must be folded with the adhesive side inwards. All used or unused patches must be kept out of the 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 wastewater systems.

#### 6. Contents of the pack and other information

What ESTRAMON conti contains

The active substances are estradiol and norethisterone acetate.

1 patch contains 4.32 mg estradiol (as estradiol hemihydrate) and 21.6 mg norethisterone acetate per 27 cm<sup>2</sup> (matrix system). It releases an average of 40 micrograms of estradiol and 130 micrograms of norethisterone acetate per day (24 hours).

The other ingredients are:

Removable protective film: Polyester, siliconized  
Self-adhesive matrix layer: Poly[(2-ethylhexyl)acrylate-co-methylacrylate-co-acrylic acid-co-(2,3-epoxypropyl) methacrylate] (62:32:5.7:0.03), Vitamin E preparation (consisting of: RRR-alpha-tocopherol, partially hydrogenated vegetable oils [main component soybean oil])

Backing film: Polyester without additives

What ESTRAMON conti looks like and contents of the pack

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

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

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

Not all pack sizes may be marketed.

Pharmaceutical entrepreneur and manufacturer

Hexal AG Industriestraße 25

83607 Holzkirchen

Phone: (08024) 908-0

Fax: (08024) 908-1290

Email: [service@hexal.com](mailto:service@hexal.com)

This package leaflet was last revised in February 2022.