

PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Verzenio 50 mg

Film-coated tablets

Active ingredient and its quantity:

Each film-coated tablet contains:
abemaciclib 50 mg

Verzenio 100 mg

Film-coated tablets

Active ingredient and its quantity:

Each film-coated tablet contains:
abemaciclib 100 mg

Verzenio 150 mg

Film-coated tablets

Active ingredient and its quantity:

Each film-coated tablet contains:
abemaciclib 150 mg

Inactive ingredients and allergens in the preparation: see section 2 "Important information about some of the ingredients of this medicine" and section 6 "Additional information".

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, contact 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 it seems to you that their illness is similar.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Early Breast Cancer

- Verzenio in combination with endocrine therapy is indicated for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2) negative, node positive early breast cancer at high risk of recurrence.

In pre- or perimenopausal women, aromatase inhibitor endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.

Advanced or Metastatic Breast Cancer

- Verzenio, in combination with a non-steroidal aromatase inhibitor, is indicated as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.
- Verzenio, in combination with fulvestrant, is indicated for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.
- Verzenio, as monotherapy, is indicated for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy in the metastatic setting and prior chemotherapy in the metastatic setting including taxane in adjuvant or metastatic setting.

Verzenio should not be used in women after prior treatment with cyclin-dependent kinases 4 and 6 (CDK4 and CDK6) inhibitor.

When Verzenio is used in combination with fulvestrant, tamoxifen, or an aromatase inhibitor, also read the Patient Information for the prescribed product. Ask your healthcare provider if you are not sure.

Therapeutic group: cyclin-dependent kinase inhibitor.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient abemaciclib or any of the other ingredients that this medicine contains. For the list of inactive ingredients, see section 6.

Special warnings regarding the use of this medicine

Before taking Verzenio, tell your doctor about your medical condition, including if:

- You suffer from fever, chills or other signs of infection.
- You have previously suffered from blood clots in your veins.
- You suffer from lung or breathing problems.
- You suffer from liver or kidney problems.

Additional warnings:

- **Diarrhea.** Diarrhea is a common side effect, which may sometimes be severe. Diarrhea may cause you to develop dehydration or an infection. The most common time to develop diarrhea is during the first month of treatment with Verzenio. If you suffer from diarrhea during treatment with Verzenio, your doctor may tell you to temporarily stop taking Verzenio, stop the treatment or decrease the dosage.
- **Low white blood cell counts (neutropenia).** Low white blood cell counts (neutropenia) are common during treatment with Verzenio and may cause serious infections that can lead to death. Your doctor has to monitor white blood cell counts before and during treatment. If you develop low white blood cell counts during treatment with Verzenio, your doctor may tell you to temporarily stop taking Verzenio, decrease the dosage, or wait before you start the next month of treatment.
- **Lung problems.** Verzenio may cause serious or life-threatening inflammation of the lungs during treatment that can lead to death. If you develop lung problems during treatment with Verzenio, your doctor may tell you to temporarily stop taking Verzenio, decrease the dosage, or stop your treatment.
- **Liver problems.** Verzenio may cause serious liver problems. Your doctor should do blood tests to check your liver before and during treatment with Verzenio. If you develop liver problems during treatment with Verzenio, your doctor may decrease the dosage or stop your treatment.
- **Blood clots in your veins, or in the arteries of your lungs.** Verzenio may cause serious blood clots that may lead to death. If you develop blood clots during treatment with Verzenio, your doctor may tell you to temporarily stop taking Verzenio.

For additional information, see section 4 "Side effects".

Children and adolescents:

The safety and efficacy of this medicine in children are unknown.

Tests and follow up

- Your doctor must monitor your white blood cell counts prior to and during treatment.
- Your doctor must perform blood tests to monitor your liver function prior to and during treatment.
- If you are able to become pregnant, your doctor will perform a pregnancy test for you before you start treatment with Verzenio.

Drug Interactions

If you are taking or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, inform your doctor or pharmacist. Verzenio may affect the way other medicines work, and other medicines may affect how Verzenio works, causing serious side effects. Particularly tell your doctor if you are taking:

- CYP3A strong and moderate inhibitors: these medicines increase the exposure to Verzenio and may lead to excessive toxicity. Your doctor may monitor side effects and, if necessary, will reduce the dosage of Verzenio.
- Ketoconazole - avoid taking medicines that contains ketoconazole during treatment with Verzenio.
- Strong or moderate CYP3A enzyme inducers reduce the blood levels of Verzenio and may lead to reduced activity of Verzenio. Avoid taking strong or moderate CYP3A enzyme inducers during treatment with Verzenio.

Know the medicines you take. Keep a list of them to show your doctor or pharmacist when you get a new medicine.

Use of this medicine and food

Verzenio can be taken with or without food. Avoid grapefruit and products that contain grapefruit during treatment with Verzenio. Grapefruit may increase the amount of this medicine in the blood.

Pregnancy, breastfeeding and fertility

Consult your doctor prior to using the medicine if you are pregnant or planning a pregnancy, are breastfeeding or planning to breastfeed.

Verzenio may harm the fetus.

- **Pregnancy**

- **Females who are able to become pregnant:**

- A pregnancy test should be performed before starting treatment with Verzenio.
 - You should use effective birth control (contraceptives) during treatment with Verzenio and for 3 weeks after taking the last dose of Verzenio.
 - Tell your doctor right away if you become pregnant or think you are pregnant during treatment with Verzenio.

- **Breastfeeding**

- It is not known whether Verzenio passes into breast milk. Do not breastfeed during treatment with Verzenio and for at least 3 weeks after taking the last dose of Verzenio.

- **Fertility**

- Based on studies in laboratory animals, Verzenio may cause fertility problems in men. This may affect your ability to have a child. Consult your doctor if it concerns you.

Driving and using machines

Verzenio can cause dizziness. Do not drive or operate machinery until you know how the medicine affects you.

Important information about some of the ingredients of this medicine

Verzenio contains lactose

Patients with lactose intolerance should be aware that Verzenio tablets contain lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor prior to taking this medicine.

Verzenio contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say it is essentially 'sodium-free'.

3. HOW TO USE THIS MEDICINE?

Always use this medicine exactly as your doctor has told you. 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 be determined only by your doctor. Your doctor may change the medicine dosage if required.

Take the medicine approximately at the same time every day.

Do not exceed the recommended dose.

How to use: swallow the medicine whole. Do not chew, crush or split the tablets prior to swallowing them. Do not take Verzenio tablets if they are broken, cracked or damaged.

If you have accidentally taken a higher dose

If you have taken an overdose, or if a child has accidentally swallowed the medicine, go immediately to the doctor or a hospital Emergency Room and bring the medicine package with you.

If you forgot to take this medicine at the scheduled time or if you vomited, do not take a double dose to make up for the missed dose. Take the next dose at the usual time and consult your doctor.

Persist with the treatment as recommended by your doctor. Even if your health condition has improved, do not stop the treatment or change the dosage without consulting your doctor.

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

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

4. SIDE EFFECTS

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

Verzenio may cause serious side effects including:

- **Diarrhea** is a common side effect, which may sometimes be severe. Diarrhea may cause you to develop dehydration or an infection.

- **Low white blood cell counts (neutropenia)** are common during treatment with Verzenio and may cause serious infections that can lead to death.
- **Liver problems**
- **Lung problems.** Verzenio may cause serious or life-threatening inflammation of the lungs during treatment that can lead to death.
- **Blood clots in the veins or in the arteries of the lungs.** Verzenio may cause serious blood clots that may lead to death.

Contact your doctor immediately if:

- **You suffer from loose stools.** Start taking a medicine for the treatment of diarrhea (such as loperamide). Be sure to drink more fluids and contact your doctor right away.
- **You suffer from signs and symptoms of low white blood cell counts or infections, such as fever and chills.**
- **You suffer from one of the following signs or symptoms of liver problems:** feeling very tired, pain on the upper right side of your stomach area, loss of appetite, bleeding or bruising more easily than normal.
- **You suffer from one of the following signs or symptoms of a blood clot:** pain or swelling in the arms or legs, shortness of breath, chest pain, rapid breathing, rapid heart rate.
- **You have life-threatening pneumonia symptoms:** contact your doctor immediately if you have new symptoms of breathing problems or worsening of existing symptoms such as: trouble breathing or shortness of breath, coughing with or without mucus, chest pain.

Side effects observed in clinical trials

Early Breast Cancer

- **The most common side effects of Verzenio combined with tamoxifen or an aromatase inhibitor (effects that occur in 20% or more of patients):** diarrhea, infections, neutropenia, fatigue, leucopenia, nausea, anemia and headache.
- **Side effects that occur in 10% or more of patients treated with Verzenio combined with tamoxifen or an aromatase inhibitor:**
 - **Gastrointestinal disorders:** diarrhea, nausea, vomiting, and inflammation of the oral mucosa (stomatitis).
 - **Infection and infestations:** infections.
 - **General disorders:** fatigue.
 - **Nervous system disorders:** headache, dizziness.
 - **Metabolism and nutrition disorders:** decreased appetite.
 - **Skin and subcutaneous tissue disorders:** rash, alopecia.
- **Side effects that occur in less than 10% of patients treated with Verzenio combined with tamoxifen or an aromatase inhibitor:** pruritus, digestive problems (dyspepsia), nail disorder, lacrimation increased, impaired sense of taste (dysgeusia), Interstitial lung disease (ILD) or pneumonia, Venous thromboembolic events (VTEs).
- **Abnormal results in laboratory tests that occur in 10% or more patients treated with Verzenio:** creatinine increase in the blood, decrease in white blood cells, low neutrophil count in the blood, anemia, low lymphocyte count in the blood, low platelet

count in the blood, increase in liver enzymes (ALT and AST) in the blood, low level of potassium in the blood (hypokalemia).

Advanced or Metastatic Breast Cancer

- **The most common side effects of Verzenio combined with non-steroidal aromatase inhibitor (effects that occur in 20% or more of patients):** diarrhea, nausea, abdominal pain, vomiting, infections, neutropenia, anemia, leucopenia, fatigue, alopecia, decreased appetite.
- **Side effects that occur in 10% or more of patients treated with Verzenio combined with non-steroidal aromatase inhibitor:**
 - **Gastrointestinal disorders:** diarrhea, nausea, abdominal pain, vomiting and constipation.
 - **Infection and infestations:** infections.
 - **General disorders:** fatigue, influenza-like illness.
 - **Skin and subcutaneous tissue disorders:** alopecia, rash, pruritus.
 - **Metabolism and nutrition disorders:** decreased appetite.
 - **Laboratory tests:** weight decreased.
 - **Respiratory, thoracic, and mediastinal disorders:** cough, dyspnea.
 - **Nervous system disorders:** dizziness.
- **Additional side effects of Verzenio combined with a non-steroidal aromatase inhibitor:** Venous thromboembolic events (VTEs).
- **The most common side effects of Verzenio combined with fulvestrant (effects that occur in 20% or more of patients):** nausea, infections, anemia, decreased appetite, headache, abdominal pain, fatigue, low white blood cell counts (neutropenia, leucopenia), vomiting and diarrhea.
- **Side effects that occur in 10% or more of patients treated with Verzenio combined with fulvestrant:**
 - **Gastrointestinal disorders:** diarrhea, nausea, abdominal pain, vomiting, inflammation of the oral mucosa (stomatitis).
 - **Infection and infestations:** infections.
 - **General disorders:** fatigue, peripheral edema, fever.
 - **Metabolism and nutrition disorders:** decreased appetite.
 - **Respiratory, thoracic and mediastinal disorders:** cough.
 - **Skin and subcutaneous tissue disorders:** alopecia, pruritus, rash.
 - **Nervous system disorders:** headache, impaired sense of taste, dizziness.
 - **Laboratory tests:** weight decreased.
- **Additional side effects of Verzenio combined with fulvestrant:** Venous thromboembolic events (VTEs).
- **The most common side effects of Verzenio when administered as monotherapy (effects that occur in 20% or more of patients):** diarrhea, fatigue, nausea, decreased appetite, abdominal pain, low white blood cell counts (neutropenia), vomiting, infections, anemia, headache, and low platelet count (thrombocytopenia).

- **Side effects that occur in 10% or more of patients treated with Verzenio when administered as monotherapy:**
 - **Gastrointestinal disorders:** diarrhea, nausea, abdominal pain, vomiting, constipation, dry mouth, inflammation of the oral mucosa (stomatitis).
 - **Infection and infestations:** infections.
 - **General disorders:** fatigue, fever.
 - **Metabolism and nutrition disorders:** decreased appetite, dehydration.
 - **Respiratory, thoracic and mediastinal disorders:** cough.
 - **Musculoskeletal and connective tissue disorders:** joint pain (arthralgia).
 - **Nervous system disorders:** headache, impaired sense of taste, dizziness.
 - **Skin and subcutaneous tissue disorders:** alopecia.
 - **Laboratory tests:** weight decreased.
- **Abnormal results in laboratory tests that occur in 10% or more patients treated with Verzenio:** creatinine increase in the blood, decrease in white blood cells, low neutrophil count in the blood, anemia, low lymphocyte count in the blood, low platelet count in the blood, increase in liver enzymes (ALT and AST) in the blood.
- **Side effects that have been observed during post-approval use with unknown frequency:**
Respiratory system disorders: Interstitial lung disease (ILD) or pneumonia.

If a side effect occurs, if one of the side effects worsens, or if you are suffering from a side effect not mentioned in this leaflet, consult the doctor.

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting side effects due to drug treatment" that can be found 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 any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use this medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- Store at a temperature below 30°C.
- Store in the original package.
- 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 to protect the environment.

6. ADDITIONAL INFORMATION

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

microcrystalline cellulose 102, microcrystalline cellulose 101, lactose monohydrate, lactose hydrate, croscarmellose sodium, sodium stearyl fumarate, silicon dioxide; silica, colloidal hydrate, hydrated silicone dioxide.

150 mg:

color mixture: polyvinyl alcohol, titanium dioxide, macrogol 4000/PEG MW 3350, talc, iron oxide yellow.

100 mg:

color mixture: polyvinyl alcohol, titanium dioxide, macrogol 4000/PEG MW 3350, talc.

50 mg:

color mixture: polyvinyl alcohol, titanium dioxide, macrogol 4000/PEG MW 3350, talc, iron oxide yellow, iron oxide red.

Each Verzenio 50 mg tablet contains 0.7 mg sodium and 14 mg lactose (as monohydrate).

Each Verzenio 100 mg tablet contains 1.4 mg sodium and 28 mg lactose (as monohydrate).

Each Verzenio 150 mg tablet contains 2.0 mg sodium and 42 mg lactose (as monohydrate).

What the medicine looks like and the contents of the pack

Verzenio 50 mg:

An oval shaped beige tablet, with "Lilly" embossed on one side and "50" on the other side. Each pack contains a blister of 14 tablets.

Verzenio 100 mg:

An oval shaped white to practically white tablet, with "Lilly" embossed on one side and "100" on the other side. Each pack contains a blister of 14 tablets.

Verzenio 150 mg:

An oval shaped yellow tablet, with "Lilly" embossed on one side and "150" on the other side. Each pack contains a blister of 14 tablets.

License Holder and address:

Eli Lilly Israel Ltd., 4 HaSheizaf St., P.O.B 4246, Ra'anana 4366411.

Manufacturer and address:

Eli Lilly and Company, Indianapolis, Indiana 46285, USA.

Revised in August 2022 according to MOHs guidelines.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:

Verzenio 50 mg: 161-43-35390-00

Verzenio 100 mg: 161-44-35391-00

Verzenio 150 mg: 161-45-35392-00