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

This medicine is dispensed with a doctor's prescription only

Rozlytrek 100 mg	**Rozlytrek 200 mg**
Hard capsules	**Hard capsules**

Composition:

Each capsule contains:	**Each capsule contains:**
entrectinib 100 mg	entrectinib 200 mg

For information about inactive ingredients and allergens, see section 2 under 'Important information about some of this medicine's ingredients' and see also section 6, 'Further information'.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, contact the doctor or pharmacist. Keep this leaflet. You may need to read it again.

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

1. WHAT IS THE MEDICINE INTENDED FOR?

Rozlytrek is intended to treat adults with:

A. A solid tumor that:
- was caused by a change in a NTRK-class gene **and**
- has spread to other parts of the body, or in instances when surgery to remove the tumor may cause severe complications **and**
- there is no satisfactory alternative treatment or the tumor grew or spread during the receipt of another treatment.

B. Non-small cell lung cancer (NSCLC) that has spread to other parts of the body and has a change in ROS1 gene.

Therapeutic group:
kinase inhibitor

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

You are sensitive (allergic) to the active ingredient (entrectinib) or to any of the other ingredients in this medicine (see section 6, 'Further information').

Special warnings regarding use of the medicine:

Before taking Rozlytrek, tell the doctor about all of your previous medical conditions, including if:
- you are suffering from liver or kidney problems
- you have bone fractures
- you are suffering from any heart problems, including a medical condition called long QT syndrome
- you are suffering from neurological problems (in the nervous system)
- you suffered or are suffering from eye or vision problems
- you are pregnant or plan to become pregnant. Rozlytrek can harm your unborn baby. Tell your doctor **immediately** if you become pregnant or think that you may be pregnant while taking Rozlytrek.
  Women of childbearing age:
  - Your doctor will refer you to take a pregnancy test before starting treatment with Rozlytrek.
  - You should use effective means of birth control during treatment with Rozlytrek and for at least 5 weeks after taking the last dose of Rozlytrek.

  Men whose women partners are of childbearing age:
  - you should use effective means of birth control during treatment with Rozlytrek and for 3 months after taking the last dose of Rozlytrek.
- you are breastfeeding or plan to breastfeed. It is not known whether Rozlytrek passes into breast milk. Do not breastfeed during treatment with Rozlytrek and for 7 days (one week) after taking the last dose of Rozlytrek. Talk with your doctor about the best way to feed your baby during this period.
- you have been told by the doctor that you have an intolerance to certain sugars, because Rozlytrek contains lactose (a type of sugar).

Children and adolescents:

This medicine is not approved for children and adolescents under the age of 18 years.

Tests and follow-up:
- Your doctor will refer you to blood tests in order to check your liver function during treatment with Rozlytrek.
- Your doctor will do tests before and during treatment with Rozlytrek in order to check the electrical activity of your heart and your body salts (electrolytes).
- Your doctor may refer you to blood tests before and during treatment with Rozlytrek in order to check the level of uric acid in your blood.
- Women of childbearing age: your doctor will refer you to take a pregnancy test before you start treatment with Rozlytrek.

Drug interactions:

If you are taking or have recently taken or may take other medicines, including non-prescription medications and nutritional supplements, tell the doctor or pharmacist. Taking Rozlytrek with certain other medicines may affect the level of Rozlytrek or other medicines in your blood and cause side effects or affect the way that Rozlytrek or other medicines work. Know and keep a list of the medicines you take and show the list to your doctor and pharmacist when you receive a new medicine.

Using the medicine, food and drink:

You may take the capsules with or without food.
Do not drink grapefruit juice or eat grapefruit during treatment with Rozlytrek because it may increase the amount of the active ingredient, entrectinib, in your blood to a harmful level and increase your risk of side effects.

Pregnancy, breastfeeding and fertility:

Before taking Rozlytrek, tell the doctor about any previous medical condition, including if:
- you are pregnant or plan to become pregnant. Rozlytrek can harm your unborn baby. Tell your doctor **immediately** if you become pregnant or think that you may be pregnant while taking Rozlytrek.
  Women of childbearing age:
  - your doctor will refer you to take a pregnancy test before starting treatment with Rozlytrek.
  - you should use effective means of birth control during treatment with Rozlytrek and for at least 5 weeks after taking the last dose of Rozlytrek.

  Men whose women partners are of childbearing age:
  - You should use effective means of birth control during treatment with Rozlytrek and for 3 months after taking the last dose of Rozlytrek.
- you are breastfeeding or plan to breastfeed. It is not known whether Rozlytrek passes into breast milk. Do not breastfeed during treatment with Rozlytrek and for 7 days (one week) after taking the last dose of Rozlytrek. Talk with your doctor about the best way to feed your baby during this period.

Driving and using machines:

Do not drive or operate heavy machines until you know how Rozlytrek affects you. If you experience dizziness, fainting, tiredness, blurred vision, memory loss, changes in mental state, confusion or hallucinations, do not drive or operate heavy machines until your symptoms resolve.

Important information about some of this medicine's ingredients:
- Rozlytrek 100 mg and Rozlytrek 200 mg contain lactose (a type of sugar). If you have been told by the doctor that you have an intolerance to certain sugars, consult with your doctor before starting treatment with this medicine.
- Rozlytrek 200 mg contains a coloring agent called sunset yellow FCF (E110), which may cause allergic reactions.

3. HOW SHOULD YOU USE THE MEDICINE?

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

Dosage:

The dosage and treatment regimen will be determined by the doctor only.
The usual dosage is: 3 capsules of Rozlytrek 200 mg once a day (total of 600 mg per day).
Do not exceed the recommended dose.
Do not change your dose or stop taking Rozlytrek unless your doctor tells you to.
The doctor may change the dosage, temporarily discontinue or permanently stop treatment with Rozlytrek if you develop certain side effects.

Form of administration:

Swallow whole capsules with drinking water, according to your doctor's instructions.
Do not open, crush or chew the capsules, and do not dissolve the capsule contents because the contents have a bitter taste.
You may take the capsules with or without food.
Do not drink grapefruit juice or eat grapefruit during treatment with Rozlytrek because it may increase the amount of the active ingredient, entrectinib, in your blood to a harmful level and increase the risk of side effects.

If you vomit right after taking a dose of Rozlytrek, you may take the dose again.

If you have accidentally taken a higher dosage or if a child or other person has accidentally swallowed some of the medicine, refer **immediately** to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine at the required time, take it as soon as you remember. If you are supposed to take your next dose within 12 hours, skip the missed dose and take your next dose at the regular time. Do not take a double dose to make up for a forgotten dose.

It is important to take Rozlytrek every day for the period of time determined by your doctor. Adhere to the treatment as recommended by the doctor. Even if your health improves, do not stop the treatment with this medicine without consulting with the doctor.

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 use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Rozlytrek 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.

Rozlytrek may cause serious side effects, including:
- **Congestive heart failure.** Rozlytrek may cause congestive heart failure or exacerbate existing congestive heart failure. Tell your doctor **immediately** if you experience any of the following signs and symptoms of congestive heart failure:
  - wheezing or persistent cough
  - trouble breathing when lying down
  - sudden weight gain
  - increasing shortness of breath
  - fatigue or weakness
  - swelling of ankles, feet or legs
- **Central nervous system effects.** Rozlytrek may cause dizziness, mood changes, or may affect how you think and cause confusion, hallucinations, problems with your concentration, attention, memory, speaking, understanding what you hear or read, and sleep. Tell your doctor **immediately** if you experience any of these symptoms.
- **Bone fractures.** Rozlytrek may increase your risk of bone fractures. Bone fractures may happen with or without a fall or other injury. Tell the doctor if you develop pain, changes in movement or bone abnormalities.
- **Liver problems (hepatotoxicity).** The doctor will refer you to blood tests in order to check your liver function during treatment with Rozlytrek. Tell the doctor **immediately** if you develop any of the following symptoms of liver problems, including:
  - loss of appetite
  - nausea or vomiting
  - pain on the upper right side of your stomach area
  - yellowing of your skin or the white part of your eyes
  - dark urine
- **Increased uric acid level in the blood (hyperuricemia).** Rozlytrek may cause too high a level of uric acid in your blood. The doctor may refer you to blood tests before and during treatment with Rozlytrek in order to check the uric acid level in your blood. If you have a high level of uric acid in your blood, the doctor may prescribe you medicines to treat this situation. Tell your doctor if you develop any of the following symptoms of an increase in the level of uric acid (hyperuricemia), including:
  - red, hot, tender, or swollen joints, especially in your big toe
  - pain in your stomach-area or sides
  - nausea or vomiting
  - pink or brown urine
- **QT prolongation – changes in the electrical activity of the heart.** QT prolongation can cause irregular heartbeats that may be life-threatening. The doctor will do tests before and during treatment with Rozlytrek in order to check the electrical activity of your heart and your body salts (electrolytes). Tell the doctor **immediately** if you feel faint, dizzy or feel your heart beating irregularly or fast during treatment with Rozlytrek. These may be symptoms related to QT prolongation.
- **Vision problems.** Rozlytrek may cause vision problems. If you develop severe vision problems during treatment with Rozlytrek, the doctor may stop treatment with Rozlytrek and refer you to an eye specialist. Tell the doctor **immediately** if you have any loss of vision or any change in vision, including:
  - double vision
  - blurred vision
  - new or increased floaters
  - seeing flashes of light
  - light hurting your eyes

Additional side effects:

Very common side effects (may affect more than one in 5 patients):
- tiredness
- constipation
- change in sense of taste
- swelling
- dizziness
- diarrhea
- nausea
- abnormal touch sensation
- shortness of breath
- muscle pain
- confusion, changes in mental state, memory problems and hallucinations
- weight gain
- cough
- vomiting
- fever
- joint pain
- vision changes

Your doctor may temporarily stop treatment, decrease your dose or completely stop Rozlytrek if you develop certain side effects during treatment with the preparation. These are not all the possible side effects of Rozlytrek. **If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.**

Reporting side effects:

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, 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 the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the outer package. The expiry date refers to the last day of that month.
- Do not store above 30°C.
- To protect from moisture, store the medicine in its original packaging and keep the bottle tightly closed.
- Do not throw away medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines that you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

Rozlytrek contains the active ingredient entrectinib.

Rozlytrek 100 mg: every capsule contains 100 mg of active ingredient.
Rozlytrek 200 mg: every capsule contains 200 mg of active ingredient.

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

Capsule content ingredients:
- lactose anhydrous, tartaric acid, crospovidone, hypromellose, microcrystalline cellulose, magnesium stearate, colloidal silicon dioxide.

Capsule shell ingredients:
- hypromellose, titanium dioxide (E171), yellow iron oxide (E172; for Rozlytrek 100 mg capsule), FD&C Yellow #6 (E110; for Rozlytrek 200 mg capsule).
- Printing ink: shellac, propylene glycol, strong ammonia solution, and FD&C blue #2 aluminum lake.

What the medicine looks like and the contents of the package:

Rozlytrek 100 mg is provided as hard yellow opaque capsules. "ENT 100" is printed in blue ink on the capsule body. This medicine is available in a bottle containing 30 capsules.

Rozlytrek 200 mg is provided as hard orange opaque capsules. "ENT 200" is printed in blue ink on the capsule body. This medicine is available in a bottle containing 90 capsules.

License holder and address: Roche Pharmaceuticals (Israel) Ltd., P.O.B. 6391, Hod Hasharon 4524079.

Manufacturer's name and address: Hoffmann–La Roche Ltd., Basel, Switzerland.

Revised in December 2023 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry:

Rozlytrek 100 mg: 36185
Rozlytrek 200 mg: 36186