Indivina® 1mg/2.5mg Tablets

Ref: 1000/020525/1/F

(estradiol valerate / medroxyprogesterone acetate)

Patient Information Leaflet

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, 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.

Your medicine is called Indivina 1mg/2.5mg Tablets, but will be referred to as Indivina throughout this leaflet. *Please note that this leaflet also contains information about other strengths of this medicine.*

What is in this leaflet

1 What Indivina is and what it is used for
2 What you need to know before you take Indivina
3 How to take Indivina
4 Possible side effects
5 How to store Indivina
6 Contents of the pack and other information

1 What Indivina is and what it is used for

Indivina is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an oestrogen and progestogen. Indivina is used in menopausal women with at least three years since their last natural period. Indivina 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"). Indivina alleviates these symptoms after menopause. You will only be prescribed Indivina 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 Indivina to prevent osteoporosis after menopause.

2 What you need to know before you take Indivina

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

Do not take Indivina
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 Indivina.
Do not take Indivina
* 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 valerate** or **medroxyprogesterone 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 Indivina, stop using it at once and consult your doctor immediately.

Warnings and precautions
Talk to your doctor before starting the treatment if you have ever had any of the following problems, as these may return or become worse during treatment with Indivina. 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
* hereditary and acquired angioedema.

Stop taking Indivina 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 Indivina" 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: Indivina 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 Indivina protects you from this extra risk.

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

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 1 000 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 1 000 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 1 000 users (i.e. an extra 4 to 8 cases).
Women aged 50 to 59 who are not taking HRT, on average, 27 in 1 000 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 1 000 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 1 000 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 2 000 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 2 000 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 taking Indivina 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 1 000 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 1 000 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 a 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 1 000 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 1 000 users, over 5 years (i.e. an extra 3 cases).

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.
* If you are taking thyroid hormone replacement therapy (e.g. thyroxine), your doctor may monitor your thyroid function more often when you start treatment.
* If you have or have had cholasma (yellowish-brown pigmentation patches on the skin, particularly of the face); if so, minimize your exposure to the sun or ultraviolet radiation whilst using Indivina.

Indivina® 1mg/2.5mg Tablets

(estradiol valerate / medroxyprogesterone acetate)

Patient Information Leaflet (continued)

Other medicines and Indivina
Some medicines may interfere with the effect of Indivina. This might lead to irregular bleeding. This applies to the following medicines:
* Medicines for **epilepsy** (such as phenobarbital, phenytoin and carbamazepin)
* Medicines for **tuberculosis** (such as rifampicin, rifabutin)
* Medicines for **HIV infection** (such as nevirapine, efavirenz, ritonavir 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. Indivina contains estradiol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Indivina 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 Indivina, because this medicine can affect the results of some tests.

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

Driving and using machines
Indivina has no influence on your ability to drive or use machines.

Indivina contains lactose
This medicine contains 78.9 mg (1 mg/2.5 mg tablet), 76.5 mg (1 mg/5 mg tablet) or 75.5 mg (2 mg/5 mg tablet) lactose (as monohydrate). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3 How to take Indivina

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. 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.
Take one Indivina tablet every day, preferably at about the same time each day. Calendar days are printed on the blister sheet to help you follow your daily tablet intake. Swallow the tablet whole with a drink. You will normally start on the lowest dose of Indivina and this will be increased, if necessary. Your doctor should aim to prescribe the lowest dose for the shortest time that gives you relief from your symptoms. Talk to your doctor if your symptoms are not better after three months. If you feel that the effect of Indivina is too strong or too weak, do not change the dose or stop taking the tablets yourself, but ask your doctor for advice.
If you are not having periods and you have not previously taken HRT or you are changing from another continuous combined HRT product, treatment with Indivina may be started on any day.
If you switch from a cyclic HRT regimen, start Indivina treatment one week after taking the last tablet of the cyclic HRT. Talk to your doctor or pharmacist if you are unsure.
Whilst taking this medicine
When you first start taking Indivina you may get some bleeding at odd times for a few months (Please also refer to the section above on Endometrial cancer). However, if this is still happening after a few months or if you experience heavy bleeding tell your doctor.

If you take more Indivina than you should
If you or somebody else has taken too many Indivina tablets, talk to your doctor or pharmacist. An overdose of Indivina could make you feel sick, or make you get a headache or uterine bleeding.
If you forget to take Indivina
It is best to take the tablet at the same time each day. Do not take a double dose to make up for a forgotten tablet. You should then continue by taking the next tablet at your usual time. Missing a tablet or irregular use of Indivina tablets may cause breakthrough bleeding or spotting.
If you stop taking Indivina
If you want to stop taking Indivina, talk to your doctor first. He/she will explain the effects of stopping treatment and discuss other possibilities with you.
If you need to have surgery
If you are going to have surgery, tell the surgeon that you are taking Indivina. You may need to stop using Indivina 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 Indivina again.
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, particularly early on (in the first few months of treatment), for example irregular bleeding may occur, although not everybody gets them. These often disappear with continued treatment.
There are a number of situations in which you may have to **stop taking Indivina.** Tell your doctor immediately if you develop any of the following conditions:
* develop signs of jaundice (yellowing of the skin or the whites of the eyes)
* experience a migraine type headache for the first time
* become pregnant
* experience a significant increase in your blood pressure

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 is a list of side effects that have been linked to the use of HRT:

Common side effects (may affect up to 1 in 10 people):
* weight increase or decrease, swelling caused by fluid retention
* depression, nervousness, lack of energy
* headache, dizziness
* hot flushes, increased sweating
* feeling sick, vomiting, stomach cramps, gas
* breast tension and pain, vaginal discharge, bleeding or spotting, disorder of vulva/vagina, menstrual disorder.

Uncommon side effects (may affect up to 1 in 100 people):
* benign breast tumor, benign growths in the lining of the womb
* allergic (hypersensitivity) reaction
* increased appetite, high level of cholesterol in the blood
* anxiety, inability to sleep, apathy, mood swings, poor concentration, changes in sex drive or mood, euphoria, agitation
* migraine, sensation of tingling, prickling or numbness in skin, trembling
* visual impairment, dry eye
* feeling your heartbeat
* increased blood pressure, inflammation of a vein, purple patches like bruising
* breathlessness, runny or blocked nose
* constipation, indigestion/heartburn, diarrhea, rectal disorder
* acne, hair loss, dry skin, nail problems, skin nodule, excessive hair growth (hirsutism), painful reddish skin nodules (erythema nodosum), generalized itchy rash
* joint disorders, muscle cramps
* increased frequency or urge to pass urine, lack of bladder control, bladder infections, discoloured urine, blood in the urine
* breast enlargement, breast tenderness, thickening of the lining of the womb, uterine disorder
* tiredness, abnormal laboratory tests, weakness, fever, flu-like symptoms, feeling generally unwell.

Rare side effects (may affect up to 1 in 1 000 people):
* contact lens intolerance
* alterations in liver function and biliary flow
* skin rash
* blood clot, usually in a leg or lung, which causes pain, swelling or redness
* menstrual pain, pre-menstrual like syndrome

Frequency not known side effects (frequency cannot be estimated from the available data)
* tumours in uterus
* worsening of the symptoms of angioedema (hereditary and acquired)
* reduced blood supply to the brain or to a section of the brain
* stomach pain, bloating, yellowing of the skin or eyes
* eczema

The following side effects have been reported with other HRTs:
* heart disease (heart attack)
* gall bladder disease
* inflammation of pancreas (pancreatitis)
* skin disorders:
  - yellowish-brown pigmentation patches on the skin, particularly of the face (chloasma)
  - rash with target-shaped reddening or sores (erythema multiforme).
* Probable memory loss over the age of 65

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 the Yellow Card Scheme at: www.mhra.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 Indivina

* Do not store above 25ºC.
* Store in the original package in order to protect from moisture.
* KEEP THIS MEDICINE OUT OF THE SIGHT AND REACH OF CHILDREN.
* Do not use this medicine after the expiry date shown on the carton label or blister strip. Only keep this medicine if your doctor tells you to. If your tablets become discoloured or show any any other signs of deterioration, consult your pharmacist (chemist) who will tell you what to do.
* Medicines should not be disposed 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 Contents of the pack and other information

What Indivina contains:
Indivina 1mg/2.5mg tablets contain 1mg estradiol valerate and 2.5mg medroxyprogesterone acetate.
The tablets also contain lactose monohydrate, maize starch, gelatine, magnesium stearate

What Indivina looks like and contents of the pack
Indivina 1mg/2.5mg tablets are white, round, flat tablets embossed with "1 + 2.5" on one side and plain on the other.
Each pack contains either 1 x 28 tablets or 3 x 28 tablets.

Manufacturer and Licence Holder
This medicine is manufactured by Delpharm Lille Sas Lys Lez Lannoy, Parc D Activites Roubaix-Est, 22 Rue De Toufflers, CS 50070 59452 Lys Lez Lannoy, France and is procured from within the EU and repackaged by the Product Licence Holder: Lexon (UK) Limited, Unit 18, Oxleasow Road, East Moons Moat, Redditch, Worcestershire, B98 0RE.

If you have any questions or are not sure about anything, ask your doctor or pharmacist. They will have additional information about this medicine and will be able to advise you.

POM PL 15184/1000 Indivina 1mg/2.5mg Tablets

Revision date: 02/05/25

Blind or partially sighted?
Is this leaflet hard to see or read?
Phone Lexon (UK) Limited,
Tel: 01527 505414 to obtain the leaflet in a format suitable for you

Duova® 1mg/2.5mg Tablets

Ref: 1000/020525/2/F

(estradiol valerate / medroxyprogesterone acetate)

Patient Information Leaflet

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, 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.

Your medicine is called Duova 1mg/2.5mg Tablets, but will be referred to as Duova throughout this leaflet. *Please note that this leaflet also contains information about other strengths of this medicine.*

What is in this leaflet

1 What Duova is and what it is used for
2 What you need to know before you take Duova
3 How to take Duova
4 Possible side effects
5 How to store Duova
6 Contents of the pack and other information

1 What Duova is and what it is used for

Duova is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an oestrogen and progestogen. Duova is used in menopausal women with at least three years since their last natural period. Duova 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"). Duova alleviates these symptoms after menopause. You will only be prescribed Duova 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 Duova to prevent osteoporosis after menopause.

2 What you need to know before you take Duova

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

Do not take Duova
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 Duova.
Do not take Duova
* 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 valerate** or **medroxyprogesterone 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 Indivina, stop using it at once and consult your doctor immediately.

Warnings and precautions
Talk to your doctor before starting the treatment if you have ever had any of the following problems, as these may return or become worse during treatment with Duova. 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
* hereditary and acquired angioedema.

Stop taking Duova 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 Duova" 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: Duova 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 Duova protects you from this extra risk.

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

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 1 000 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 1 000 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 1 000 users (i.e. an extra 4 to 8 cases).
Women aged 50 to 59 who are not taking HRT, on average, 27 in 1 000 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 1 000 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 1 000 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 2 000 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 2 000 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 taking Duova 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 1,000 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 1 000 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 a 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 1 000 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 1 000 users, over 5 years (i.e. an extra 3 cases).
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.
* If you are taking thyroid hormone replacement therapy (e.g. thyroxine), your doctor may monitor your thyroid function more often when you start treatment.

If you have or have had cholasma (yellowish-brown pigmentation patches on the skin, particularly of the face); if so, minimize your exposure to the sun or ultraviolet radiation whilst using Duova.

Duova® 1mg/2.5mg Tablets

Ref: 1000/020525/2/B

(estradiol valerate / medroxyprogesterone acetate)

Patient Information Leaflet (continued)

Other medicines and Duova
Some medicines may interfere with the effect of Duova. This might lead to irregular bleeding. This applies to the following medicines:
* Medicines for **epilepsy** (such as phenobarbital, phenytoin and carbamazepin)
* Medicines for **tuberculosis** (such as rifampicin, rifabutin)
* Medicines for **HIV infection** (such as nevirapine, efavirenz, ritonavir 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. Duova contains estradiol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Duova 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 Duova, because this medicine can affect the results of some tests.

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

Driving and using machines
Duova has no influence on your ability to drive or use machines.

Duova contains lactose
This medicine contains 78.9 mg (1 mg/2.5 mg tablet), 76.5 mg (1 mg/5 mg tablet) or 75.5 mg (2 mg/5 mg tablet) lactose (as monohydrate). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3 How to take Duova

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. 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.
Take one Duova tablet every day, preferably at about the same time each day. Calendar days are printed on the blister sheet to help you follow your daily tablet intake. Swallow the tablet whole with a drink. You will normally start on the lowest dose of Duova and this will be increased, if necessary. Your doctor should aim to prescribe the lowest dose for the shortest time that gives you relief from your symptoms. Talk to your doctor if your symptoms are not better after three months. If you feel that the effect of Duova is too strong or too weak, do not change the dose or stop taking the tablets yourself, but ask your doctor for advice.
If you are not having periods and you have not previously taken HRT or you are changing from another continuous combined HRT product, treatment with Duova may be started on any day.
If you switch from a cyclic HRT regimen, start Duova treatment one week after taking the last tablet of the cyclic HRT. Talk to your doctor or pharmacist if you are unsure.
Whilst taking this medicine
When you first start taking Duova you may get some bleeding at odd times for a few months (Please also refer to the section above on Endometrial cancer). However, if this is still happening after a few months or if you experience heavy bleeding tell your doctor.

If you take more Duova than you should
If you or somebody else has taken too many Duova tablets, talk to your doctor or pharmacist. An overdose of Duova could make you feel sick, or make you get a headache or uterine bleeding.
If you forget to take Duova
It is best to take the tablet at the same time each day. Do not take a double dose to make up for a forgotten tablet. You should then continue by taking the next tablet at your usual time. Missing a tablet or irregular use of Duova tablets may cause breakthrough bleeding or spotting.
If you stop taking Duova
If you want to stop taking Duova, talk to your doctor first. He/she will explain the effects of stopping treatment and discuss other possibilities with you.
If you need to have surgery
If you are going to have surgery, tell the surgeon that you are taking Duova. You may need to stop using Duova 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 Duova again.
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, particularly early on (in the first few months of treatment), for example irregular bleeding may occur, although not everybody gets them. These often disappear with continued treatment.
There are a number of situations in which you may have to **stop taking Duova.** Tell your doctor immediately if you develop any of the following conditions:
* develop signs of jaundice (yellowing of the skin or the whites of the eyes)
* experience a migraine type headache for the first time
* become pregnant
* experience a significant increase in your blood pressure

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 is a list of side effects that have been linked to the use of HRT:

Common side effects (may affect up to 1 in 10 people):
* weight increase or decrease, swelling caused by fluid retention
* depression, nervousness, lack of energy
* headache, dizziness
* hot flushes, increased sweating
* feeling sick, vomiting, stomach cramps, gas
* breast tension and pain, vaginal discharge, bleeding or spotting, disorder of vulva/vagina, menstrual disorder.

Uncommon side effects (may affect up to 1 in 100 people):
* benign breast tumor, benign growths in the lining of the womb
* allergic (hypersensitivity) reaction
* increased appetite, high level of cholesterol in the blood
* anxiety, inability to sleep, apathy, mood swings, poor concentration, changes in sex drive or mood, euphoria, agitation
* migraine, sensation of tingling, prickling or numbness in skin, trembling
* visual impairment, dry eye
* feeling your heartbeat
* increased blood pressure, inflammation of a vein, purple patches like bruising
* breathlessness, runny or blocked nose
* constipation, indigestion/heartburn, diarrhea, rectal disorder
* acne, hair loss, dry skin, nail problems, skin nodule, excessive hair growth (hirsutism), painful reddish skin nodules (erythema nodosum), generalized itchy rash
* joint disorders, muscle cramps
* increased frequency or urge to pass urine, lack of bladder control, bladder infections, discoloured urine, blood in the urine
* breast enlargement, breast tenderness, thickening of the lining of the womb, uterine disorder
* tiredness, abnormal laboratory tests, weakness, fever, flu-like symptoms, feeling generally unwell.

Rare side effects (may affect up to 1 in 1 000 people):
* contact lens intolerance
* alterations in liver function and biliary flow
* skin rash
* blood clot, usually in a leg or lung, which causes pain, swelling or redness
* menstrual pain, pre-menstrual like syndrome

Frequency not known side effects (frequency cannot be estimated from the available data)
* tumours in uterus
* worsening of the symptoms of angioedema (hereditary and acquired)
* reduced blood supply to the brain or to a section of the brain
* stomach pain, bloating, yellowing of the skin or eyes
* eczema

The following side effects have been reported with other HRTs:
* heart disease (heart attack)
* gall bladder disease
* inflammation of pancreas (pancreatitis)
* skin disorders:
  - yellowish-brown pigmentation patches on the skin, particularly of the face (chloasma)
  - rash with target-shaped reddening or sores (erythema multiforme).
* Probable memory loss over the age of 65

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 the Yellow Card Scheme at: www.mhra.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 Duova

* Do not store above 25ºC.
* Store in the original package in order to protect from moisture.
* KEEP THIS MEDICINE OUT OF THE SIGHT AND REACH OF CHILDREN.
* Do not use this medicine after the expiry date shown on the carton label or blister strip. Only keep this medicine if your doctor tells you to. If your tablets become discoloured or show any any other signs of deterioration, consult your pharmacist (chemist) who will tell you what to do.
* Medicines should not be disposed 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 Contents of the pack and other information

What Duova contains:
Duova 1mg/2.5mg tablets contain 1mg estradiol valerate and 2.5mg medroxyprogesterone acetate.
The tablets also contain lactose monohydrate, maize starch, gelatine, magnesium stearate

What Duova looks like and contents of the pack
Duova 1mg/2.5mg tablets are white, round, flat tablets embossed with "1 + 2.5" on one side and plain on the other.
Each pack contains either 1 x 28 tablets or 3 x 28 tablets.

Manufacturer and Licence Holder
This medicine is manufactured by Delpharm Lille Sas Lys Lez Lannoy, Parc D Activites Roubaix-Est, 22 Rue De Toufflers, CS 50070 59452 Lys Lez Lannoy, France and is procured from within the EU and repackaged by the Product Licence Holder: Lexon (UK) Limited, Unit 18, Oxleasow Road, East Moons Moat, Redditch, Worcestershire, B98 0RE.

If you have any questions or are not sure about anything, ask your doctor or pharmacist. They will have additional information about this medicine and will be able to advise you.

POM PL 15184/1000 Duova 1mg/2.5mg Tablets

Revision date: 02/05/25

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