Package leaflet: Information for the user
ESTRAMON comp 2 mg/1 mg film-coated tablets
Estradiol, Norethisterone acetate

Read the entire package leaflet carefully before you start taking 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 leaflet. See section 4.

What is in this leaflet

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

ESTRAMON comp is a preparation for continuous combined hormone replacement therapy (HRT), taken every day without interruption. ESTRAMON comp is used in women after menopause, whose last menstrual period (menopause) was at least 1 year ago.

The tablets contain 2 hormones: Estradiol 2 mg (an estrogen identical to the estradiol produced in the ovaries) and Norethisterone acetate 1 mg (a progestogen that acts similarly to the body's own progesterone).

ESTRAMON comp 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 comp alleviates these post-menopausal symptoms. ESTRAMON comp is only prescribed to you if your symptoms significantly affect your daily life.

Prevention of osteoporosis
After menopause, some women may experience brittle bones (osteoporosis). You should discuss all available treatment options with your doctor. You can use ESTRAMON comp to prevent osteoporosis after menopause if you have an increased risk of osteoporosis-related bone fractures and other medications are not suitable for you.

ESTRAMON comp is prescribed to women whose uterus has not been removed and whose last menstrual period was more than 1 year ago.

There is only limited experience in treating women over 65 years of age with ESTRAMON comp.

2. What should you consider before taking ESTRAMON comp?

Medical history and regular check-ups

Hormone replacement therapy 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) hormone replacement therapy, 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. He/She should inform you about changes in the breast that you need to be aware of and may recommend that you have a breast X-ray (a mammogram).

After you have started hormone replacement therapy, you should see your doctor regularly (at least once a year) for check-ups. Please discuss the benefits and risks associated with continuing treatment with ESTRAMON comp during these examinations with your doctor. Please go for regular breast screenings as recommended by your doctor.

ESTRAMON comp must not be taken,

if the following points apply to you. If you are unsure whether this is the case, please talk to your doctor before taking ESTRAMON comp. You must not take ESTRAMON comp if

you are allergic to estradiol or norethisterone acetate or any of the other ingredients of this medicine listed in section 6

- you have or have had breast cancer or if there is a suspected case
- you have a form of cancer whose growth is dependent on estrogens, such as cancer of the uterine lining (endometrium), or if there is a suspected case
- unexplained vaginal bleeding occurs
- vaginal bleeding of unclear cause occurs
- 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 suffer from 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 sudden chest pain with chest tightness (angina pectoris)
- you have or have had a liver disease and your liver function tests have not yet normalized

- you suffer from a rare, hereditary blood disorder called porphyria
- if you are pregnant or suspect you might be pregnant

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

Warnings and precautions
Please talk to your doctor or pharmacist before taking ESTRAMON comp.

Talk to your doctor if you have ever had any of the following health problems, as they may recur or worsen during treatment with ESTRAMON comp. In this case, you should see your doctor more frequently for check-ups:

- benign tumors in the uterus (fibroids)
- 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 '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
- Disease of the immune system that affects many organ functions of the body (systemic lupus erythematosus [SLE])
- Epilepsy
- Asthma
- Disease affecting the eardrum and hearing (otosclerosis)
- Very high blood fat levels (triglycerides)
- Fluid retention due to heart or kidney diseases
- Hypothyroidism (a condition where your thyroid does not produce enough thyroid hormones and you are treated with thyroid hormone replacement therapy)
- Congenital and acquired angioedema or episodes of rapidly swelling hands, feet, face, lips, 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 hormone replacement therapy:

- Diseases mentioned in the section "ESTRAMON comp must not be taken"
- 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 occurring for the first time, with or without visual disturbance. Such headaches can be an early sign of a stroke. If you have already had a stroke, discuss with your doctor whether the benefits of treatment outweigh the potentially increased risks.

- If you have chest pain radiating to your arms or neck. This pain can be a sign of a heart attack.
- 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, e.g.
  - Painful swelling and redness of the legs
  - Sudden chest pain
  - Shortness of breath

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

Note: ESTRAMON comp 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 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-only therapy, 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 comp protects you from this additional risk.

In women aged 50 to 65 who still have a uterus and do not use HRT, an average of 5 cases of endometrial carcinoma per 1,000 women are diagnosed.
In women aged 50 to 65 who still have a uterus and use estrogen-only therapy, 10 to 60 cases of endometrial carcinoma per 1,000 women (i.e., 5 to 55 additional cases), depending on the dose and duration of therapy, are diagnosed.

Irregular bleeding
During the first 3 to 6 months of taking ESTRAMON comp, irregular bleeding or spotting may occur.
However, if the irregular bleeding

- persists beyond the first 6 months of treatment
- starts after you have been taking ESTRAMON comp for more than 6 months
- persists after stopping treatment,

please see your doctor as soon as possible.

Breast cancer
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 more 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 per 1,000 women are diagnosed over a 5-year period.
In women aged 50 years who start taking HRT with estrogen only 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 years who start taking 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 between 50 and 59 years who do not use HRT, about 27 cases of breast cancer per 1,000 women are diagnosed over a 10-year period on average.
In women aged 50 years who start taking HRT with estrogen only 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 taking HRT with estrogen and progestogen for a period of 10 years, 48 cases occur per 1,000 users (i.e., 21 additional cases).

Examine your breasts regularly. 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 the breast cancer screening program (mammography screening program), you should take advantage of this offer. Inform the professional conducting the mammography that you are taking a hormone replacement therapy medication. Medications taken for hormone replacement therapy 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 medications or combined estrogen-progestogen medications for hormone replacement therapy 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 per 2,000 women are diagnosed 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 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.

You have a higher likelihood of developing a blood clot as you 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 planning an operation')
- if you are severely overweight (BMI > 30 kg/m2)
- if you suffer from a bleeding 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 hormone replacement therapy, over a 5-year period, an average of 4 to 7 out of 1,000 women are expected to have a venous blood clot. In women in their 50s who have used hormone replacement therapy with estrogen and progestogen for 5 years, 9 to 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 years old 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
Considering 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 use hormone replacement therapy, there are 11 cases per 1,000 users (i.e., 3 additional cases).

Other conditions
Hormone replacement therapy 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 hormone replacement therapy. Consult your doctor for advice.

Hypothyroidism
In the case of thyroid hormone replacement therapy, you should regularly monitor your thyroid function while taking ESTRAMON comp to ensure that your thyroid hormone levels remain within the permissible range.

Angioedema

Medicines containing estrogens can cause or worsen symptoms of hereditary and acquired angioedema.

Taking ESTRAMON comp with other medicines

Inform your doctor or pharmacist if you are taking/using, have recently taken/used, or intend to take/use other medicines.

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

- Medicines for epilepsy, such as those containing phenobarbital, phenytoin, or carbamazepine
- Medicines for tuberculosis, such as those containing rifampicin or rifabutin
- Certain medicines for the treatment of HIV infections, such as those containing nevirapine, efavirenz, ritonavir, or nelfinavir
- Certain medicines for the treatment of hepatitis C infections, such as those containing 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 of the liver enzyme ALT) in women using CHC containing ethinylestradiol. ESTRAMON comp contains estradiol instead of ethinylestradiol. It is not known whether an increase in the liver enzyme ALT can occur when using ESTRAMON comp with this combination treatment against HCV. Your doctor will be happy to advise you.
- Herbal medicines containing St. John's wort (Hypericum perforatum),
- Phenylbutazone, a medicine for pain and inflammation
- Meprobamate, a medicine for mental disorders

Medicines containing ketoconazole (antifungal medicines) can enhance the side effects and action of ESTRAMON comp.

ESTRAMON comp can affect the efficacy or tolerability of other medicines, such as:

- Ciclosporin, a medicine to suppress the immune system
- Lamotrigine, a medicine for epilepsy

Please inform your doctor or pharmacist if you are taking or have recently taken other medicines, even if they are not prescription medicines, herbal preparations, or natural remedies.

Laboratory tests
If you require a blood test, inform your doctor or the laboratory staff that you are taking ESTRAMON comp, as this medicine can affect the results of some laboratory tests.

Pregnancy and breastfeeding
The use of ESTRAMON comp is intended only for women after menopause. If you become pregnant, stop taking ESTRAMON comp and consult your doctor.

Do not take ESTRAMON comp if you are pregnant or breastfeeding.

If you are pregnant or breastfeeding, or if you suspect you might be pregnant or are planning to become pregnant, consult your doctor or pharmacist before taking this medicine.

Driving and using machines
ESTRAMON comp has no known effect on the ability to drive and use machines.

ESTRAMON comp contains lactose.
Please only take ESTRAMON comp after consulting your doctor if you know you have an intolerance to certain sugars.

How to take ESTRAMON comp?
Always take this medicine exactly as agreed with your doctor. Ask your doctor or pharmacist if you are unsure.

The recommended dose is:
Take 1 film-coated tablet every day at about the same time without interruption.

Your doctor will try to prescribe 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 comp is too strong or too weak.

If you are scheduled for surgery
If you are scheduled for surgery, inform the operating doctor that you are taking ESTRAMON comp. You may need to stop taking ESTRAMON comp 4 to 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 taking ESTRAMON comp.

Start of treatment
For women who have not previously used HRT, or for women switching from continuous-combined HRT, treatment can be started on any day.
For women switching from cyclic or continuous-sequential HRT, treatment should begin directly on the day after finishing the previous cycle.

Duration of treatment
You should use ESTRAMON comp for as short a time as possible. It is important that you follow these instructions. Please contact your doctor if you wish 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.

If you have taken more ESTRAMON comp than you should
If you have taken too much ESTRAMON comp, contact your doctor or pharmacist immediately. Symptoms of an overdose with oral estrogens include breast tenderness, nausea, vomiting, and/or metrorrhagia. An overdose with progestogens can lead to depressive mood, fatigue, acne, and hirsutism.

If you forget to take ESTRAMON comp

If you forget to take your tablet at the usual time, take it within the next 12 hours. If more than 12 hours have passed, skip the missed dose and continue the treatment as usual the next day. Do not take a double dose if you have forgotten the previous film-coated tablet. Forgetting a film-coated tablet increases the likelihood of breakthrough or spotting bleeding.

If you stop taking ESTRAMON comp
Stopping the intake of ESTRAMON comp can increase the risk of breakthrough bleeding or spotting. If this occurs after you have stopped the treatment, contact your doctor immediately. Your doctor will determine the cause.
After a long treatment break, consult your doctor before resuming ESTRAMON comp.

If you have further questions about taking this medicine, contact your doctor or pharmacist.

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
- Possibly memory loss (dementia), if the Hormone replacement therapy was started over the age of 65

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

Hypersensitivity/Allergy (occasionally occurring side effect: may affect up to 1 in 100 treated individuals) Hypersensitivity/allergies can occur, even if it is only an occasionally occurring side effect. Signs of a hypersensitivity/allergic reaction may include one or more of the following symptoms: hives, itching, swelling, shortness of breath, low blood pressure (paleness and coldness of the skin, rapid heartbeat), dizziness, sweating; these may also be signs of an anaphylactic reaction/shock.

Other serious side effects:

- Worsening of high blood pressure
- Swelling of the face, lips, mouth, tongue, or throat (angioedema)

If any of the mentioned symptoms occur, stop taking ESTRAMON comp and seek medical help immediately.

Other side effects
The most common side effects during treatment with Estradiol/Norethisterone acetate are irregular bleeding, breast pain, or breast tenderness.

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

- Headaches
- Breast pain or breast tenderness
- Painful menstruation
- Menstrual disorders
- Irregular vaginal bleeding

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

- Fungal infections or inflammation in the vagina
- Water retention (fluid accumulation)
- Depression or worsening of depression
- Nervousness
- Mood swings
- Migraine or worsening of migraine
- Dizziness
- Sleep disturbances
- Nausea
- Abdominal pain
- Flatulence
- Malaise
- Diarrhea
- Indigestion
- Acne
- Rash
- Itching
- Dry skin
- Back pain
- Pain in the extremities
- Leg cramps
- Fluid retention in the breast
- Breast enlargement
- Development, recurrence, or enlargement of benign tumors in the uterus
- Prolonged menstrual bleeding (Menorrhagia)
- Vaginal discharge
- Uterine cramps
- vaginal inflammations
- endometrial hyperplasia
- fluid retention in the arms or legs
- pain
- weakness (asthenia)
- weight gain

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

- allergic reaction (hypersensitivity)
- dizziness (sensation of spinning)
- superficial vein inflammation associated with thrombosis

- feeling of fullness
- vomiting
- hair loss
- increased facial or body hair
- hives
- skin discoloration
- insufficient effect
- increase in transaminases

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

- Libido changes
- Feeling of stabbing, tingling, or burning skin
- Gallstones
- Gallbladder diseases
- Myasthenia
- Uterine leiomyoma
- Fallopian tube cysts
- Endocervical polyps

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

- Cholestatic jaundice
- Insomnia
- Anxiety
- Visual disturbances
- Feeling of fullness
- Vomiting
- Gallbladder disease, recurrence or worsening of gallstones
- Oily skin
- Rash
- Itching in the vagina
- Weight loss
- Increase in blood pressure

The following side effects are summarized from clinical studies and spontaneous reports. The frequency is not known (frequency cannot be estimated from the available data).

- Irritability
- rapid and irregular heartbeat
- Nosebleed
- Muscle cramps
- Breast tenderness, vaginal discharge, possibly irregular bleeding during the first months of therapy
- Decrease in glucose tolerance, abnormal liver function tests
- Fatigue

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

- 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)
  - small skin hemorrhages (vascular purpura)
- Yellowing of the skin or the whites of the eyes (cholestatic jaundice)
- possible dementia in those over 65 years of age
- Gallbladder disease
- Diarrhea
- dry eyes
- Changes in the composition of tear fluid

It is important that you consult your doctor if you do not feel well or if unusual symptoms occur that you cannot explain.

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

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

How to store ESTRAMON comp?
Keep this medicine out of the reach of children.

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

Do not store above 25 °C.

Never dispose of medicines via wastewater (e.g., do not dispose of via the toilet or sink). Ask your pharmacist how to dispose of the medicine if you no longer use it. This helps protect the environment. For more information, visit www.bfarm.de/medicinedisposal.

Contents of the pack and other information
What ESTRAMON comp contains
The active substances are estradiol and norethisterone acetate.
One film-coated tablet contains 2 mg estradiol (as hemihydrate) and 1 mg norethisterone acetate.

The other ingredients are:
Tablet coating: Hypromellose, lactose monohydrate, macrogol 4000, titanium dioxide

Tablet core: Microcrystalline cellulose, lactose monohydrate, magnesium stearate (Ph.Eur.) [vegetable], corn starch, colloidal silicon dioxide

What ESTRAMON comp looks like and contents of the pack

ESTRAMON comp is a white, round film-coated tablet with a score line on one side. The tablet can be divided into equal doses.

ESTRAMON comp is available in aluminum/polyvinyl chloride/PVDC blister packs with 1x28 and 3x28 film-coated tablets.

Not all pack sizes may be marketed.

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This medicinal product is authorized in the Member States of the European Economic Area (EEA) and in the United Kingdom (Northern Ireland) under the following names:
Denmark: Femanor
Germany: ESTRAMON comp 2 mg/1 mg film-coated tablets
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