Package leaflet: Information for the user

Elleste Duet™ 1 mg Tablets
1 mg + 1 mg/1 mg film-coated tablets
(estradiol + estradiol/norethisterone acetate)
and
Elleste Duet™ 2 mg Tablets
2 mg + 2 mg/1 mg film-coated tablets
(estradiol + estradiol/norethisterone acetate)

Read all of this leaflet carefully before you start taking 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, please 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 ELLESTE DUET IS AND WHAT IT IS USED FOR

Elleste Duet is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an oestrogen (estradiol hemihydrate) and a progestogen (norethisterone acetate).

Elleste Duet 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"). Elleste Duet alleviates these symptoms after menopause. You will only be prescribed Elleste Duet 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 Elleste Duet 2 mg to prevent osteoporosis after menopause.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ELLESTE DUET

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

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

Do not take Elleste Duet

if any of the following applies to you. If you are not sure about any of the points below, **talk to your doctor** before taking Elleste Duet,

Do not take Elleste Duet

• 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** to **estradiol hemihydrate** or **norethisterone acetate** or any of the other ingredients of this medicine (listed in section 6)

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

When to take special care with Elleste Duet

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 Elleste Duet. 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 a 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
• hereditary and acquired angioedema

Stop taking Elleste Duet and see a doctor immediately

If you notice any of the following when taking HRT:
• any of the conditions mentioned in the 'DO NOT take Elleste Duet' 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: Elleste Duet 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 Elleste Duet protects you from this extra risk.

Unexpected bleeding

You will have a bleed once a month (so-called withdrawal bleed) while taking Elleste Duet. But, if you have unexpected bleeding or drops of blood (spotting) besides your monthly bleeding, which:
• carries on for more than the first 6 months
• starts after you have been taking Elleste Duet more than 6 months
• carries on after you have stopped taking Elleste Duet
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/m2)
• 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 taking Elleste Duet 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).

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.

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).

Underactive thyroid gland

If you are having medicine for treatment of an underactive thyroid gland, your doctor will carry out tests while you are taking HRT, to ensure that your thyroid hormone levels remain acceptable.

Angioedema

If you have angioedema (a serious allergic reaction often involving swelling of the face, mouth and

throat), oestrogens may make this worse.

Other conditions

• 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.

Children

Do not give this medicine to children.

Other medicines and Elleste Duet

Some medicines may interfere with the effect of Elleste Duet. 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 and nelfinavir)
• Herbal remedies containing **St John's Wort** (Hypericum perforatum)

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 combination regimen ombitasvir/paritaprevir/ritonavir with or without dasabuvir as well as a regimen with glecaprevir/pibrentasvir) may cause increases in liver function blood test results (increase in ALT liver enzyme) in women using CHCs containing ethinylestradiol. Elleste Duet contains estradiol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Elleste Duet 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 taking Elleste Duet, because this medicine can affect the results of some tests.

Pregnancy and breast-feeding

Elleste Duet is for use in postmenopausal women only. If you become pregnant, stop taking Elleste Duet and contact your doctor.

Driving and using machines

No effects on driving or using machinery have been observed for Elleste Duet.

Elleste Duet 2 mg contains **Sunset yellow colouring** which can cause allergic-type reactions, including asthma. This allergy is more common in people who are allergic to aspirin.

Elleste Duet contains **lactose**.
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW TO TAKE ELLESTE DUET

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Your doctor will aim to prescribe the lowest possible dose to treat your symptoms for as short a time as necessary. Speak to your doctor if you think the dose is too strong or not strong enough.

The Elleste Duet **1 mg** pack contains 16 white tablets and 12 pale green tablets.
- You must start with the white tablets.

The Elleste Duet **2 mg** pack contains 16 orange tablets and 12 grey tablets.
- You must start with the orange tablets.

If you are still having regular periods, start on the first day of bleeding.

If you are not having regular periods you can start straight away.
- Take one tablet each day. You can take the tablet at a time of the day that suits you but it is best to take it at about the same time each day.
- Swallow the tablets whole, with some water.
- Follow the direction of the arrows on the pack and take a tablet each day until the pack is empty.
- When you finish your first foil strip, start a new strip on the next day. Remember to put a fresh sticker on your new foil strip.

To help you remember to take your tablets, we have included stickers in the pack with the days of the week marked on them. For example, if you are starting the tablets on a Friday, use the sticker which starts with 'Fri'. Stick this at the top of the foil strip on the side where you can see the tablets.

If you are taking

- Elleste Duet 1 mg, the first day should be above the white tablet which has the start arrow next to it.
- Elleste Duet 2 mg, the first day should be above the orange tablet which has the start arrow next to it.

Changing from another type of HRT

If you are changing from another type of HRT, start taking Elleste Duet when you finish the pack of HRT you are taking at the moment.

If your doctor gives you instructions on changing from another type of HRT you should follow these instructions. If you have any doubts you should contact your doctor.

Will I have periods?

You will probably have a monthly bleed. This may start any time between day 21 of the pack to day 5 of the next pack. This pattern will usually be the same from month to month. Some women may have no bleeds.
In the first few months you may get irregular bleeding. However, if this carries on you should tell your doctor.

If you need to have surgery

If you are going to have surgery, tell the surgeon that you are taking Elleste Duet. You may need to stop taking Elleste Duet 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 taking Elleste Duet again.

If you forget to take Elleste Duet

Take the tablet as soon as you remember, and take the next one at the normal time.
If you have missed your tablet by more than 12 hours, dispose of this tablet safely and take the next one at the normal time. Do not take a double dose to make up for the forgotten tablet. You may experience some breakthrough bleeding or spotting.

If you take more Elleste Duet than you should

There should be no problems, but you may experience breast tenderness, feel sick or actually be sick, have irregular periods, feel down, feel tired, develop acne or experience an increase in body and facial hair. If you are worried, contact your doctor. Take the usual tablet the following day.

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

4. POSSIBLE SIDE EFFECTS

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

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.

The following side effects have been associated with Elleste Duet:

Frequencies are defined as follows:

Very common: may affect more than 1 in 10 people
Common: may affect up to 1 in 10 people
Uncommon: may affect up to 1 in 100 people
Rare: may affect up to 1 in 1,000 people
Very rare: may affect up to 1 in 10,000 people
Not known: frequency cannot be estimated from the available data

Very common: headache, breast pain, breast tenderness, painful periods, problems with your menstrual cycle.

Common: feeling down**,** feeling anxious, mood changes, changes in sex drive, feeling dizzy, difficulty sleeping, feeling sick, bloating, diarrhoea, indigestion, stomach cramps, acne, rashes, itchiness, dry skin, back pain, pain in the extremities, breast enlargement, heavy periods, vaginal discharge, break-through bleeding, spasms (contractions) of the womb, vaginal infection, excessive thickening of the lining of the womb, pain, feeling of weakness, swelling of the ankles, feet or fingers, increase in weight.

Uncommon: migraine, a feeling of dizziness or “spinning”, high blood pressure, varicose veins, being sick, gallstones and gallbladder disease, change in colour of the skin, breast cancer, muscle cramps, increased levels of chemicals in the blood which may indicate disease.

Rare: hypersensitivity, tingling or numbness, blood clot in a vein, inflammation of a vein, muscle weakness, growths in the womb (myoma, cysts, polyps).

Very rare: increase in body and facial hair, yellowing of the skin.

Not known: loss of hair from the scalp.

The following side effects have been reported with other HRTs:
• various skin disorders
- discolouration 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)

• dry eyes
• tear film changes

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
By reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE ELLESTE DUET

Keep this medicine out of the sight and reach of children.

Do not store Elleste Duet 1 mg Tablets above 30ºC.

Do not store Elleste Duet 2 mg Tablets above 25ºC.

Store in the original package.

Do not use this medicine after the 'expiry date' which is stated on the carton after "EXP". The expiry date refers to the last day of that month.
.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Elleste Duet contains

Each strip of Elleste Duet **1 mg** Tablets contains the active substances:
- 16 white tablets containing 1 milligram estradiol (as hemihydrate)
- 12 pale green tablets containing 1 milligram estradiol (as hemihydrate) and 1 milligram norethisterone acetate.

Each strip of Elleste Duet **2 mg** Tablets contains the active substances:
- 16 orange tablets containing 2 milligrams estradiol (as hemihydrate).
- 12 grey tablets containing 2 milligrams estradiol (as hemihydrate) and 1 milligram norethisterone acetate

(The estradiol hemihydrate used to make Elleste Duet does not come from animals).

The tablets also contain: lactose monohydrate, maize starch, povidone, talc, magnesium stearate, macrogol 400 and hypromellose (E464).

- Elleste Duet 1 mg contains the colours indigo carmine (E132), quinoline yellow (E104) and titanium dioxide (E171).
- Elleste Duet 2 mg contains the colours sunset yellow (E110), titanium dioxide (E171) and black iron oxide (E172). (*see also the warning at the end of section 2*)

What Elleste Duet looks like and contents of the pack

One pack of Elleste Duet 1 mg Tablets contains white and pale green film-coated tablets with an embossing.
One pack of Elleste Duet 2 mg Tablets contains orange and grey film-coated tablets with an embossing.
They are supplied in packs containing blister strips of 28 or 84 tablets.

Not all packs sizes may be marketed.

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This leaflet was last revised in March 2025.