Package leaflet: Information for the patient

DUAVIVE 0.45 mg/20 mg modified-release tablets
conjugated oestrogens/bazedoxifene

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.

What is in this leaflet

1. What DUAVIVE is and what it is used for

DUAVIVE is a medicine that contains two active substances called conjugated oestrogens and bazedoxifene. Conjugated oestrogens is a medicine that belongs to a group of medicines called hormone replacement therapy (HRT). Bazedoxifene belongs to a group of non-hormonal medicines called selective oestrogen receptor modulators (SERMs).

DUAVIVE is used in postmenopausal women who still have their uterus (womb) and have not had a natural period in the last 12 months.

DUAVIVE 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"). DUAVIVE alleviates these symptoms after menopause. You will only be prescribed this medicine if your symptoms seriously hinder your daily life and your doctor determines that other types of HRT are not appropriate for you.

2. What you need to know before you take DUAVIVE

Medical history and regular check-ups

The use of DUAVIVE carries risks, which need to be considered when deciding whether to start taking it, or whether to carry on taking it.

There is no experience in treating women with a premature menopause (due to ovarian failure or surgery) with DUAVIVE.

Before you start taking this medicine, your doctor will ask you 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, or if you have any special concerns. Tell your doctor if you have any medical problems or illnesses.

Once you have started this medicine you should see your doctor for regular check-ups (at least once a year). During these check-ups, discuss with your doctor the benefits and risks of continuing with DUAVIVE. You are advised to:

- go for regular breast screening and cervical smear tests, as recommended by your doctor.
- regularly check your breasts for any changes such as dimpling of the skin, changes in the nipple, or any lumps you can see or feel.

Do not take DUAVIVE

- If you are allergic to conjugated oestrogens, bazedoxifene or any of the other ingredients of this medicine (listed in section 6).
- If you have or have ever had breast cancer, or if you are suspected of having it.
- If you have or have had 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 recently had 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), the lungs (pulmonary embolism) or eyes (retinal vein thrombosis).
- 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 liver disease and your liver function tests have not returned to normal.
- If you are pregnant or could still become pregnant or you are breast-feeding.
- If you have a rare blood problem called porphyria, which is passed down in families (inherited).

If you are not sure about any of the points above, **talk to your doctor** before taking this medicine.
If any of the above conditions appear for the first time while taking this medicine, stop taking it at once and consult your doctor immediately.

Warnings and precautions

Talk to your doctor before taking this medicine if you have ever had any of the following problems, as these may return or become worse during treatment with DUAVIVE. 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 rare disease of the immune system that affects many organs of the body (systemic lupus erythematosus, SLE)
- seizures (epilepsy)

- asthma
- a disease affecting the eardrum and hearing (otosclerosis)
- a high level of fat in your blood (triglycerides)
- fluid retention due to cardiac or kidney problems

Stop taking DUAVIVE and see a doctor immediately

If you notice any of the following:
- any of the conditions mentioned under 'Do not take DUAVIVE'
- yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease
- a large increase in your blood pressure (symptoms may be headache, tiredness, dizziness)
- migraine-like headaches which happen for the first time
- if you become pregnant
- you notice signs of a blood clot, such as painful swelling and redness of the legs, sudden chest pain, or difficulty in breathing. For more information, see 'Blood clots in a vein (thrombosis)'

DUAVIVE and cancer

Excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)
This medicine contains conjugated oestrogens and bazedoxifene and is used to treat women with a uterus (womb).

When you take DUAVIVE do not take additional oestrogens as this may increase the risk of endometrial hyperplasia.

If you have any unexpected vaginal bleeding, **you must contact your doctor as soon as possible**.

Breast cancer
Evidence shows that taking 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.

The effect of DUAVIVE on the risk of breast cancer is unknown.

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

Ovarian cancer
Ovarian cancer is rare - much rarer than breast cancer. The use of oestrogen-only 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). Talk to your doctor if you have any concerns.

The effect of DUAVIVE on the risk of ovarian cancer is unknown.

DUAVIVE and your heart or circulation

Blood clots in a vein (thrombosis)
DUAVIVE may increase the risk of blood clots.

Oestrogen-only and bazedoxifene monotherapy increase the risk of blood clots in the veins (also called deep vein thrombosis, or DVT), especially during the first year of taking these medicines.

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

Since 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 promptly:

- if 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)
- if you are seriously overweight (BMI >30 kg/m^2)
- if 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
- if you have systemic lupus erythematosus (SLE).
- if you have cancer.

If any of these conditions apply to you, talk to your doctor before you take this medicine.

Heart disease (heart attack)
There is no evidence that HRT will prevent a heart attack. Randomised controlled data found no increased risk of coronary artery disease in hysterectomised women using oestrogen-only therapy.

Stroke
The risk of having 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.

For 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., 3 extra cases).

The effect of DUAVIVE on the risk of stroke is unknown.

Other things that can increase the risk of stroke include:

- getting older
- high blood pressure
- smoking
- drinking too much alcohol
- an irregular heartbeat

If you are having an operation

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

In case of doubt, talk to your doctor before you take this medicine.

Other conditions

If you have any of the following your doctor should monitor you:

- kidney problems
- pre-existing high level of fat in your blood (triglycerides)
- liver problems
- asthma
- seizures (epilepsy)
- migraine
- systemic lupus erythematosus (SLE – a rare disease of the immune system that affects many organs of the body)
- fluid retention

Oestrogen therapy will not prevent memory loss. There is some evidence of a higher risk of memory loss in women who start using oestrogen therapy after the age of 65. Speak to your doctor for advice.

Children and adolescents

This medicine is not for use in children and adolescents below 18 years old.

Other medicines and DUAVIVE

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Some medicines may interfere with the effect of DUAVIVE. 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 and nelfinavir);
- Herbal remedies containing St John's Wort (Hypericum perforatum)

Pregnancy and breast-feeding

This medicine is for use only by postmenopausal women. Do not take this medicine if you are pregnant, or if you think you might be pregnant. Do not take this medicine if you are breast-feeding.

Driving and using machines

DUAVIVE has a minor effect on the ability to drive or use machines.

If you feel drowsy after taking this medicine, you should avoid driving or operating machines.

The bazedoxifene component of this medicine has been reported to cause problems with eyesight such as blurred vision. If this happens, you should avoid driving or operating machines until your doctor tells you that it is safe to do so.

DUAVIVE contains lactose, sucrose, maltitol liquid, glucose and sorbitol

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before using this medicinal product.
This medicine contains 0.0088 mg sorbitol in each tablet.

3. How to take DUAVIVE

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.

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

The recommended dose is one tablet once daily.
Swallow the tablet whole with a glass of water.

You can take the tablet at any time of the day, with or without food; however, it is advisable to take your tablet at the same time each day as this will help to remind you to take your medicine.

You should continue taking this medicine for as long as your doctor tells you. In order for this medicine to work, it should be taken daily as prescribed.

If you take more DUAVIVE than you should

Call your doctor or pharmacist.
If you take too many tablets you may have nausea (feel sick) or vomit. You may experience breast tenderness, dizziness, abdominal pain, drowsiness/fatigue or experience a short period of vaginal bleeding.

If you forget to take DUAVIVE

If you forget to take a tablet, take it as soon as you remember. However, if it is almost time to take your next tablet, skip the tablet you missed and only take your next scheduled tablet. Do not take a double dose to make up for a forgotten tablet.

If you stop taking DUAVIVE

If you decide to stop taking this medicine before finishing the prescribed course of treatment, you should talk to your doctor first.

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.

Stop taking DUAVIVE and see a doctor immediately if you get any of the following serious side effects:

Uncommon: may affect 1 in 100 people
- If you begin to get migraine-like headaches, or severe headaches

Rare: may affect up to 1 in 1,000 people
- Signs of a blood clot, such as painful swelling and redness of the legs, sudden chest pain or difficulty in breathing
- Signs of a blood clot in the eye (retinal vein), such as one sided visual disturbance including loss of vision, pain and swelling of the eye especially if sudden
- A severe allergic reaction - symptoms may include sudden wheezing and chest pain or tightness, swelling of the eyelids, face, lips, mouth, tongue or throat, difficulty breathing, collapse
- Swelling of the eyes, nose, lips, mouth, tongue or throat, difficulty in breathing, severe dizziness or fainting, skin rash (symptoms of angioedema)
- Symptoms of pancreatitis which may include severe upper abdominal pain which may spread to your back, accompanied by abdominal swelling, fever, nausea and vomiting
- Abrupt onset of abdominal pain and passage of bright red blood in the stool, with or without diarrhoea due to sudden blockage of an artery supplying the intestines (ischaemic colitis)

- A heart attack - symptoms will usually include pain, including chest pain spreading to the jaw, neck and upper arm. You may feel sweaty, breathless, fatigued, nauseous and faint in addition to the pain

Very rare: may affect up to 1 in 10,000 people
- A large rise in your blood pressure (symptoms may be headache, tiredness, dizziness)
- Erythema multiforme: symptoms may include skin rash with pink-red blotches especially on palms of hands or soles of feet which may blister. You may also have ulcers in the mouth, eyes or genitals and have a fever

Not known: frequency cannot be estimated from the available data
- Other ocular reactions (seeing sparks or flashes of light, narrowing of visual field, and swelling of eye or eye lid)

Other side effects

Very common: may affect more than 1 in 10 people
- Abdominal pain (stomach ache)

Common: may affect 1 in 10 people
- Muscle spasms (including leg cramps)
- Constipation
- Diarrhoea
- Nausea
- Thrush (vaginal yeast infection)
- Increases in your triglyceride levels (fatty substances in the blood)

Uncommon: may affect 1 in 100 people
- Gall bladder disease (e.g. gallstones, inflammation of the gall bladder (cholecystitis))

The following side effects have been observed when either conjugated oestrogens and/or bazedoxifene (the active ingredients in this medicine) has been used alone and may occur also with this medicine:

Very common: may affect more than 1 in 10 people
- Hot flushes
- Muscle cramps
- Visible swelling of the face, hands, legs, feet or ankles (peripheral oedema)

Common: may affect 1 in 10 people
- Breast pain, breast tenderness, swollen breasts
- Discharge from the nipples
- Joint pain
- Alopecia (hair loss)
- Changes in weight (increase or decrease)
- Increases in liver enzymes (identified in routine liver function testing)
- Dry mouth
- Drowsiness
- Hives (urticaria)
- Rash
- Itching

Uncommon: may affect up to 1 in 100 people

- Vaginal inflammation
- Vaginal discharge
- Cervical erosion found on medical examination
- Blood clot in the leg veins
- Blood clot in the lungs
- Blood clot in a vein at the back of the eye (retinal vein) which may lead to loss of vision
- Nausea (feeling sick)
- Headache
- Migraine
- Dizziness
- Changes in mood
- Feeling nervous
- Depression
- Memory loss (dementia)
- Changes in your interest in sex (increased or decreased libido)
- Discolouration of the skin on the face or other parts of the body
- Increase in hair growth
- Difficulty wearing contact lenses

Rare: may affect up to 1 in 1,000 people

- Pelvic pain
- Changes in breast tissue
- Vomiting
- Feeling irritable
- An effect on the way in which your blood sugar (glucose) levels are controlled including increased glucose levels in the blood
- A worsening of asthma
- A worsening of epilepsy (seizures)
- Growth of benign meningioma, a non-cancerous tumour of the membranes around the brain or spinal cord

Very rare: may affect up to 1 in 10,000 people

- Painful red bumps on the skin
- A worsening of chorea (an existing neurological disorder characterised by involuntary spasmodic movements of the body)
- Enlargement of hepatic haemangiomas, a benign (non-cancerous) tumour of the liver
- Low levels of blood calcium (hypocalcaemia); frequently there will be no symptoms to suggest that your blood calcium is low, but when hypocalcaemia is severe you may feel tired, generally unwell, depressed and become dehydrated. This may be accompanied by bone pain and abdominal pain. Kidney stones may develop and cause severe pain in the mid-back region (renal colic).
- Worsening of porphyria, a rare blood disorder which is passed down in families (inherited).

Not known: frequency cannot be estimated from the available data

- Palpitations (awareness of your heart beat)
- Dry eye, eye pain, visual acuity reduced, visual impairment, blepharospasm (abnormal, involuntary blinking or spasm of the eyelids)

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 DUAVIVE

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

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

Do not store above 25°C.

Store in the original package in order to protect from moisture.

After opening the blister pouch, use within 60 days.

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

6. Contents of the pack and other information

What DUAVIVE contains

The active substances are conjugated oestrogens and bazedoxifene. Each tablet contains 0.45 mg of conjugated oestrogens and bazedoxifene acetate equivalent to 20 mg bazedoxifene.

The other ingredients are: lactose monohydrate, sucrose, sucrose monopalmitate, polydextrose (E1200, containing glucose and sorbitol) and maltitol liquid (see section 2), microcrystalline cellulose, powdered cellulose, hydroxypropylcellulose, hydroxyethylcellulose, magnesium stearate, ascorbic acid, hypromellose (E464), povidone (E1201), poloxamer 188, calcium phosphate, titanium dioxide (E171), macrogol (400), red iron oxide (E172), black iron oxide (E172) and propylene glycol (E1520).

What DUAVIVE looks like and contents of the pack

The DUAVIVE 0.45 mg/20 mg modified-release tablet is a pink, oval-shaped, tablet marked on one side with “0.45/20”.

The modified-release tablets are provided in PVC/Aclar/PVC blister packs containing 28 tablets.

Marketing Authorisation Holder

Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium.

Manufacturer

Pfizer Ireland Pharmaceuticals, Little Connell, Newbridge, County Kildare, Ireland.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
Pfizer Limited,
Tel: +44 (0) 1304 616161

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

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