Package leaflet: Information for the user

ESTALIS 50 micrograms/250 micrograms/24 hours transdermal patch
Estradiol/Norethisterone Acetate

Read all of this leaflet carefully, before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Estalis is and what it is used for

Estalis is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an oestrogen and a progestogen. Estalis is used in postmenopausal women with at least 12 months since their last natural period.

Estalis is used for:

Relief of symptoms occurring after menopause
During the menopause, the amount of the oestrogen produced by a woman's body drops. This can cause symptoms such as hot face, neck and chest ("hot flushes"), sleeping problems, irritability and dryness of the vagina. Estalis alleviates these symptoms after menopause. You will only be prescribed Estalis if your symptoms seriously hinder your daily life.

Prevention of osteoporosis
After the menopause some women may develop fragile bones (osteoporosis). You should discuss all available options with your doctor.
If you are at an increased risk of fractures due to osteoporosis and other medicines are not suitable for you, you can use Estalis to prevent osteoporosis after menopause.

2. What you need to know before you use Estalis

Medical history and regular check-ups
The use of HRT carries risks which need to be considered when deciding whether to start using it, or whether to carry on using it.

The experience in treating women with a premature menopause (due to ovarian failure or surgery) is limited. If you have a premature menopause the risks of using HRT may be different. Please talk to your doctor

Before you start (or restart) HRT, your doctor will ask about your own and your family's medical history. Your doctor may decide to perform a physical examination. This may include an examination of your breasts and/or an internal examination, if necessary.

Once you have started on Estalis you should see your doctor for regular check-ups (at least once a year). At these check-ups, discuss with your doctor the benefits and risks of continuing with Estalis.

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

Do not use Estalis
if any of the following applies to you. If you are not sure about any of the points below, **talk to your doctor** before using Estalis.

Do not use Estalis:
- if you have or have ever had **breast cancer,** or if you are suspected of having it;
- if you have **cancer which is sensitive to oestrogens**, such as cancer of the womb lining (endometrium), or if you are suspected of having it;
- if you have **any unexplained vaginal bleeding**;
- if you have **excessive thickening of the womb lining** (endometrial hyperplasia) that is not being treated;
- if you have or have ever had a **blood clot in a vein** (thrombosis), such as in the legs (deep venous thrombosis) or the lungs (pulmonary embolism);
- if you have a **blood clotting disorder** (such as protein C, protein S, or antithrombin deficiency);
- if you have or recently have had a disease caused by blood clots in the arteries, such as a **heart attack**, **stroke** or **angina**;
- if you have or have ever had a **liver disease** and your liver function tests have not returned to normal;
- if you have a rare blood problem called "**porphyria"** which is passed down in families (inherited);
- if you are **allergic** (hypersensitive) to **estradiol or norethisterone** or any of the other ingredients of Estalis (listed in section 6 Further information).

If any of the above conditions appear for the first time while using Estalis, stop using it at once and consult your doctor immediately.

When to take special care with Estalis
Tell your doctor if you have ever had any of the following problems, before you start the treatment, as these may return or become worse during treatment with Estalis. If so, you should see your doctor more often for check-ups:

- fibroids inside your womb;
- growth of womb lining outside your womb (endometriosis) or a history of excessive growth of the womb lining (endometrial hyperplasia);
- increased risk of developing blood clots (see "Blood clots in a vein (thrombosis)");
- increased risk of getting an oestrogen-sensitive cancer (such as having a mother, sister or grandmother who has had breast cancer);
- high blood pressure;
- a liver disorder, such as a benign liver tumour;
- diabetes;
- gallstones;
- migraine or severe headaches;
- a disease of the immune system that affects many organs of the body (systemic lupus erythematosus, SLE);
- epilepsy;

- asthma;
- a disease affecting the eardrum and hearing (otosclerosis);
- a very high level of fat in your blood (triglycerides);
- fluid retention due to cardiac or kidney problems;
- a condition called hypothyroidism (your thyroid gland fails to produce enough thyroid hormone) and you are taking a thyroid hormone replacement therapy;
- hereditary and acquired angioedema.

Stop using Estalis and see a doctor immediately
If you notice any of the following when using HRT:
- any of the conditions mentioned in "Do not use Estalis" section;
- yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease;
- swollen face, tongue and/or throat and/or difficulty swallowing or hives, together with difficulty breathing which are suggestive of an angioedema;
- a large rise in your blood pressure (symptoms may be headache, tiredness, dizziness);
- migraine-like headaches which happen for the first time;
- if you become pregnant;
- if you notice signs of a blood clot, such as:
  - painful swelling and redness of the legs;
  - sudden chest pain;
  - difficulty in breathing.

  For more information, see 'Blood clots in a vein (thrombosis)'.

Note: Estalis is not a contraceptive. If it is less than 12 months since your last menstrual period or you are under 50 years old, you may still need to use additional contraception to prevent pregnancy. Speak to your doctor for advice.

HRT and cancer

Excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)
Taking oestrogen-only HRT will increase the risk of excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the womb lining (endometrial cancer).

The progestogen in Estalis protects you from this extra risk.

In women who still have a womb and who are not taking HRT, on average, 5 in 1000 will be diagnosed with endometrial cancer between the ages of 50 and 65.
For women aged 50 to 65 who still have a womb and who take oestrogen-only HRT, between 10 and 60 women in 1000 will be diagnosed with endometrial cancer (i.e. between 5 and 55 extra cases), depending on the dose and for how long it is taken.

Irregular bleeding
You may have irregular bleeding or drops of blood (spotting) during the first 3-6 months of using Estalis. However, if the irregular bleeding:
- carries on for more than the first 6 months;
- starts after you have been using Estalis for more than 6 months;
- carries on after you have stopped using Estalis;

see your doctor as soon as possible.

Breast cancer
Evidence shows that taking combined oestrogen-progestogen or oestrogen-only hormone replacement therapy (HRT) increases the risk of breast cancer. The extra risk depends on how long you use HRT.

The additional risk becomes clear within 3 years of use. After stopping HRT the extra risk will decrease with time, but the risk may persist for 10 years or more if you have used HRT for more than 5 years.

Compare
Women aged 50 to 54 who are not taking HRT, on average, 13 to 17 in 1000 will be diagnosed with breast cancer over a 5-year period.
For women aged 50 who start taking oestrogen-only HRT for 5 years, there will be 16-17 cases in 1000 users (i.e. an extra 0 to 3 cases).
For women aged 50 who start taking oestrogen-progestogen HRT for 5 years, there will be 21 cases in 1000 users (i.e. an extra 4 to 8 cases).

Women aged 50 to 59 who are not taking HRT, on average, 27 in 1000 will be diagnosed with breast cancer over a 10-year period.
For women aged 50 who start taking oestrogen-only HRT for 10 years, there will be 34 cases in 1000 users (i.e. an extra 7 cases).
For women aged 50 who start taking oestrogen-progestogen HRT for 10 years, there will be 48 cases in 1000 users (i.e. an extra 21 cases).

Regularly check your breasts. See your doctor if you notice any changes, such as:
- dimpling of the skin;
- changes in the nipple;
- any lumps you can see or feel.

Additionally, you are advised to join mammography screening programs when offered to you. For mammogram screening, it is important that you inform the nurse/healthcare professional who is actually taking the x-ray that you use HRT, as this medication may increase the density of your breasts which may affect the outcome of the mammogram. Where the density of the breast is increased, mammography may not detect all lumps.

Ovarian cancer
Ovarian cancer is rare - much rarer than breast cancer. The use of oestrogen-only or combined oestrogen-progestagen HRT has been associated with a slightly increased risk of ovarian cancer.

The risk of ovarian cancer varies with age. For example, in women aged 50 to 54 who are not taking HRT, about 2 women in 2000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there will be about 3 cases per 2000 users (i.e. about 1 extra case).

Effect of HRT on heart and circulation

Blood clots in a vein (thrombosis)
The risk of **blood clots in the veins** is about 1.3 to 3- times higher in HRT users than in non-users, especially during the first year of taking it.

Blood clots can be serious, and if one travels to the lungs, it can cause chest pain, breathlessness, fainting or even death.

You are more likely to get a blood clot in your veins as you get older and if any of the following applies to you. Inform your doctor if any of these situations applies to you:
- you are unable to walk for a long time because of major surgery, injury or illness (see also section 3, If you need to have surgery);
- you are seriously overweight (BMI>30 kg/m^2);
- you have any blood clotting problem that needs long-term treatment with a medicine used to prevent blood clots;

- if any of your close relatives has ever had a blood clot in the leg, lung or another organ;
- you have systemic lupus erythematosus (SLE);
- you have cancer.

For signs of a blood clot, see "Stop using Estalis and see a doctor immediately".

Compare
Looking at women in their 50s who are not taking HRT, on average, over a 5-year period, 4 to 7 in 1000 would be expected to get a blood clot in a vein.
For women in their 50s who have been taking oestrogen-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).

It is uncertain if varicose veins increase the risk for venous thrombosis.

Heart disease (heart attack)
There is no evidence that HRT will prevent a heart attack.

Women over the age of 60 years who use oestrogen-progestogen HRT are slightly more likely to develop heart disease than those not taking any HRT.

If you have had a heart attack or chest pain (angina pectoris), discuss with your doctor the benefits and risks of using Estalis.

Stroke
The risk of getting stroke is about 1.5-times higher in HRT users than in non-users. The number of extra cases of stroke due to use of HRT will increase with age.

Compare
Looking at women in their 50s who are not taking HRT, on average, 8 in 1000 would be expected to have a stroke over a 5-year period. For women in their 50s who are taking HRT, there will be 11 cases in 1000 users, over 5 years (i.e. an extra 3 cases).

Other conditions
- Using HRT may cause fluid retention (*oedema*), especially for patients already suffering from heart or kidney problems.
- HRT may increase blood fat levels (*triglycerides*) which for women with raised levels of blood fats may lead to inflammation of the pancreas (*pancreatitis*). This could lead to nausea, vomiting, upper abdominal pain and fever.
- HRT will not prevent memory loss. There is some evidence of a higher risk of memory loss in women who start using HRT after the age of 65. Speak to your doctor for advice.
- All medicines used on the skin (*like patches*) may cause allergic skin reactions. Although it occurs very rarely, you should tell your doctor if you have, or have ever had, a severe allergic reaction to any of the ingredients of the patch.

Other medicines and Estalis
Some medicines may interfere with the effect of Estalis. This might lead to irregular bleeding. This applies to the following medicines:
- Medicines for **epilepsy** (such as phenobarbital, phenytoin and carbamazepine);
- Medicines for **tuberculosis** (such as rifampicin, rifabutin);
- Medicines for **HIV infection** (such as nevirapine, efavirenz, ritonavir, telaprevir, nelfinavir);
- Herbal remedies containing **St John's Wort** (Hypericum perforatum);
- Other **anti-infective medicines** (such as ketoconazole, erythromycin).

HRT can affect the way some other medicines work:
- A medicine for epilepsy (lamotrigine), as this could increase frequency of seizures

- Medicines for **Hepatitis C virus (HCV)** (such as combinations regimens ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin; glecaprevir/pibrentasvir or sofosbuvir/velpatasvir/voxilaprevir) may cause increases in liver function blood test results (increase in ALT liver enzyme) in women using combined hormonal contraception (CHCs) containing ethinylestradiol. Estalis contains estradiol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Estalis with this HCV combination regimen.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription, herbal medicines or other natural products. Your doctor will advise you.

Laboratory tests
If you need a blood test, tell your doctor or the laboratory staff that you are using Estalis, because this medicine can affect the results of some tests.

Pregnancy and breast-feeding
Estalis is for use in postmenopausal women only. If you become pregnant, stop using Estalis and contact your doctor.

Do not use Estalis while you are breast-feeding.

Driving and using machines
No known adverse effect of Estalis on the ability to drive or operate machines have been reported.

3. How to use Estalis

Always use this medicine exactly as your doctor has told you. Your doctor will aim to prescribe the lowest dose to treat your symptom for as short as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.

When to start treatment
- If you are currently not using any form of hormone replacement therapy (patches or tablets), or if you have been using a continuous combined hormone replacement therapy product (in which oestrogen and progestogen are given every day without interruption), you can start to use Estalis on any convenient day.
- If you are changing from a cyclic or sequential hormone replacement therapy treatment should be complete the on-going treatment cycle before treatment with oestrogen/progestogen therapy. The appropriate time to begin treatment with oestrogen/progestogen therapy, would be the first day of a withdrawal bleeding or seven days after finishing the previous treatment cycle.

When to apply the Estalis transdermal patch
- An Estalis patch should be replaced twice weekly (every 3 to 4 days). It is best to always replace it on the same two days of the week (e.g. Monday and Thursday). Your Estalis pack contains a calendar checklist on the back to help you remember your schedule. Mark the twice-a-week schedule that you plan to follow. Always change the patch on the two days of the week you have marked.
- Estalis should be worn continuously until it is time to replace it with a new patch.

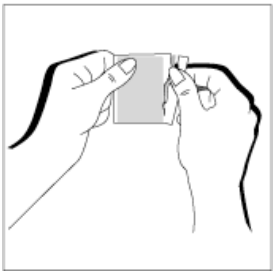
Where to apply Estalis
Apply the patch to the lower abdomen, below the waistline. Avoid the waistline, as clothing may cause the patch to rub off.
You may wish to try different areas of the skin when applying a new patch, to find ones that are most comfortable for you and where clothing will not rub on the patch.

Do not apply the patch to your breasts.

When changing your patch, apply your new patch to a different area of skin in the lower abdomen. Do not apply a new patch to that same area for at least one week.

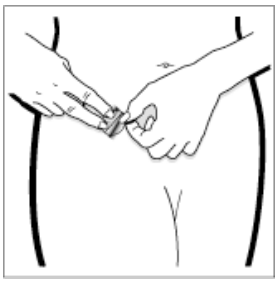
How to apply Estalis
If you store the patches in the refrigerator, allow them to reach room temperature before applying to the skin.

Before you apply Estalis, make sure that your skin is:
- clean, dry and cool
- free of any powder, oil, moisturiser, or lotion
- free of cuts and/or irritation.

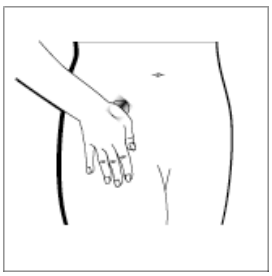


Each patch is individually sealed in a protective pouch. Tear open this pouch at the notch and remove the patch. Do not use scissors to open the pouch – this could damage the patch. Apply the patch immediately after opening the pouch and removing the protective backing.

Hold the patch with the protective backing facing you. Peel off one side of the protective backing and discard it. Try to avoid touching the sticky side of the patch, as the patch will not attach properly if you do.



Holding the other half of the backing, apply the sticky side of the patch to the skin. Remove the other half of the protective film and stick down the rest of the patch.



Press the patch tightly to the skin with the palm of your hands for at least 10 seconds so that it sticks properly, particularly around the edges.

When changing the patch, peel it off and fold it in half with the sticky side inwards. Please see section 5, *How to store Estalis* for instructions on safe disposal of the patch. Do not flush used patches down the toilet. You can easily remove any adhesive residue from your skin by gently rubbing the area with an oil-based cream or lotion.

Other useful information
Bathing, swimming, showering or exercising should not affect the patch if it has been correctly applied. If a patch falls off, for instance during bathing or showering, shake it to remove the water. After drying and cooling of the skin, reapply the same patch on a different area of the skin (see "where to apply Estalis").

Make sure you choose a clean, dry, lotion-free area of the skin. If the patch does not stick completely to your skin, use a new patch. No matter what day this happens, go back to changing this patch on the same days as the initial schedule.

When sunbathing or using a solarium, the patch should be covered. When swimming, the patch can be worn under your bathing suit.

The patch should not be applied to sweaty skin or immediately after a bath or shower. Wait until the skin is dry and cooled off.

How long to use Estalis
From time to time, you will need to discuss with your doctor the possible risk and benefits associated with Estalis, and benefits associated with Estalis, and whether you still need the treatment. It is important that you use Estalis **only as long as needed**, and that you **have regular check-ups**.

If you use more Estalis than you should
Overdose is unlikely due to the way Estalis is used (the patch releases the drug gradually). The effects of overdosage with oral oestrogens are breast tenderness, nausea, vomiting and/or metrorrhagia. Overdosage with progestogens may lead to a depressive mood, fatigue, acne and hirsutism. Remove the patch and contact your doctor or pharmacist, if any of these effects occurs.
Do not use a double dose to make up for the forgotten patch.

If you forget to use Estalis
If you forget to change the patch, reapply another patch as soon as you remember. No matter what day this happens, go back to changing the patch on the same days as your initial schedule.
Do not use two patches to make up for a forgotten one.

If you need to have surgery
If you are going to have surgery, tell the surgeon that you are using Estalis. You may need to stop using Estalis about 4 to 6 weeks before the operation to reduce the risk of a blood clot (see section 2, Blood clots in a vein). Ask your doctor when you can start using Estalis again.

If you stop using Estalis
Stopping use of Estalis may increase the likelihood of recurrent of symptoms and irregular bleeding and spotting. If this occurs after you stop treatment, consult your doctor immediately. Your doctor will need to work out the reasons for this and to rule out cancer of the womb.
After a long treatment break, consult your doctor before starting to use the patches again.

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

4. Possible side effects

The following diseases are reported more often in women using HRT compared to women not using HRT:
- breast cancer;
- abnormal growth or cancer of the lining of the womb (endometrial hyperplasia or cancer);
- ovarian cancer;
- blood clots in the veins of the legs or lungs (venous thromboembolism);

- heart disease;
- stroke;
- probable memory loss if HRT is started over the age of 65.

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

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

The following side effects have been reported with Estalis 50/250. **If any of these gets severe, tell your doctor or pharmacist.**

Very common (may affect more than 1 in 10 people):
Headache, application site reactions (including irritation, burning, rash, dryness, bleeding, bruising, inflammation, swelling, skin pigmentation, hives, and blisters), breast pain, breast tenderness, dysmenorrhoea, menstrual disorder.

Common (may affect up to 1 in 10 people):
Dizziness, nervousness, insomnia, mood changes, nausea, abdominal distension, dyspepsia, diarrhoea, abdominal pain, acne, rash, pruritus, dry skin, back pain, pain in extremity, pain, asthenia, weight changes, peripheral oedema, breast enlargement, menorrhagia, leucorrhoea, irregular vaginal bleeding, uterine spasms, vaginitis, endometrial hyperplasia, , depression

Uncommon (may affect up to 1 in 100 people):
Migraine, vertigo, vomiting, skin discoloration, increase in blood pressure, varicose veins, breast cancer, transaminases increase.

Rare (may affect up to 1 in 1,000 people):
Myasthenia, venous thromboembolism, allergic reactions (including rash, itching and breathing difficulties), libido changes, paraesthesia, gallstones, gallbladder disease, uterine leiomyoma, paratubular cysts, endocervical polyps.

Very rare (may affect up to 1 in 10,000 people):
Cholestatic jaundice.

Not known, frequency cannot be estimated from the available data:
Hair loss, allergic skin inflammation, severe allergic reaction (including difficulties to breath; swelling of face, tongue, throat or skin; dizziness and hives).

The following side effects have been reported with other HRT:
- gallbladder disease
- various skin disorders:
  - discoloration of the skin especially of the face or neck known as “pregnancy patches” (chloasma);
  - painful reddish skin nodules (erythema nodosum);
  - rash with target-shaped reddening or sores (erythema multiforme).
- decline in memory or mental ability
- dry eyes
- contact lens discomfort

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist**.** This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [to be completed nationally]. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Estalis

Store in a refrigerator (2°C – 8°C). Store below 25°C for a maximum period of 1 month. Do not freeze. Store in the original (sealed) pouch. Use the patch immediately after opening the pouch.

All patches (used and unused) must always be kept out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the patch. The expiry date refers to the last day of that month.

After removing a patch, fold it in half with the sticky side inwards and dispose of it safely out of the reach of children. Any used or unused transdermal patches should be disposed of in accordance with local requirements or returned to the pharmacy, preferably in the original packaging.

Do not throw away any medicine via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Estalis contains
Each Estalis 50 µg/250 µg/24 hours transdermal patch contains estradiol hemihydrate equivalent to 0.51 mg estradiol and 4.80 mg norethisterone acetate in a patch of 16 cm^2, releasing nominal 50 micrograms estradiol and 250 micrograms norethisterone acetate per 24 hours.

- The active substances in the Estalis patch are estradiol (as hemihydrate) and norethisterone acetate.
- The other ingredients in the Estalis patch are: **Adhesive matrix**: silicone and acrylic adhesive matrix, povidone, oleic acid and dipropylene glycol. **Backing layer**: polyester film laminate. **Release liner** (to be removed before application): fluoropolymer-coated polyester film**.**

What Estalis looks like and contents of the pack
Estalis patch is a 16 cm^2 round patch. The patch comprises a pressure sensitive adhesive layer, releasing the active substance, with a translucent polymeric backing on one side and a protective liner on the other.

Estalis 50 µg/250 µg/24 hours is available in cartons of 2, 8 or 24 round transdermal patches.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder

{Name And address}
<{tel}>
<{fax}>
<{e-mail}>

Manufacturer

{Name And address}
<{tel}>
<{fax}>
<{e-mail}>

<[To be completed nationally]>

This medicinal product is authorized in the Member States of the EEA under the following names:

Estalis 50/250: AT, BE, ES, FI, PT, SE

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2025-07-17