1. WHAT ESTRADOT IS AND WHAT IT IS USED FOR

Estradot is a hormone replacement therapy (HRT) and contains the hormone oestrogen. Estradot comes as a patch that is applied to the skin. The patch releases small amounts of estradiol, which pass directly through the skin into your bloodstream. Estradiol is identical to the natural hormone oestrogen that is produced by the ovaries until the menopause (the time when your menstrual periods stop).

Estradot is used for:

Relief of symptoms of the menopause
During the menopause, the amount of oestrogen produced by a woman’s body drops. For some women this can cause unpleasant symptoms such as hot face, neck and chest (“hot flushes”), sleep problems, irritability and depression. Some women also have problems with dryness of the vagina, which may cause discomfort during or after sexual intercourse. Estradot can reduce or stop these symptoms after the menopause.

Prevention of osteoporosis (for Estradot 50, 75 and 100 only)
Reduced oestrogen can increase the risk of osteoporosis. Osteoporosis is a thinning of the bones that makes them weaker and more likely to break. Taking oestrogens after the menopause slows down bone loss and can help to prevent osteoporosis. Estradot may be used to prevent osteoporosis after the menopause in women who are at an increased risk of fractures but who are unable to use other drugs approved for the prevention of osteoporosis. Your doctor should discuss all the available options with you.

The experience treating women older than 65 years is limited.

2. BEFORE YOU USE ESTRADOT
**Do not use Estradot**

- if you have, or have ever had breast cancer, or think you might have it;
- if you have or have ever had any cancer which is sensitive to oestrogens, such as cancer of the lining of the womb (endometrium), or think you might have it;
- if you have vaginal bleeding of unknown cause;
- if you have abnormal growth of the womb lining (endometrial hyperplasia) and you have not been treated for this yet;
- if you have or have ever had a blood clot in your veins. This may cause blockage of a blood vessel in the legs (deep vein thrombosis) leading to thromboembolism, e.g. in the lungs (pulmonary embolism) or other organs;
- if you have or have ever had a heart attack, stroke or severe chest pain due to angina (angina pectoris);
- if you have or have ever had a liver disease and your liver function has not returned to normal;
- if you have porphyria (red blood pigment in your urine);
- if you are allergic to estradiol or any of the other ingredients of Estradot;

Tell your doctor if any of these applies to you. You should not receive Estradot.

**Take special care with Estradot**

Estradot is not a transdermal contraceptive nor a fertility treatment. If you are still capable of becoming pregnant you must not use any hormone replacement therapy.

Estradot is a hormone replacement therapy. You need to be aware of the general risks when using HRT.

**If you have or have ever had any of the following conditions, you need to let your doctor know.** They may come back or get worse during treatment with Estradot:

- **Benign tumours** of the womb (e.g. myoma), **endometrial hyperplasia** (abnormal growth of the womb lining) or **endometriosis** (endometrial growths outside the uterus): Using HRT products containing only oestrogens (such as Estradot) for a long period can increase the risk of abnormal growth of the womb lining (the endometrium) and endometrial cancer. Adding a progestogen for at least 12 days every month greatly decreases this risk. During the first months of treatment, irregular bleeding may occur. **Contact your doctor** immediately:
  - if unexpected bleeding or spotting (breakthrough bleeding) occurs after having used Estradot for some time or if this continues after you stop treatment
  - if you have painful menstrual periods.
  Your doctor should examine what the cause is.

- If your womb has not been removed, you should also use the hormone progestogen for 12-14 days a month, in addition to Estradot, as directed by your doctor.

- **Blood clots** (thrombosis, lung embolism): You should not use Estradot if you have ever had a blood clot in your veins. HRT may increase the risk of blood clots, especially during the first year of treatment. **Stop using Estradot and contact your doctor** immediately if you get:
  - painful swelling and redness of the legs
  - sudden chest pain
  - difficulty in breathing.
  These symptoms may be signs of a blood clot. **Tell your doctor** if any of the following applies to you:
  - if you are extremely overweight (BMI>30)
  - if you have had a blood clot before or if you or someone in your close family has had blood clots
  - if you have any blood-clotting problem needing treatment with a medicine (anticoagulant)
- if you have had more than one miscarriage
- if you are off your feet for a long time because of surgery, injury or illness
- if you are about to have an operation; it is best to stop treatment 4 to 6 weeks before surgery. Any of these will make your risk of a blood clot higher.

**High blood pressure:** Stop using Estradot and contact your doctor immediately,
- if an increase in blood pressure occurs while using Estradot.

**Liver problems:** You need to let your doctor know if you have ever had liver problems, such as a benign tumour in the liver (liver adenoma).

Stop using Estradot and contact your doctor immediately,
- if you get yellowing of the eyes and face (jaundice); this could be a sign of liver problems.

**Migraine or severe headache:** Some studies with HRT have shown a slightly increased risk of stroke.

Stop using Estradot and contact your doctor immediately
- if you get unexplained migraine-like headaches, with or without disturbed vision. Headaches like these can be an early sign of a stroke. If you have already had a stroke, talk with your doctor about whether the benefits of the treatment outweigh the possibly increased risk.

**Breast cancer:** You should not use Estradot if you have ever had breast cancer. There is a slightly increased risk of breast cancer related to HRT. The risk increases the longer the treatment lasts and decreases when treatment is stopped. Five years after stopping treatment, the risk returns to that of women who have never used HRT. The risk of breast cancer seems to be higher for women using oestrogen in combination with progestogen than for women who use products containing only oestrogen (such as Estradot).

Contact your doctor if you notice any changes to your breasts, such as:
- dimpling of the breast skin
- changes in the nipple
- lumps that you can see or feel.

Your doctor may advise you to have regular breast check-ups, including mammography. You need to let your doctor know if you have a history of breast cancer or other oestrogen-sensitive cancers in your immediate family (mother, sister or daughter).

**Heart disease:** You should not use Estradot if you have ever had a heart attack or chest pain (angina pectoris). Studies with HRT tablets have shown that women may be slightly more likely to get heart disease during the first year of treatment. For Estradot, it is not certain whether the risk is similar.

Stop using Estradot and contact a doctor immediately,
- if you get pain in your chest that spreads to your arm or neck. This pain may be a sign of heart disease.

**Stroke:** You should not use Estradot if you have ever had a stroke. See “migraine or severe headache” These can be warning signs of a stroke.

**Cancer of the ovaries:** Some studies have shown that using hormone therapy with oestrogens alone (such as Estradot) for 5-10 years may lead to an increased risk of cancer of the ovaries compared to women never treated with HRT. It is not known whether the use of oestrogens combined with progestogen increases the risk of ovarian cancer.

**High fat levels in your blood** which in rare cases may cause inflammation of the pancreas.

**Diabetes**

**Gallstones**

**Systemic lupus erythematosus** (SLE), an autoimmune disorder
• Epilepsy
• Asthma
• Hearing loss due to otosclerosis (a problem with the bones in your ear)
• Kidney problems

Tell your doctor before taking Estradot if you have ever had any of the conditions above.

Medical check-ups
Before you start using Estradot your doctor should ask you about your own and your family's medical history. Your doctor should examine your breasts and your abdomen and may do an internal examination. He/she should tell you what kind of changes in the breast you should report to the doctor and may advise you to have a breast X-ray (a mammogram). Once you have started Estradot, you should see your doctor for regular check-ups (at least once a year). At these check-ups your doctor should discuss with you the benefits and risks of continuing to take Estradot.

Effects on laboratory tests
Using oestrogens may influence the results of certain laboratory results. Tell your doctor that you use Estradot before undergoing a blood test.

Taking other medicines
Tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Some medicines may increase or decrease the effect of Estradot, such as medicines containing:
• phenobarbital, phenytoin or carbamazepine (used to treat epilepsy),
• rifampicin, rifabutin (used to treat tuberculosis),
• nevirapine, efavirenz, ritonavir, nelfinavir (used to treat HIV infection),
• St John's wort (herbal medicine used to treat depression).

Pregnancy and breast-feeding
You should not use Estradot if you are pregnant or can still become pregnant or while you are breast-feeding. Stop using Estradot and contact your doctor immediately if you become pregnant during Estradot treatment. Ask your doctor or pharmacist for advice before taking any medicine.

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

3. HOW TO USE ESTRADOT

Always use Estradot exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. During the treatment your doctor may adjust the dose according to your individual needs.

How long to use Estradot
It is important that you use the lowest possible effective dose and only as long as needed. From time to time, you should discuss with your doctor whether you still need the treatment.

When to start treatment
• If you are currently not using any form of HRT (patches or tablets), or if you have been using a continuous combined HRT product (where oestrogen and the progestogen are given every day without interruption), you can start to use Estradot on any convenient day.
• If you are changing from a cyclic or sequential HRT treatment (where the progestogen is added for 12-14 days of the cycle), you should start to use Estradot on the day after you complete your previous cycle.

**When to apply Estradot**

• An Estradot 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 Estradot 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.

• Estradot should be worn continuously until it is time to replace it with a new patch.

Any adhesive that might remain on your skin can be easily rubbed off. Then place the new Estradot patch onto a different area of skin.

**Women without a uterus**
The Estradot patch is applied continuously without a break. Additional use of another type of hormone called progestogen is not required, unless you have a condition where the lining of the uterus also grows outside the uterus (*endometriosis*). Check the risks to be aware of with HRT in general in section 2, *Take special care with Estradot*.

**Women with a uterus**

Your doctor should give you another hormone called progestogen in addition to Estradot to reduce the risk of cancer of the uterus. While Estradot is applied continuously without a break, the progestogen tablet should be taken for at least 12-14 days every month. Check the risks to be aware of with HRT in general in section 2, *Take special care with Estradot*.

**Where to apply Estradot**

Apply the patch to the lower abdomen, below the waistline. Avoid the waistline itself, since clothing may cause the patch to rub off. Do not apply the patch to the breasts or any area near to the breasts.

When changing your patch, based on your twice-a-week schedule, apply your new patch to a different site. Do not apply a new patch to that same area for at least one week.

Before you apply Estradot, make sure that your skin is:

• clean, dry and cool,

• free of any powder, oil, moisturiser, or lotion,

• free of cuts and/or irritation.

**How to apply Estradot**

Each patch is individually sealed in a protective pouch. Tear open this pouch at the indentation and remove the patch (do not use scissors to open the pouch as this could damage the patch).

A stiff protective backing covers the sticky side of the patch. This backing must be removed before the patch is stuck to the skin. Apply the patch immediately after opening the pouch and removing the protective backing.

Hold the patch with the protective backing facing you. Peel one side of the protective backing and discard it. Try to avoid touching the sticky side of the patch with your fingers.
Holding the other half of the backing, apply the sticky side of the patch to a dry area of your lower abdomen. Press the sticky side to the skin and smooth down. Fold back the remaining side of the patch.

Grasp the straight edge of the protective backing and pull it off the patch.

Press the sticky remaining side of the patch to the skin and smooth down. Press the patch firmly in place with the palm of your hand for about 10 seconds.

Make sure that the patch sticks properly to your skin and go over the edges with your finger to ensure good contact between the patch and skin.

When changing the patch, peel it off, fold it with the sticky side inside, and discard it with normal household waste.

**Further useful information**

Bathing, swimming, showering or exercising should not affect the patch if it has been correctly applied. If a patch falls off, e.g. during bathing or showering, shake it to remove the water. After careful drying and cooling down of the skin, reapply the same patch on a different area of the lower abdomen (see ‘Where to apply Estradot’).

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 your original schedule.

When sunbathing or using a solarium, the patch should be covered. When swimming, the patch can be worn under your bathing suit.
If you have used more Estradot than you should
Remove the patch if you have used too much Estradot. Symptoms of overdose are usually tenderness of the breasts and/or vaginal bleeding. Acute overdose is unlikely due to the way Estradot is used (patch). If symptoms persist contact your doctor.

If you forget to use Estradot
If you forget to change the patch, change the patch as soon as you remember. No matter what day this happens, go back to changing the newly applied patch on the same days as your original schedule. Do not use a double dose to make up for the forgotten patch.

If you stop using Estradot
Stopping use of Estradot may increase the risk of breakthrough bleeding or spotting. Talk to your doctor if this occurs. After a long break in treatment, consult your doctor before starting to use the patch again.

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

4. POSSIBLE SIDE EFFECTS
Like all medicines, Estradot patches can cause side effects, although not everybody gets them.

Some effects could be serious
These symptoms need immediate medical attention:

- Sudden chest pain
- Pain in your chest that spreads to your arm or neck
- Difficulty in breathing
- Painful swelling and redness of the legs
- Yellowing of the eyes and face (jaundice)
- Unexpected vaginal bleeding or spotting (breakthrough bleeding) after using Estradot for some time, or after you stop treatment
- Breast changes, including dimpling of the breast skin, changes in the nipple, lumps that you can see or feel.
- Painful menstrual periods
- Unexplained migraine-like headaches

Stop using Estradot and tell your doctor immediately if you get any of the effects mentioned above. Check the risks to be aware of with HRT in general in section 2, Take special care with Estradot.

Other side effects
In addition, the following side effects have been reported with Estradot. If any of these gets severe, tell your doctor or pharmacist.

Very common (affects more than 1 user in 10):
- Headache, skin reactions at the patch application site (redness, rash, itching), breast tension and pain, menstrual pains, menstrual disorders.

Common (affects 1 to 10 users in 100):
- Depression, nervousness, mood changes, sleeplessness, nausea (feeling sick), indigestion, diarrhoea, abdominal pain, bloated feeling, acne, rash, dry skin, itching, breast enlargement, heavy menstrual periods, a white or yellowish discharge from the vagina, irregular vaginal bleeding, severe uterine contractions, inflammation of the vagina, abnormal growth of the womb lining (endometrial hyperplasia), pain, back pain, weakness, fluid retention (oedema) in the extremities (hands and feet), weight changes.
Uncommon (affects 1 to 10 users in 1,000):
Migraine, dizziness, increase in blood pressure, vomiting (being sick), skin discoloration, impaired liver function tests.

Rare (affects 1 to 10 users in 10,000):
Tingling or numbness of hand and feet, blood clot, gallstones, hair loss, muscular weakness, benign smooth muscle growth in uterus, cysts close to uterine tubes, polyps (small growths) in the uterine cervix (neck of the womb), changes in sexual desire, allergic reactions such as rash.

Very rare (affects less than 1 user in 10,000):
Hives, signs of serious allergic reaction such as sudden trouble breathing, tightness of the chest, general rash, swelling or itching, decreased carbohydrate tolerance, involuntary movements which may affect the eyes, head and neck, contact lens discomfort, severe skin lesions, excessive hair growth.

Other side effects that have been linked to HRT:
Hard painful lumps looking like bruises on the legs, skin eruptions (redness, spots and sometimes blistering, possibly also affecting the inside of the mouth) and decline in memory or mental ability (possible dementia), gallbladder disease.

If any of the side effects gets severe, or if you notice any side effects not listed in this leaflet, tell your doctor or pharmacist.

5. HOW TO STORE ESTRADOT

- Keep Estradot out of the reach and sight of children.
- Store Estradot in the original package in a cool, dry place. Once opened or once the protective pouch has been removed, the patch should be applied to the skin immediately.
- Do not refrigerate or freeze Estradot.
- Do not use Estradot after the expiry date which is stated on the carton and patch after ‘EXP’. The expiry date refers to the last date of the month.
- Do not use any Estradot pack that is damaged or shows signs of tampering.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Estradot contains

Each 25 micrograms/24 hours patch contains estradiol hemihydrate corresponding to 0.39 mg estradiol and releases about 25 micrograms estradiol per 24 hours.
Each 37.5 micrograms/24 hours patch contains estradiol hemihydrate corresponding to 0.585 mg estradiol and releases about 37.5 micrograms estradiol per 24 hours.
Each 50 micrograms/24 hours patch contains estradiol hemihydrate corresponding to 0.78 mg estradiol and releases about 50 micrograms estradiol per 24 hours.
Each 75 micrograms/24 hours patch contains estradiol hemihydrate corresponding to 1.17 mg estradiol and releases about 75 micrograms estradiol per 24 hours.
Each 100 micrograms/24 hours patch contains estradiol hemihydrate corresponding to 1.56 mg estradiol and releases about 100 micrograms estradiol per 24 hours.

- The active substance is estradiol (as hemihydrate).
- The other ingredients in the adhesive layer of the patch are acrylic adhesive, silicone adhesive, oleyl alcohol, dipropylene glycol, povidone (E1201).
• The backing layer is composed of: ethylene/vinyl acetate copolymer, polyethylene, vinylidene/vinyl chloride copolymer, polyethylene, ethylene/vinyl acetate copolymer co-extruded film, silicon dioxide/titanium dioxide.
• The release liner (to be removed before application) is a fluoropolymer-coated polyester film.

What Estradot looks like and contents of the pack
Estradot 25 is a 2.5 cm$^2$ rectangular patch with rounded corners, comprising a pressure-sensitive adhesive layer containing estradiol, with a translucent polymeric backing on one side and a protective liner on the other.
Estradot 37.5 is a 3.75 cm$^2$ rectangular patch with rounded corners, comprising a pressure-sensitive adhesive layer containing estradiol, with a translucent polymeric backing on one side and a protective liner on the other.
Estradot 50 is a 5 cm$^2$ rectangular patch with rounded corners, comprising a pressure-sensitive adhesive layer containing estradiol, with a translucent polymeric backing on one side and a protective liner on the other.
Estradot 75 is a 7.5 cm$^2$ rectangular patch with rounded corners, comprising a pressure-sensitive adhesive layer containing estradiol, with a translucent polymeric backing on one side and a protective liner on the other.
Estradot 100 is a 10 cm$^2$ rectangular patch with rounded corners, comprising a pressure-sensitive adhesive layer containing estradiol, with a translucent polymeric backing on one side and a protective liner on the other.

Estradot is available in five different strengths: 25, 37.5, 50, 75 and 100 micrograms/24 hours. Not all strengths may be marketed in your country.

Estradot is available in cartons of 2, 8, 24 and 26 patches. Not all pack sizes may be marketed in your country.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
{Name and address}
	<{tel}>
	<{fax}>
	<{e-mail}>

Manufacturer:
Novartis Pharma S.A.S.
Site Industriel de Huningue
26 rue de la Chapelle
F-68330 Huningue
France

This medicinal product is authorised in the Member States of the EEA under the following name:
Austria: Estradot
Belgium: Vivelle dot
Denmark: Vivelle dot
Finland: Estradot
France: Vivelledot
Germany: Estradot
Greece: Estradot
Iceland: Vivelle dot
Ireland: Estradot
Luxembourg: Estradot
Norway: Estradot
Portugal: Estradot
Spain: Estradot
Sweden: Estradot
The Netherlands: Estradot
United Kingdom: Estradot

This leaflet was last approved in {MM/YYYY}. Proposal