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

This medicine is dispensed with a doctor's prescription only

Lorviqua® 25 mg
Lorviqua® 100 mg

Film-coated tablets

Each tablet contains:
lorlatinib 25 mg or 100 mg

A list of inactive ingredients and allergens in the preparation: 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.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Lorviqua® is intended for treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) which is positive for a mutation in a gene called ALK (anaplastic lymphoma kinase).

Therapeutic group: protein kinase inhibitors.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine, listed in section 6.
- You take medicines inducing the activity of CYP3A enzyme, called strong inducers, such as rifampicin used to treat tuberculosis, carbamazepine and phenytoin used to treat epilepsy, enzalutamide used to treat prostate cancer, mitotane used to treat adrenal cancer, medicines containing St. John's wort (hypericum), a herbal preparation. If you are not sure, refer to the doctor for the full list of medications.

Special warnings regarding use of the medicine

Before treatment with Lorviqua®, tell your doctor if:

- you have had episodes of depression or seizures
- you have high blood levels of cholesterol or triglycerides
- you have problems with your heart beat
- you have lung or breathing problems
- you have high blood pressure
- you have diabetes or high blood sugar
- you are pregnant or plan to become pregnant
- you are breastfeeding or plan to breastfeed

Children and adolescents
It is not known if Lorviqua® is effective and safe for use in children.

Tests and follow-up
Your doctor will perform a test to make sure that Lorviqua® is right for you.
Your doctor will perform blood tests to check the levels of cholesterol and triglycerides before starting treatment, one to two months after starting treatment and during the treatment, blood tests to check your blood sugar levels before starting and during treatment, check your blood pressure before starting treatment, two weeks after starting treatment, and then at least every month during treatment and an ECG test before and during the treatment.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.
Particularly if you are taking:

- boceprevir, used to treat viral hepatitis C.
- dihydroergotamine, ergotamine, used to treat migraine.
- cobicistat, ritonavir, paritaprevir in combination with ritonavir and ombitasvir and/or dasabuvir, and ritonavir in combination with elvitegravir or indinavir or lopinavir or tipranavir, used to treat AIDS/HIV.
- ketoconazole, itraconazole, voriconazole and posaconazole, used to treat fungal infections.
- troleandomycin, used to treat certain types of bacterial infections.
- quinidine, used to treat irregular heartbeats and other heart problems.
- pimozide, used to treat mental health problems.
- alfentanil and fentanyl, used to treat severe pain.
- cyclosporine, sirolimus and tacrolimus, medicines used in organ transplantation procedures to prevent organ rejection.

Lorviqua® can affect the way other medicines work, and other medicines can affect the way Lorviqua® works and cause side effects.

Please see section 2 "Before using this medicine" for the list of medicines which should not be taken together with Lorviqua®.

Using this medicine and food
Lorviqua® can be taken with or without food. However, you must avoid drinking grapefruit juice or eating grapefruit during the treatment, since they may change the levels of Lorviqua® in your body.

Pregnancy, breastfeeding, and fertility
Inform the doctor if you are pregnant or plan to become pregnant. Lorviqua® may harm the fetus. The doctor will perform a pregnancy test before starting treatment with Lorviqua®. Immediately inform the doctor if you are pregnant or think you may be pregnant during the treatment with Lorviqua®.
Females who are able to become pregnant, should use effective non-hormonal contraceptives during the treatment with Lorviqua® and for at least 6 months after the last dose of Lorviqua®.

Birth control pills and other hormonal contraceptives may not be effective if used during treatment with Lorviqua®. Consult the doctor about methods of contraception suitable for you during the treatment.
Males who have female partners who are able to become pregnant, should use effective contraceptives during the treatment with Lorviqua® and for at least 3 months after the last dose of Lorviqua®.

Lorviqua® may cause decreased fertility in males. This may affect your ability to have children. Contact your doctor for advice if you have concerns regarding fertility.

Inform the doctor if you are breastfeeding or plan to breastfeed. It is not known if Lorviqua® passes into breast milk. Do not breastfeed during the treatment with Lorviqua® and for 7 days after the last dose of Lorviqua®. Consult the doctor about the best way to feed your baby during this period.

Driving and using machines
Care must be taken while driving and operating machines during the treatment with Lorviqua® because of its possible effects on the central nervous system.

Important information about some of this medicine's ingredients
Lorviqua® contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact the doctor before taking this medicine.

Lorviqua® contains sodium. The medicine contains less than 1 mmol (23 mg) sodium per 25 mg or 100 mg tablet; it is considered essentially 'sodium free'.

3. HOW TO USE THE MEDICINE?

Always use this preparation 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 standard dosage is usually: 100 mg once a day.

Swallow the tablets whole with or without food. There is no information about crushing, splitting or chewing the tablets.
Take Lorviqua® at the same time every day.

Do not exceed the recommended dose.

Persist with the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

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.

If you forget to take this medicine at the designated time, take the dose as soon as you remember. However, if the time is close to your next dose (within 4 hours), take only your next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you vomit after taking Lorviqua®, do not take another dose. Take only your next dose at the usual time.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take 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 Lorviqua® may cause side effects in some users. Do not be alarmed by the list of side effects; you may not experience any of them.

Lorviqua® can cause severe side effects including:

- **Liver problems due to interactions with other medicines.** It is important to know which medicines should not be taken together with Lorviqua®.

- **Central nervous system effects.** Lorviqua® may cause central nervous system effects including:
  - problems with thinking such as forgetfulness or confusion
  - changes in mood such as depression and thoughts about suicide or dying
  - psychotic effects such as seeing or hearing things that are not real (hallucinations)
  - seizures
  - changes in speech
  - changes in sleep

  Tell your doctor if you experience new or worsening symptoms of these central nervous system effects during treatment with Lorviqua®.

- **Increase in the cholesterol and triglycerides (lipid) levels in the blood.** Most people will have an increase in their blood lipid levels during treatment with Lorviqua®.
  - If you have an increase in the blood lipid levels during treatment with Lorviqua®, your doctor may need to start you on a medicine to lower the levels. If you are already taking a medicine to lower the lipid levels in your blood, your doctor may need to increase the dose of this medicine.
  - Your doctor will perform blood tests to check your blood lipid levels before starting treatment, one to two months after starting treatment and during the treatment with Lorviqua®.

- **Heart problems.** Lorviqua® can cause very slow or irregular heartbeats. Your doctor will check your heart rate (ECG) before starting treatment and during the treatment with Lorviqua®. Contact the doctor immediately if you feel dizzy or fainting or if you have irregular heartbeats. In some people, these problems are severe and your doctor may need to stop your treatment with Lorviqua® or have a pacemaker placed.

- **Lung problems.** Lorviqua® can cause severe or life-threatening swelling (inflammation) of the lungs during the treatment, that can lead to death. The symptoms may be similar to those of lung cancer. Refer to the doctor immediately if you experience new or worsening symptoms of lung problems, including difficulty breathing, shortness of breath, cough or fever.

- **High blood pressure (hypertension).** Your doctor will check your blood pressure before starting treatment, 2 weeks after starting treatment, and then at least every month during treatment with Lorviqua®. Your doctor may need to start or change your blood pressure medicine if you have high blood pressure during treatment with Lorviqua®. Contact your doctor right away if you have signs or symptoms of high blood pressure, including: headaches, dizziness, blurred vision, chest pain or shortness of breath.

- **High blood sugar (hyperglycemia).** Lorviqua® may increase your blood sugar levels. Your doctor will perform blood tests to check your blood sugar levels before starting and during treatment with Lorviqua®. Your doctor may need to start or change your blood sugar medicine to control your blood sugar levels. Tell your doctor right away if you have new or worsening signs and symptoms of high blood sugar, including: feeling very thirsty, needing to urinate more than usual, you feel very hungry, feeling sick to your stomach, feeling weak or tired, feeling confused.

If you have serious side effects during your treatment with Lorviqua®, your doctor may change your dose, stop your treatment for a period of time, or completely stop your treatment with Lorviqua®.

The most common side effects include:

- swelling of the arms, legs, hands and feet (edema)
- numbness and tingling in your joints or arms and legs (peripheral neuropathy)
- problems with thinking, such as forgetfulness or confusion
- difficulty breathing
- tiredness
- weight gain
- pain in the joints
- changes in mood, such as depression and irritability
- diarrhea
- high cholesterol and triglyceride levels in the blood
- cough

Lorviqua® may cause decreased fertility in males. This may affect your ability to have children. Contact your doctor for advice if you have concerns regarding fertility.

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 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 expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

- No special storage conditions. It is recommended to store at room temperature.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
microcrystalline cellulose, dibasic calcium phosphate anhydrous, sodium starch glycolate, magnesium stearate, HPMC 2910/hypromellose, titanium dioxide, lactose monohydrate, macrogol 4000/PEG 3350, triacetin, ferrosoferric oxide/ black iron oxide and iron oxide red.

What the medicine looks like and contents of the pack:
Lorviqua® 25 mg: Round light pink film-coated tablets, debossed with "Pfizer" on one side and "25" and "LLN" on the other side.
Lorviqua® 25 mg is marketed in blisters of 10 tablets, which are available in packs containing 90 or 120 tablets.

Lorviqua® 100 mg: Oval dark pink film-coated tablets, debossed with "Pfizer" on one side and "LLN 100" on the other side.
Lorviqua® 100 mg is marketed in blisters of 10 tablets, which are available in packs containing 30 tablets.

Not all pack sizes may be marketed.

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

Registration number of the medicine in the Ministry of Health's National Drug Registry:
Lorviqua® 25 mg: 164-03-35884
Lorviqua® 100 mg: 164-04-35887

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