

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 in this medicine, see section 2 ‘Important information about some of this medicine’s ingredients’, and section 6 ‘Additional information’.

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

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

- Rozlytrek is intended to treat:
- Adults and children older than 1 month with a solid tumour that:
 - was caused by a change in a neurotrophic tyrosine receptor kinase (NTRK) gene **and**
 - has spread to other parts of the body or in instances when surgery to remove the tumour may cause severe complications, **and**
 - There is no satisfactory alternative therapy or the tumour grew or spread when receiving other treatment.
 - Adults with non-small cell lung cancer (NSCLC) that has spread to other parts of the body, with a change in the ROS1 gene.

Therapeutic group:
Antineoplastic, protein kinase inhibitor

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

Rozlytrek may slow down or stop the growth of the cancer. It may also help to shrink your cancerous tumour.

2. Before using this medicine

Do not use this medicine if:
You are sensitive (allergic) to the active ingredient entrectinib or to any of the other ingredients in this medicine listed in section 6 ‘Additional information’.

Special warnings about using this medicine:
Before using Rozlytrek, tell your doctor if:

- You have recently had memory loss, confusion, hallucinations, or mental status changes.
- You have had fractured bones, or conditions which may increase your risk of breaking bones, called “osteoporosis” or “osteopaenia”.
- You take medicine to lower the uric acid in your blood.
- You have heart failure (when your heart struggles to pump blood to supply oxygen to the body) – signs can include cough, feeling short of breath, or swelling in your legs or arms.
- You have ever had heart problems or a heart conduction problem called “prolonged QTc interval” – this is shown on an ECG test, or by low levels of electrolytes in your blood.
- You have an inherited problem called “galactose intolerance”, “congenital lactase deficiency” or “glucose-galactose malabsorption”.

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

Interactions with other medicines

Rozlytrek may affect the way other medicines work, and other medicines may affect the way Rozlytrek works. **Therefore, if you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.** Particularly if you are taking medicines for:

- Fungal infections (anti-fungals) - such as ketoconazole, itraconazole, voriconazole, posaconazole.
- AIDS/HIV infection - such as ritonavir or saquinavir.
- Depression - such as paroxetine, fluvoxamine or a herbal medicine for depression - St. John’s Wort (Hypericum).
- Stopping epileptic seizures - such as phenytoin, carbamazepine, phenobarbital.
- Tuberculosis - such as rifampicin or rifabutin.
- Solid cancer tumours and blood cancer - topotecan, lapatinib, mitoxantrone, apalutamide or methotrexate.
- Inflammation of joints or joint autoimmune disease (rheumatoid arthritis) - methotrexate.
- Migraines - ergotamine.
- Severe pain - fentanyl.
- Mental illness (psychoses) or Tourette Syndrome - pimozide.
- Arrhythmias - quinidine.
- Stopping the formation of blood clots - warfarin or dabigatran etexilate.
- Gastric reflux (heartburn) - cisapride or omeprazole.
- Lowering blood cholesterol - atorvastatin, pravastatin or rosuvastatin.
- Suppressing your body’s immune system or preventing rejection of an organ transplant - sirolimus, tacrolimus or cyclosporin.
- Lowering blood sugar levels - repaglinide or tolbutamide.
- High blood pressure - bosentan, felodipine, nifedipine or verapamil.
- Inflammation or nausea - dexamethasone.

If you are taking any of the aforementioned medicines (or you are not sure), consult 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 grapefruits or Seville oranges during your treatment with this medicine, 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 must avoid becoming pregnant during treatment with Rozlytrek, 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 (contraceptive pills or implanted hormonal contraceptives). You should use another reliable method of birth control such as a barrier method (such as a condom).

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

Men and contraception:

Your female partner must avoid becoming pregnant during treatment with Rozlytrek, because the medicine 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.

Consult 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 the medicine may harm your baby.
If you become pregnant when taking Rozlytrek or during the 5 weeks after taking your last dose of Rozlytrek, tell your doctor straight away.

Breast-feeding:
Do not breast-feed during treatment with Rozlytrek. This is because it is not known if the medicine passes into breast milk and could therefore harm your baby.

Driving, cycling and using machines

Rozlytrek may affect your ability to drive, ride a bicycle or use machines. Rozlytrek may cause you to:

- have blurred vision
- feel tired, dizzy or pass out
- have changes in your mental status, feel confused or see things that are not there (hallucinations)

If any of the above happen to you, do not drive, ride a bicycle, or operate heavy machines until you feel better. Consult your doctor or pharmacist about whether it is okay for you to drive, ride a bicycle 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, consult 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 to use this medicine?

Always use this medicine according to your doctor’s instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Dosage:
Only your doctor will determine your dose and how you should take this medicine.

- Adults:**
- The recommended dose is usually: 3 capsules of Rozlytrek 200 mg, once a day (total of 600 mg per day).
 - If you feel unwell, your doctor may lower your dosage, stop treatment for a short time or stop treatment completely.

Adolescents and children older than 1 month:
Your child’s doctor will work out the correct dosage to use – based on your child’s height and weight.
Your child’s doctor will check the dose and change it as needed.

Do not exceed the recommended dose.

Method of administration:

Rozlytrek may be taken with or without food. There are two ways your doctor may tell you to take the capsules:

- Swallow each capsule whole by mouth. Do not crush or chew the capsules.
- Take the medicine orally when it is prepared as a suspension (using an oral syringe) or through a feeding tube, if needed.

Read the ‘Instructions for use’ at the end of the leaflet.

Read and follow the ‘Instructions for use’ at the end of this leaflet carefully on how to take or give Rozlytrek. It shows you details on how to prepare, measure and take or give Rozlytrek prepared as a suspension:

- by mouth, or
- through a feeding tube (such as a gastric or nasogastric tube).

If you vomit after taking Rozlytrek:

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

For capsules administered as an oral suspension

If partial or total vomiting or spitting occurs immediately after administration of the dose to the patient, consult the patient’s doctor or pharmacist for the next steps.

If you have accidentally taken a higher dose:

- 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 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 possible.
- If there are less than 12 hours until your next dose, do not take the missed dose. Take your next dose at the usual time.
- Do not take a double dose to make up for the forgotten dose.

If you stop taking the medicine:

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

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

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose every time 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, using Rozlytrek may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Serious side effects:

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

Tell your doctor straight away if you notice any of the side effects mentioned above.

Additional 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 users):

- Feeling tired
- Changes in sense of taste
- Feeling unsteady or dizzy
- Blurred vision
- Swelling
- Diarrhoea or constipation
- Being or feeling sick
- Difficulty swallowing
- Abnormal sense of touch which feels like itching, tingling or burning sensation
- Rash
- Feeling short of breath
- Cough or fever
- Headache
- Weight gain
- Vomiting
- Muscle pain or weakness
- Pain, including back pain, neck pain, musculoskeletal pain, pain in limbs
- Stomach pain
- Joint pain
- 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
- Inability to empty your bladder completely
- Loss of appetite
- Low blood pressure
- Decreased number of a type of white blood cell called neutrophils
- Lack of red blood cells (anaemia)
- Increased blood levels of certain liver enzymes (AST/ALT)
- Increased blood level of creatinine (a substance normally removed by the kidneys into the urine)

Common side effects (may affect up to one in ten users):

- Mood disorders
- Dehydration
- Fluid around your lungs
- Fainting
- Skin being more sensitive to sunlight

Uncommon side effects (may affect up to 1 in 100 users):

- Changes in certain chemicals in your blood caused by fast breakdown of the cancerous tumour cells - this may cause damage to organs, including the kidneys, heart and liver
- Inflammation of the heart muscle

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

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.

Reporting side effects:

You can report side effects to the Ministry of Health by following the ‘Reporting Side Effects of Drug Treatment’ link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or you can also use this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by your doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the outer package and bottle. The expiry date refers to the last day of that month.
- Capsules: Do not store above 30°C.
- Store the capsules in the original package and keep the bottle tightly closed to protect from moisture.
- Suspension: After preparing the suspension, store below 30°C and use within two hours of preparation.
- Do not throw away medicines via wastewater. Ask the pharmacist how to dispose of medicines that are no longer needed. These measures will help protect the environment.

6. Additional 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, this medicine also contains:

- Capsule content ingredients:
- lactose anhydrous, tartaric acid, crosopovidone, 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 aluminium lake.

What the medicine looks like and contents of the pack:

Rozlytrek 100 mg comes as hard yellow opaque capsules. “ENT 100” is printed in blue ink on the capsule body. The medicine is available in a bottle containing 30 capsules.

Rozlytrek 200 mg comes as hard orange opaque capsules. “ENT 200” is printed in blue ink on the capsule body. The medicine is available in a bottle containing 90 capsules.

Registration holder’s name and address: Roche Pharmaceuticals (Israel) Ltd., POB 6391, Hod Hasharon 4524079.

Manufacturer’s name and address: Hoffmann-La Roche Ltd., Basel, Switzerland.

Revised in May 2025.

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

7. Instructions for use

These Instructions for Use contain information on how to prepare, take and give Rozlytrek capsules.

Rozlytrek capsules can be swallowed whole or prepared as a suspension that is taken or given by mouth or through a gastric or nasogastric tube.

Before starting

- Read these instructions for use** before taking or giving Rozlytrek capsules.
- Ask your healthcare professional to show you how to use Rozlytrek before treatment is started.
- If you have any further questions on the use of Rozlytrek, ask your healthcare professional.

Important information you need to know before preparing and taking or administering Rozlytrek

- Your healthcare professional should show you how to correctly prepare and take or give a dose of Rozlytrek capsules. Always take or give Rozlytrek capsules exactly as your healthcare professional tells you.
- Do not take or give Rozlytrek to someone else, until you have been shown how to properly prepare and take or give Rozlytrek.**
- Wash your hands before and after using Rozlytrek. **Do not** touch your eyes, nose or mouth during the preparation of the oral suspension.
- Check the expiry date and whether the product is damaged before use. **Do not** use if expired or damaged.
- For whole capsules, if you vomit immediately after taking a dose of Rozlytrek, take another dose.
- For capsules administered as an oral suspension, if partial or total vomiting or spitting occurs immediately after administration of the dose to the patient, consult the patient’s doctor or pharmacist for the next steps.
- The suspension should be used **within 2 hours** of preparing.

Rozlytrek administration as a whole capsule by mouth

Your healthcare professional will decide the right daily dose of Rozlytrek for you or your child.

- Swallow whole capsules, with or without food, with some drinking water, as directed by your healthcare professional.
- Do not crush or chew the capsules.

Rozlytrek administration as a liquid suspension – orally or via gastric or nasogastric tube

If you or your child cannot swallow capsules whole, Rozlytrek capsules can be prepared as a suspension (in water or milk) and taken or given by mouth or through a feeding tube.

Your healthcare professional will tell you the number of capsules to use, the exact amount of liquid (water or milk) to be mixed with the contents of the capsule(s) needed to prepare the suspension, and the exact amount of suspension (mL) to withdraw in order to reach the prescribed dose of Rozlytrek to be taken or given.

Table 1 shows the prescribed dose, the number and strength of capsules needed, the amount of water or milk to be mixed with the contents of the capsule(s) and prepare the suspension, and the amount of suspension to withdraw in order to reach the prescribed dose to be taken or given.

You may need to measure a smaller amount of suspension than you prepared to take or give the correct prescribed dose of Rozlytrek.

Amount of suspension to withdraw in order to reach the prescribed dose	Amount of water or milk to be mixed with the content of the capsule(s) to prepare the suspension	Number of 100 mg or 200 mg capsules needed	Prescribed dose of Rozlytrek to be given
1 mL	5 mL	One 100 mg	20 mg
1.5 mL	5 mL	One 100 mg	30 mg
2 mL	5 mL	One 100 mg	40 mg
2.5 mL	5 mL	One 100 mg	50 mg
3 mL	5 mL	One 100 mg	60 mg
3.5 mL	5 mL	One 100 mg	70 mg
4 mL	5 mL	One 100 mg	80 mg
4.5 mL	5 mL	One 100 mg	90 mg
5 mL	5 mL	One 100 mg	100 mg
5.5 mL	10 mL	One 200 mg	110 mg
6 mL	10 mL	One 200 mg	120 mg
6.5 mL	10 mL	One 200 mg	130 mg
7 mL	10 mL	One 200 mg	140 mg
7.5 mL	10 mL	One 200 mg	150 mg
10 mL	10 mL	One 200 mg	200 mg
15 mL	15 mL	Three 100 mg	300 mg
20 mL	20 mL	Two 200 mg	400 mg
30 mL	30 mL	Three 200 mg	600 mg

- To prepare the suspension you will need:
- The number of capsules prescribed by your healthcare professional
 - A clean and empty cup (not included in the package)
 - A cup of room temperature (below 30°C) drinking water or milk
 - An oral syringe (to be provided by your pharmacist) with 0.5 mL graduation marks
 - A paper towel

Preparing a suspension of Rozlytrek

Step 1. Wash your hands.

Step 2. Count the number of capsules as prescribed by your healthcare professional to prepare the suspension.

Figure A

Step 3. Place a clean empty cup on a paper towel.

Step 4. Tap the capsule to loosen the contents inside.

Step 5. Hold the capsule above the clean empty cup to avoid spilling.

Step 6. Open the capsule by gently pressing in on the capsule and gently twisting both sides apart. Pour the contents into the clean cup (Figure A).

Step 7. Tap both sides of the capsule shell and check to ensure all contents have gone into the cup.

- If the contents of the capsule are spilled outside of the cup, empty the cup contents, and use another capsule. Go to Step C1 for clean-up instructions and then start over at Step 1.

Figure B

Step 8. Push the syringe plunger all the way down to remove any air in the oral syringe (Figure B).

Figure C

Step 9. Take the cup of room temperature (below 30°C) drinking water or milk. Using the syringe, withdraw the exact volume* of room temperature drinking water or milk from the cup (Figure C). *Your healthcare professional will tell you how much liquid to use.

Do not use any other type of liquid.

Step 10. Add the drinking water or milk from the syringe to the cup with the content of the capsule(s) (Figure D).

Figure D

Step 11. Let the suspension sit for 15 minutes (Figure E).

Note: It is important to do this to get an even suspension, otherwise you may not get the correct dose.

Figure E

Step 12. Swirl the suspension several times to evenly mix the medicine in the liquid (Figure F).

Note: The suspension will be cloudy if you have used water.

Figure G

Step 13. Push the plunger of the syringe all the way down to remove any air in the syringe (Figure G).

Figure H

Step 14. Swirl the medicine cup again before placing the syringe in the cup (Figure H).

Figure I

Step 15. Immediately place the syringe into the cup and slowly pull back the plunger and withdraw the exact volume of suspension to reach your prescribed dose of Rozlytrek (Figure I).

- Your healthcare professional will tell you how much suspension to withdraw for the dose prescribed for you.
- Do not** wait to withdraw the suspension. If it sits for too long, the medicine may settle to the bottom, and you may not get the correct dose.

Step 16. Check the amount in the syringe (Figure J).

- With the tip of the syringe pointing up, check:
- you have withdrawn the correct volume of suspension
 - there are no large bubbles
- Note:** If you have not withdrawn the correct volume, or if there are large bubbles inside:
- put the syringe into the cup again
 - push the medicine back into the cup
 - then withdraw the medicine again (start at Step 15)
- Shake the syringe quickly. Give Rozlytrek immediately after it is drawn up into the syringe.

If the medicine was not taken **within 2 hours**, discard the medicine from the syringe. Go to Step C1 for clean-up instructions and then start at Step 2 to remix a new dose.

Administration by mouth

Figure K

Step A1. Sit the patient upright when giving a dose of Rozlytrek by mouth (Figure K). Place the oral syringe into the mouth with the tip along either cheek. Slowly push the plunger all the way down.

Note: Administering Rozlytrek too fast may cause choking.

Figure L

Step A