Patient package insert in accordance with the pharmacists' regulations (preparations) – 1986

The medicine is dispensed by a doctor's prescription only

EVISTA

Film coated tablets

Active ingredient and quantity:
Each film coated tablet contains:
Raloxifene HCl 60 mg.

For the list of inactive ingredients and allergens, please see section “important information about some of the ingredients of this medicine” in chapter 2 and chapter 6 "Additional information".

Please read this package insert carefully in its entirety before using this medicine. This package insert contains concise information on the medicine. If you have any further questions, please ask your doctor or pharmacist.

This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them even if their condition seems similar to yours.

1. WHAT IS THE MEDICINE INTENDED FOR?

Evista is used for the treatment and prevention of osteoporosis in postmenopausal women.
Evista is used for the prevention of osteoporosis in postmenopausal women when estrogen therapy is considered unsuitable.

Prevention of breast cancer - **Evista** reduces the risk of invasive breast cancer in postmenopausal women with osteoporosis and in postmenopausal women at high risk for invasive breast cancer.

Therapeutic group:
Evista belongs to the non-hormonal drug group known as Selective Estrogen Receptor Modulators (SERMs). When a woman reaches menopause, the level of the sex hormone estrogen decreases. **Evista** simulates some of the supporting effects of estrogen at the postmenopausal stage.

Osteoporosis is a disease which causes a decrease in bone mass and increases the bones’ tendency to fracture - this disease is especially common in postmenopausal women, although it is possible that initially no symptoms will appear. Osteoporosis increases the risk of bone fractures, especially those of the spinal column, hips and wrists, and may cause back pain, loss of height and a curved back.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- you are receiving or have received in the past treatment for blood clots in the legs (deep vein thrombosis), in the lungs (pulmonary embolism), or in the eyes (retinal vein thrombosis).
- you suffer or have suffered in the past from blood clots in the veins, including blood clots in the eyes, deep veins in the legs or lungs.
- you are sensitive (allergic) to the active ingredient or to any of the other ingredients this medicine contains (see chapter 6 *"Additional information"*). Signs of an allergic reaction

include: rash, difficulties swallowing or breathing, swelling of the lips, face, throat or tongue.
- you are pregnant or can still become pregnant, since **Evista** may harm your fetus.
- you are breastfeeding.
- you are likely to be immobile for a prolonged period of time.

Special warnings regarding the use of this medicine

Before starting treatment with Evista, tell your doctor if:

- you had blood clots in your legs, lungs or eyes; stroke; mini-stroke (transient ischemic attack); irregular heartbeats, hypertension or if you are smoking.
- you are likely to be immobile for an extended period of time as this can increase the risk of blood clots forming.
- you have difficulty moving for a while, such as if you are restricted to a wheel chair, if you need to be hospitalized, or if you have to lie in bed for recovery after surgery or an unexpected illness, as these might increase the risk of developing blood clots (deep vein thrombosis in the legs, pulmonary embolism, or retinal vein embolism), so it is important on long journeys/flights to get up and move around once in a while.
  Stop taking **Evista** at least 3 days (72 hours) prior to expected prolonged immobilization.
  Treatment with **Evista** should be resumed only after you are back on your feet and fully mobile again.
- you had a cerebrovascular accident (such as a stroke), or if your doctor told you that you are at high risk of experiencing a cerebrovascular accident.
- you suffer or have suffered in the past from impaired function of the heart and/or blood vessels. If you suffer or have suffered in the past from congestive heart failure, irregular heartbeat, heart attack, or other illnesses that increase the risk for a heart attack. You must consult your doctor about the possible risks versus the benefits of the medicine.
- you suffer from a liver disease.
- you suffer or have suffered in the past from impaired function of the kidney or active cancer.
- there is a history of blood clots in your immediate family.
- you suffered in the past from breast cancer, because there is not enough experience regarding the use of **Evista** in women who suffer from this disease.
- you have or have had estrogen treatment in the past and had a high increase in triglycerides (a type of blood fat).
- you are sensitive to any food or medicine, you must inform your doctor before taking this medicine.

Additional warnings

- It is unlikely for **Evista** to cause vaginal bleeding. Therefore, any vaginal bleeding while taking **Evista** is not to be expected, and in such an event you must contact your doctor for a checkup.

- **Evista** does not cause sensitivity or enlargement of the breasts, so in any case of a change in the breast, consult a doctor. Also, do not stop the routine follow-up recommended by the doctor. Before and during treatment, you should have mammograms as directed by your doctor.

- Stop treatment and consult the doctor:
  - If there is pain in the legs or a feeling of heat in the calves
  - If there is swelling of the legs, arms or feet
  - If there is a sudden chest pain, shortness of breath or bloody cough
  - If there is a sudden change in vision such as vision loss or blurred vision

Tell your doctor if any of these symptoms occur as it may cause blood clots in your legs, eyes or lungs.

Drug interactions

If you are taking or have recently taken any other medicine, including over-the-counter medicines and nutritional supplements, inform your doctor or pharmacist. The doctor or pharmacist must be informed in particular if you are taking:

- Anticoagulants, such as coumadin preparations (warfarin) or warfarin derivatives for the thinning of your blood; your doctor may need to adjust the dosage of these medications.
- Combined treatment of **Evista** with other systemic estrogens is not recommended.
- High protein-bound drugs (e.g.: diazepam, diazoxide, lidocaine). Concomitant use of one of these medicines with **Evista** may alter the concentration of these medicines in the blood.
- Combined treatment of **Evista** with cholestyramine. Medications that are mainly used to lower the level of lipids in the blood are not recommended, since they affect the absorption of **Evista** from the gastrointestinal tract and thus reduce the concentration of the medicine in the blood.

Use of this medicine and food
You may take **Evista** with or without food.

Pregnancy and breastfeeding
Evista is intended for use only by postmenopausal women and is not for women who can still become pregnant. **Evista** may harm your fetus, do not use it during pregnancy.
Do not take **Evista** if you are breastfeeding. It is not known whether **Evista** enters the breast milk or whether it may affect the baby or milk production.

Driving and operating machinery
Evista does not affect or has negligible effect on driving and operating machinery.

Important information regarding some of the ingredients of the medicine
Evista contains lactose.
If your doctor told you that you are sensitive to lactose, a type of sugar, see your doctor before taking this medicine.

3. HOW TO USE THIS MEDICINE?

Always use according to the doctor's instructions.
You must check with your doctor or pharmacist if you are unsure. You must check with your doctor or pharmacist if you are not sure about the dosage and manner of treatment with this medicine.
The dosage and manner of treatment will only be determined by the doctor.
The dosage is one tablet daily. It does not matter what time you take the tablet, but taking it at the same time each day will help you remember to take it. It can be taken with or without food.

Do not exceed the recommended dose.

The tablet is intended to be taken orally.
Swallow the tablet whole. You can drink a glass of water with it if you want. Do not break or crush the tablet before taking it. The taste of a broken or crushed tablet may be unpleasant, and you may get the wrong dosage.

Your doctor may recommend other ways to prevent osteoporosis such as taking supplemental calcium or vitamin D tablets (in case their daily nutritional intake is insufficient).

If you accidentally took a higher dose
If you are taking a higher dosage of **Evista** than prescribed, you may experience muscle cramps in the legs and dizziness. If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a hospital Emergency Room and bring the package of the medicine with you.

If you forgot to take Evista
If you forgot to take **Evista** at the specified time, take the medicine as soon as you remember. If it is close to the time of taking the next dose, skip the dose and take the next dose at the usual time. Do not take a double dose.
Treatment should be continued as recommended by the doctor.

If you stop taking Evista
Even if there is an improvement in your health condition, do not discontinue treatment with this medicine without consulting your doctor or pharmacist.
It is important that you continue to take **Evista** for the entire period that your doctor has prescribed this medicine for you.

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

4. <u>SIDE EFFECTS</u>

As with any medicine, the use of **Evista** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Side effects from clinical trials:
The most serious side effect observed during clinical trials in **Evista** is blood clots in the veins (blood clots in the deep veins of the legs, blood clots in the lungs and blood clots in the veins of the retina in the eyes). During an average exposure of 2.6 years of **Evista** treatment study, venous blood clots appeared in 1 in 100 **Evista** patients.

Side effects observed in placebo-controlled clinical trials in osteoporosis at an incidence of ≥ 2% and most women treated with Evista (60 mg once daily) compared with women treated with placebo.

Side effects observed in clinical trials for the treatment of osteoporosis:
Very common: flu-like syndrome, joint pain, runny nose.
Common: headache, leg cramps, fever, hot flashes, fainting, varicose veins, nausea, diarrhea, vomiting, peripheral edema, tendon disorder, vertigo, nerve pain, high sensitivity to skin contact, sinusitis, bronchitis, throat inflammation, Increased cough, sweating, conjunctivitis, cystitis, vaginal bleeding.

Side effects observed in clinical trials to prevent osteoporosis:
Very common: flu-like syndrome, hot flashes, joint pain, sinusitis.
Common: leg cramps, chest pain, fever, migraine, nausea, indigestion, vomiting, flatulence, indigestion, gastritis, weight gain, peripheral edema, muscle aches, arthritis, depression, insomnia, throat inflammation, Increased cough, pneumonia, inflammation of the vocal cords, rash, sweating, vaginitis, urinary tract infection, cystitis, yellowish or white vaginal discharge.

Side effects observed in clinical trials to prevent osteoporosis with Evista 60 mg once daily and continuous or cyclic hormone therapy in combination with estrogen with progestin at a frequency of ≥ 2% per treatment group.

Evista group:

Very common: hot flashes, infection.
Common: breast pain, flatulence, abdominal pain, chest pain.

Combined and continuous hormone therapy group:

Very common: breast pain, flatulence, abdominal pain.
Common: hot flashes.

Cyclic hormonal therapy group:

Very common: breast pain, abdominal pain.
Common: flatulence, hot flashes, infection.

Very rare post-marketing side effects:

Side effects that have been observed very rarely include blockage of the retinal vein, stroke and death due to blood clots in the veins (venous thrombosis).

If any of the side effects gets worse, or if you are suffering from a side effect that has not been mentioned in this leaflet, consult a doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting side effects due to drug treatment" that appears on the home page of the Ministry of Health's website (www.health.gov.il), which refers to the online form for reporting side effects, or by entering the following link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

Avoid poisoning! This medicine and all other medicines must be stored in a secured place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiration date (exp. date) appearing on the package. The expiration date refers to the last day of that month.

Storage conditions: Store at a temperature below 25°C.

Store in the original package.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, the medicine also contains:

Anhydrous lactose, lactose monohydrate, crospovidone K30, povidone, color mixture white YS-1-18027-A, polysorbate 80, magnesium stearate, carnauba wax, edible blue ink.

Each tablet of **Evista** 60 mg contains 120 mg lactose anhydrous and 29.40 mg lactose (as monohydrate).

What does the medicine look like and what are the contents of the package:
Evista 60 mg is a white oval coated tablet, marked with the number 4165. **Evista** tablets are packaged in an aluminum blister. **Evista** tablets are supplied in packages of 14 or 28 tablets.

Manufacturer name and address: Lilly S.A., Alcobendas (Madrid), Spain.
License holder and address: Eli Lilly Israel Ltd.,4 HaSheizaf Street, P.O.B. 4246, Ra'anana 4366411

The drug registration number in the National Drug Registry in the Ministry of Health:
109-37-29234-05

This leaflet format was reviewed and approved by the Ministry of Health in December 2013 and was updated according to the Ministry of Health guidelines in March 2020.

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