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

This medicine is dispensed with a doctor's prescription only

Rozlytrek 100 mg
Hard capsules

Rozlytrek 200 mg
Hard capsules

Composition:

Each capsule contains:
entrectinib 100 mg

Each capsule contains:
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:

Antineoplastic, protein kinase inhibitor

How Rozlytrek works?

Rozlytrek works by blocking the action of abnormal enzymes caused by a change in the *NTRK* or *ROS1* genes that make them. The faulty enzymes encourage the cancer cells to grow.

Rozlytrek may slow down or stop the cancer growing. It may also help to shrink your cancer.

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 treatment with Rozlytrek, tell your doctor if:
- You have recently experienced memory loss, confusion, hallucinations, or mental status changes.
- You have a history of fractured bones, or conditions which may increase the risk of bone fractures, called "osteoporosis" or "osteopaenia".
- You take medication to lower the levels of uric acid in your blood.
- You have heart failure (an inability of the heart to adequately pump blood to supply oxygen to the body) – signs can include cough, shortness of breath, and swelling in your legs or arms.
- You have or had heart disorders or a heart conduction problem called "prolonged QTc interval" – this is shown on an ECG test, or low levels of electrolytes (potassium, magnesium, calcium or phosphorus) in your blood.
- You have an inherited problem called "galactose intolerance", "congenital lactase deficiency" or "glucose-galactose malabsorption".

Children and Adolescents

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

Drug Interactions

Rozlytrek can affect the way some other medicines work. Also, some other medicines can affect the way Rozlytrek works. **Therefore, 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.** Particularly if you are taking:
- Medicines for the treatment of fungal infections (anti-fungals) – such as ketoconazole, itraconazole, voriconazole, posaconazole.
- Medicines for the treatment of Acquired Immune Deficiency Syndrome (AIDS)/Human Immunodeficiency Virus (HIV) infection – such as ritonavir or saquinavir.
- A herbal medicine for depression – St. John's Wort (Hypericum).
- Medicines to stop epileptic seizures (anti-epileptics) - such as phenytoin, carbamazepine, phenobarbital.
- Medicines for the treatment of tuberculosis – such as rifampicin, rifabutin.
- Medicines to treat solid cancers and blood cancer – topotecan, lapatinib, mitoxantrone, apalutamide, methotrexate.
- A medicine for inflammation of joints or joint autoimmune disease (rheumatoid arthritis) – methotrexate.
- A medicine for migraine-type headaches – ergotamine.
- A medicine for relief of severe pain – fentanyl.
- A medicine for mental illness (psychoses) or involuntary movements and sounds, also called Tourette Syndrome – pimozide
- A medicine for the treatment of irregular heart rate – quinidine.
- Medicines to prevent formation of blood clots – warfarin, dabigatran etexilate.
- Medicines for the treatment of gastric reflux (heartburn) – cisapride, omeprazole.
- Medicines to reduce blood cholesterol – atorvastatin, pravastatin, rosuvastatin.
- Medicines to suppress the immune system, or prevent the body from rejecting an organ transplant – sirolimus, tacrolimus, cyclosporin.
- Medicines for the treatment of depression – paroxetine, fluvoxamine.
- Medicines to reduce blood sugar levels – repaglinide, tolbutamide.
- Medicines for high blood pressure – bosentan, felodipine, nifedipine, verapamil.

If you are taking any of the aforementioned medicines (or you are not sure), talk to your doctor or pharmacist before taking Rozlytrek.

Using the medicine, food and drink

The capsules may be taken with or without food.

Do not drink grapefruit juice or eat grapefruit or Seville oranges during your treatment with Rozlytrek, because it may increase the amount of the medicine in your blood to a harmful level.

Pregnancy, breast-feeding and fertility

Women and contraception:

You should not become pregnant while taking this medicine because it could harm the baby.

If you are able to become pregnant, you must use highly effective contraception while on treatment and for at least 5 weeks after stopping treatment.

It is not known if Rozlytrek can reduce the effect of birth control medicines (pills or implanted hormonal contraceptives). You should use another reliable method of birth control such as a barrier method (e.g. condom) so you do not become pregnant while you are taking Rozlytrek and for 5 weeks after you stop treatment.

Talk to your doctor about the right methods of contraception for you and your partner.

Men and contraception:

Your female partner should not become pregnant while you are taking this medicine because it could harm the baby. If your female partner is able to become pregnant, you must use highly effective contraception while on treatment and for at least 3 months after stopping treatment.

Talk to your doctor about the right methods of contraception for you and your partner.

Pregnancy
- Do not take Rozlytrek if you are pregnant. This is because it may harm your baby.
- If you become pregnant when taking the medicine or during the 5 weeks after taking your last dose, tell your doctor straight away.

Breast-feeding:

Do not breast-feed during treatment with Rozlytrek, this is because it is not known if Rozlytrek can pass over into breast milk and could therefore harm your baby.

Driving and using machines

Rozlytrek may affect your ability to drive or operate machines. Rozlytrek may cause you to:
- Have blurred vision
- Feel dizzy
- Pass out (lose consciousness)
- Feel tired
- Have changes in your mental status, feel confused or see things that are not there (hallucinations).

If one of the aforementioned happens, you should not drive, use a bicycle, or operate heavy machinery until your symptoms resolve. Talk to your doctor or pharmacist about whether it is okay for you to drive or use machines.

Important information about some of this medicine's ingredients
- **Lactose** (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
- **Sunset yellow FCF (E110) in 200 mg capsules only.** This is a colouring agent, which may cause allergic reactions.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use this medicine 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 medicine.

Dosage:

The dosage and treatment regimen will be determined by the doctor only.

The usual dose is: 3 capsules of Rozlytrek 200 mg, once a day (total of 600 mg per day).

Do not exceed the recommended dose.

If you feel unwell, sometimes your doctor may lower your dose, stop treatment for a short time or stop treatment completely.

Form of administration:

Rozlytrek should be taken by mouth. The capsules may be taken with food or without food.

The capsules must be swallowed whole.

Do not open and disperse the contents of the capsule, do not crush, do not chew or dissolve the content of the capsules since the contents have a bitter taste.

If you vomit after taking Rozlytrek:

If you vomit immediately after taking a dose of Rozlytrek, take another dose.

If you have accidentally taken a higher dose:

If you have taken a higher dose or if a child 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 and this leaflet with you.

If you forget to take the medicine:
- If your next dose is more than 12 hours later, take the missed dose as soon as you remember.
- If there are less than 12 hours until your next dose, do not take the missed dose. Then take your next dose at the usual time.
- Do not take a double dose to make up for a missed dose.

If you stop taking the medicine:

Do not stop taking this medicine without talking to your doctor first. It is important to take Rozlytrek every day for the period of time determined by your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

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 the following side effects:

Serious side effects:

Tell your doctor straight away if you notice any of the following after taking Rozlytrek. Your doctor may lower your dose, stop your treatment for a short time or stop your treatment completely:
- you have cough, shortness of breath, and swelling in your legs or arms (fluid retention). These can be signs of heart problems.
- you feel confused, have changes in mood, memory problems or hallucinations (see things that are not there).
- you feel dizzy or light-headed, or feel your heart beating irregularly or fast, as this may be a sign of an abnormal heart rhythm.
- you notice any joint pain, bone pain, deformities or changes in your ability to move, as this may be a sign of fractures.
- you have kidney problems or arthritis, as this may be the result of high uric acid levels in your blood.

Other side effects:

Tell your doctor, pharmacist or nurse if you notice any of the following side effects:

Very common side effects (may affect more than one in ten patients):
- Feeling tired
- Constipation
- Changes in taste
- Feeling unsteady or dizzy
- Swelling
- Diarrhoea
- feeling sick
- Abnormal sense of touch which feels like itching, tingling or burning sensation
- Lack of enough red blood cells (anaemia)
- Shortness of breath
- Weight gain
- Increased blood level of creatinine (a substance normally eliminated by the kidneys into the urine)
- Vomiting
- Cough
- Fever
- Muscle pain
- Pain including back pain, neck pain, musculoskeletal pain, pain in limbs
- Stomach or joint pain
- Any bone pain, deformities or changes in your ability to move (bone fractures)
- Headache
- Low blood pressure
- Increased blood levels of certain liver enzymes (AST/ALT)
- Abnormal unpleasant sensation in your arms or legs
- Loss of muscle coordination, being unsteady when walking
- Disturbance in normal sleep patterns
- Lung infection
- Urinary tract infection
- Muscle weakness
- Decreased appetite
- Blurred vision
- Rash
- Decreased number of a type of white blood cell called neutrophils
- Inability to empty your bladder completely
- Difficulty swallowing

Common side effects (may affect 1-10 of 100 patients):
- Mood disorders
- Dehydration
- Fluid in the lungs
- Fainting
- Increased sensitivity of the skin to sunlight

Uncommon side effects (may affect 1-10 in 1,000 patients):
- Changes in certain chemicals in your blood caused by rapid breakdown of tumour cells, which may cause damage to organs, including the kidneys, heart, and liver.

Tell your doctor, pharmacist, or nurse if you notice any of the above side effects.

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 and the bottle. 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: each capsule contains 100 mg entrectinib.
Rozlytrek 200 mg: each capsule contains 200 mg entrectinib.

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 [Sunset yellow FCF (E110; for Rozlytrek 200 mg capsule)].
- Printing ink: shellac, propylene glycol, strong ammonia solution, 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.

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

Rozlytrek 100 mg: 164-36-36185-00
Rozlytrek 200 mg: 164-37-36186-00

For simplicity and ease of reading, this leaflet was drafted in the masculine form. However, the medicines is targeted at both genders.