PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) 1986

The medicine is marketed according to a doctor's prescription only

ORSERDU 86 mg

Film-coated tablets

ORSERDU 345 mg

Film-coated tablets

Active ingredients and their quantities in unit dose:

Each ORSERDU 86 mg film-coated tablet contains:
100 mg of elacestrant dihydrochloride, equivalent to approximately 86 mg elacestrant

Each ORSERDU 345 mg film-coated tablet contains:
400 mg of elacestrant dihydrochloride, equivalent to approximately 345 mg elacestrant

For the list of the inactive ingredients see section 6 “Further information”

Read the leaflet carefully in its entirety before using the medicine.

- This leaflet contains concise information about the medicine. If you have any further questions, refer to the 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.

  ORSERDU can harm unborn baby when taken by pregnant woman. Talk to your doctor before you take ORSERDU if you think you may be pregnant or are planning to have a baby.

1. WHAT IS THE MEDICINE INTENDED FOR?

ORSERDU is indicated for the treatment of postmenopausal women or adult men with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, ESR1-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy.

Your doctor will perform a test to make sure that ORSERDU is right for you.

Therapeutic group: Estrogen receptor antagonist

2. BEFORE USING THE MEDICINE

- Do not use the medicine if:

• you are sensitive (allergic) to the active ingredient (elacestrant dihydrochloride) or to any of the other ingredients contained in the medicine (see section 6 "further information").

Special warnings regarding use of the medicine

- ORSERDU may increase fat (lipid) levels in your blood (hypercholesterolemia and hypertriglyceridemia). Your doctor will do blood tests to check your lipid levels before and during your treatment with ORSERDU.

- ORSERDU may affect fertility in males and in females who are able to become pregnant. Talk to your doctor if this is a concern for you.

Before starting treatment with ORSERDU, tell your doctor if:

- you have liver problems

- you are pregnant, think you may be pregnant or are planning to have a baby. See section "Pregnancy, breast feeding and fertility" below.

- you are breastfeeding or plan to breastfeed. See section "Pregnancy, breast feeding and fertility" below.

Children and Adolescents
The safety and effectiveness of ORSERDU in children and adolescents under the age of 18 years old have not been established.

Tests and follow-up
Before starting treatment with ORSERDU**,** the doctor will do blood tests to check the ESR1 mutation.
Before starting treatment with ORSERDU and during it, the doctor will perform tests on your liver and lipid levels. The doctor may also do a pregnancy test.
During treatment with ORSERDU you may additionally be referred for blood tests.

Drug interactions/reactions

If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:
- antibiotics to treat bacterial infections (such as rifampicin)
- medicine for low blood sodium
- medicines to treat depression
- medicine to treat anxiety and alcohol withdrawal
- medicines for the treatment of other cancers
- medicines for high blood pressure or chest pain
- medicines for fungal infections (such as fluconazole, itraconazole)
- medicines for HIV infection (such as efavirenz)
- medicines to treat irregular heartbeats (such as digoxin)
- medicines used in organ transplantation to prevent rejection
- medicines to prevent cardiovascular events and to treat high levels of cholesterol (such as rosuvastatin)
- medicines used to prevent seizures
- medicines to treat vomiting
- medicines containing St. John’s wort used to treat depression

ORSERDU use and food
Do not drink grapefruit juice or eat grapefruit while on treatment with ORSERDU as it may change the amount of ORSERDU in your body and increase the side effects of ORSERDU (see Section 3 “how should you use the medicine”).

Pregnancy, breast feeding and fertility
If you are pregnant, planning a pregnancy, breastfeeding or planning to breastfeed, consult your doctor or pharmacist before using ORSERDU.

- Pregnancy
  ORSERDU may harm an unborn baby when taken by a pregnant woman. Talk to your doctor before taking ORSERDU if you think you are pregnant or are planning to become pregnant.
  Females who are able to become pregnant:
  - Your doctor may do a pregnancy test before you start treatment with ORSERDU.
  - You should use effective contraception during treatment with ORSERDU and for 1 week after the last dose. Ask your doctor for suitable birth control methods.
  - Tell your doctor right away if you become pregnant or think you may be pregnant during treatment with ORSERDU.

  Males with female partners who are able to become pregnant:
  - You should use effective (contraception) birth control during treatment with ORSERDU and for 1 week after the last dose.

- Breast-feeding

It is not known if ORSERDU passes into your breast milk. Do not breastfeed during treatment with ORSERDU and for 1 week after the last dose.

- Fertility

ORSERDU may impair fertility in women and men.

Driving and using machines
ORSERDU has no or negligible influence on the ability to drive and use machines. However, since fatigue, weakness, and difficulty sleeping have been reported in some patients taking elacestrant, caution should be observed by patients who experience those reactions when driving or operating machinery.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. You should check with the doctor or pharmacist if you are unsure regarding the dosage and treatment regimen.

The usual dose in general is:
The dosage and treatment regimen will be determined by the doctor only. The usual dosage is 345 mg (one 345 mg film-coated tablet) once daily. In certain situations (i.e. in case of liver problems, side effects, or if you are also using certain other medicines), your doctor may instruct you to take a lower dose of ORSERDU, e.g. 258 mg (3 tablets of 86 mg) once daily, or 172 mg (2 tablets of 86 mg) once daily. Your doctor will tell you exactly how many tablets to take.

Do not exceed the recommended dose.

Method of administration

Take ORSERDU 1 time each day, at about the same time each day. This will help you to remember to take your medicine.
Take ORSERDU with food. Taking ORSERDU with food may help reduce nausea and vomiting. You should avoid grapefruit and grapefruit juice during treatment with ORSERDU (see section 2 “ORSERDU use and food"). Swallow ORSERDU tablets whole. **Do not chew, crush or split** the tablets before swallowing.

Do not take any ORSERDU tablets that are broken, cracked, or that look damaged.

Crushing/halving/chewing
It is prohibited to crush/split/chew the tablets as it may alter ORSERDU absorption.

If you have accidentally taken a higher dose than you should
If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine
If you forget to take a dose of ORSERDU, take it as soon as you remember. You may still take a forgotten dose up to 6 hours after the time you should have taken it. If more than 6 hours have passed or if you vomit after taking the dose, skip the dose for that day and take the next dose at your usual time the next day. Do not take a double dose to make up for the one that you missed.

If you stop taking the medicine
Adhere to the treatment regimen as recommended by the doctor. Even if there is an improvement in your health, do not discontinue use of **ORSERDU** without consulting your doctor. **If you stop taking ORSERDU your condition may worsen**.

Do not take medicines in the dark! Check the label and dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding the use of the medicine, consult with a doctor or a pharmacist.

4. SIDE EFFECTS

As with any medicine, ORSERDU may cause side effects, in some users. Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

ORSERDU can cause serious side effects

Refer to the doctor as soon as possible if you develop any of the following signs:
- Increased fat (lipid) levels in your blood (hypercholesterolemia and hypertriglyceridemia). Your doctor will do blood tests to check your lipid levels before and during your treatment with ORSERDU.

Very common side effects - appear in 1 or more of every 10 people
- muscle and joint (musculoskeletal) pain

- nausea
- increased cholesterol and triglyceride levels in your blood
- increase in functional liver enzymes
- tiredness
- decreased red blood cell counts and hemoglobin
- vomiting
- decreased salt (sodium) levels in your blood
- increased kidney function test (for example, an increase in creatinine)
- decreased appetite
- diarrhea
- headache
- constipation
- abdominal pains
- hot flush
- indigestion or heartburn

Side effects that appear in less than 1 in 10 people:
- rash
- insomnia
- dyspnea
- cough
- dizziness
- stomatitis
- gastroesophageal reflux disease

If a side effect appears, if any of the side effects worsen or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

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

5. HOW TO STORE THE MEDICINE?

- Avoid Poisoning! This medicine and any other medicine must be kept in a safe and 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 appears on the package. The expiry date refers to the last day of that month.

Storage conditions: Store below 30°C up to the end of shelf life.

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

6. FURTHER INFORMATION

In addition to the active ingredients ORSERDU also contains:
microcrystalline cellulose, silicified microcrystalline cellulose, crospovidone, magnesium stearate (non-bovine), colloidal silicon dioxide, and Opadry II 85F105080 Blue.

What ORSERDU looks like and what are the contents of the package:

ORSERDU 86 mg film-coated tablets
Blue to light blue, unscored, round film-coated biconvex tablet, imprinted with “ME” on one side and plain on the other side.

ORSERDU 345 mg film-coated tablets
Blue to light blue, unscored, oval film-coated biconvex tablet, imprinted with “MH” on one side and plain on the other side.

ORSERDU is supplied in bottles of 30 Tablets

Registration holder and address:
Stemline Israel Ltd, 132 Begin Rd., 1 Azrieli Center, Tel Aviv

Manufacturer and address:
Stemline Therapeutics, Inc., NY, USA

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
ORSERDU 86 mg, 176-10-37711-99
ORSERDU 345 mg, 176-11-37712-99

Approved by MOH in April 2024