Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Duavive®
Modified release tablets

Each tablet contains:
0.45 mg conjugated estrogens
20 mg bazedoxifene acetate (equivalent to 20 mg bazedoxifene)

Inactive ingredients and allergens: See section 2 under "Important information about some of this medicine's ingredients" and section 6 "Further information".

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

The medicine is intended for menopausal and postmenopausal women.

Important information you should know about Duavive®:

- Do not take additional estrogen containing products while you are taking Duavive®.
- Using estrogens may increase your chance of developing cancer of the uterus.
- Report any unusual vaginal bleeding right away while you are taking Duavive®. Vaginal bleeding after menopause may be a warning sign of cancer of the uterus. Your doctor should check any unusual vaginal bleeding to find out its cause.
- Do not use estrogen to prevent heart disease, heart attacks, strokes or dementia (decline in brain function).
- Using estrogens may increase your chances of getting a stroke or blood clots.
- Based on a study conducted in women 65 years of age or older, using estrogens may increase your chance of developing dementia.
- Duavive® should be taken for the shortest possible period and only for as long as treatment is needed. You and your doctor should talk regularly about whether you still need treatment with Duavive®.

1. WHAT IS THIS MEDICINE INTENDED FOR?

For women with a uterus for the following conditions:

- Treatment of moderate to severe menopausal symptoms.
- Prevention of postmenopausal osteoporosis.

Therapeutic group: tissue selective estrogen complex.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- **You currently have or have had blood clots (for example, stroke, heart attack and pulmonary embolism).**

- **You are sensitive (allergic) to the active ingredients or to any of the additional ingredients contained in the medicine.** See the list of inactive ingredients in section 6 of this leaflet.
- **You have unusual vaginal bleeding.** Vaginal bleeding after menopause may be a warning sign of cancer of the uterus. Your doctor should check any unusual vaginal bleeding to find out its cause.
- **You have cancer or have a history of any types of cancer.** Using estrogens may increase the chances of developing various types of cancers, including cancer of the breast or uterus. If you have or have had cancer, consult your doctor about whether you should use Duavive®.
- **You currently have or have had liver problems.**
- **You have been diagnosed with a blood clotting disorder (such as protein C, protein S or antithrombin deficiency).**
- **You are pregnant.**

Special warnings regarding use of the medicine
Before treatment with Duavive®, tell your doctor if:

- **You have unusual vaginal bleeding.** Vaginal bleeding after menopause may be a warning sign of cancer of the uterus. Your doctor should check any unusual vaginal bleeding to find out its cause.
- **You have any other medical condition**. Your doctor may need to check you more carefully if you have certain conditions, such as asthma (wheezing), epilepsy (seizures), diabetes, migraine, endometriosis, lupus, or problems with your heart, liver, thyroid, kidney function, or if you have high blood calcium levels.
- **You are planning to undergo surgery or to be on extended bed rest.** Your doctor will let you know if you need to stop taking Duavive®.

Drug interactions
If you are taking or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.
It is especially important to inform the doctor or pharmacist if you are taking other hormonal medicines, including progestins or other medicines similar to Duavive®. Ask your doctor if you do not know whether you are taking these medicines.

Certain medicines may affect how Duavive® works in the body, and Duavive® may affect how other medicines such as itraconazole, Hypericum (St. John's wort), phenobarbital, carbamazepine, phenytoin, rifampin, work in the body.

Keep an orderly list of all the medicines that you are taking and inform your doctor and pharmacist of every new medicine that is prescribed for you.

Using this medicine and food
Duavive® may be taken with or without food.

Pregnancy, breastfeeding and fertility
Duavive® is not intended for use in women of childbearing age.
Do not take Duavive® if you are pregnant or think that you are pregnant.
If you think that you may be pregnant, you should perform a pregnancy test and await the result. If the test is positive, do not take Duavive® and contact your doctor.
Do not take Duavive® while breastfeeding.

Important information about some of the ingredients of the medicine
Duavive® contains lactose, sucrose, polydextrose and maltitol
This medicine contains lactose (as monohydrate), sucrose, glucose (in polydextrose and maltitol) and sorbitol (in polydextrose) (types of sugars). If you have been told by your doctor that you have intolerance to certain sugars, contact your doctor before taking this medicine.

Duavive® can cause glucose intolerance.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.
The dosage and treatment regimen will be determined by your doctor only.

The usual dose is generally one tablet at the same time each day.

Do not exceed the recommended dose.

- The tablet should be swallowed whole. Do not crush/halve/chew as it is a modified release tablet.

- Take the medicine with or without food.

- You should remove the tablet from the blister right before you take it. Remove only one tablet at a time. Do not store the tablets in a pill box.

- If you are taking calcium or vitamin D, you may take them at the same time that you take Duavive®.

If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.
Signs of an overdose include nausea, vomiting, breast tenderness, dizziness, abdominal pain, feeling tired and vaginal bleeding.

If you forgot to take this medicine at the scheduled time, take a dose as soon as you remember, but never take a double dose. If it is almost time for your next dose, skip the forgotten dose. Take the next dose at the regular time and consult your doctor.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take a medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Duavive® may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Side effects are grouped by the level of their severity and frequency.
Serious side effects include:

- blood clots
- stroke
- heart attack
- endometrial cancer
- breast cancer
- ovarian cancer
- dementia
- gallbladder problems
- loss of vision
- high blood pressure
- increased fat levels in the blood
- liver problems
- thyroid problems
- fluid retention
- low calcium levels
- swelling of the mouth or tongue
- worsening of other medical problems such as asthma, diabetes, epilepsy, migraines, porphyria (a genetic problem), lupus and liver problems.

Contact the doctor immediately if you experience any of the following symptoms:

- appearance of new breast lumps
- unusual vaginal bleeding
- changes in vision or speech
- sudden new severe headaches
- severe pain in the chest or legs with or without shortness of breath, weakness and fatigue

Less serious, but common side effects include:

- muscle spasms
- nausea
- diarrhea
- upset stomach
- abdominal pain
- throat pain
- dizziness
- neck pain

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This and any other medicine should be kept in a closed place, out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- Do not store above 25°C, store in the original package to protect from moisture. Use within 60 days after opening the pouch containing the blister.

6. FURTHER INFORMATION

In addition to the active ingredients, this medicine also contains:
Sucrose, hypromellose, lactose monohydrate, microcrystalline cellulose, hydroxypropyl cellulose, calcium phosphate tribasic**,** macrogol 400, ascorbic acid, sucrose palmitic acid ester, magnesium stearate, titanium dioxide (E171), red iron oxide (E172), hydroxyethylcellulose, povidone (E1201), polydextrose, maltitol liquid, poloxamer 188, black iron oxide (E172), isopropyl alcohol and propylene glycol (E1520).

What the medicine looks like and contents of the pack:
A carton package containing a single blister of 28 tablets within a pouch. The tablet is an oval, convex, film coated pink tablet, imprinted with “0.45/20” in black ink on one side.

Registration holder's name and address: Pfizer PFE Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

Manufacturer’s name and address: Pfizer Ireland Pharmaceuticals, Newbridge, Ireland.

Registration number of the medicine in the Ministry of Health’s National Drug Registry: 157-37-34551.

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