Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Retevmo 40 MG
Retevmo 80 MG

Capsules

Active ingredient and its quantity:
Each capsule of Retevmo 40 mg contains 40 mg of selpercatinib.
Each capsule of Retevmo 80 mg contains 80 mg of selpercatinib.

Inactive ingredients and allergens in the preparation: see Chapter 6 "Additional Information".

Read this patient leaflet carefully in its entirety before using this medicine. This leaflet contains concise information regarding this medicine. If you have any further questions, contact your doctor or pharmacist.
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.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Retevmo is used to treat certain cancers caused by abnormal RET genes and is indicated:
- for the treatment of adult patients with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC).
- for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy.
- for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).
- as monotherapy for the treatment of adults with advanced *RET* fusion-positive solid tumors, when treatment options not targeting *RET* provide limited clinical benefit, or have been exhausted.

Therapeutic group: Antineoplastic and immunomodulating agents, antineoplastic agents, protein kinase inhibitors.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- you are hypersensitive (allergic) to the active ingredient (selpercatinib) or any of the other ingredients of this medicine (listed in Chapter 6).

Special warnings regarding the use of this medicine
Before and during treatment with Retevmo, talk to your doctor if:
- you have liver problems
- you have lung or breathing problems other than lung cancer
- you have high blood pressure
- you have heart problems including a condition called QT prolongation

- you have bleeding problems
- you plan to have surgery. You should stop taking Retevmo at least 7 days before your planned surgery. See Chapter 4 “Side effects”.
- you are pregnant or plan to become pregnant. Retevmo can harm your fetus. See section “Pregnancy, breastfeeding and fertility”.

For further details about warnings regarding the use of this medicine, see Chapter 4 "Side effects”.

Children and Adolescents
The medicine is intended for ages 12 years and older.
It is not known if Retevmo is safe and effective when used:
- in children younger than 12 years of age for the treatment of:
  - advanced or metastatic MTC who require systemic therapy.
  - advanced or metastatic thyroid cancer who require systemic therapy and have received radioactive iodine and it did not work or is no longer working.
- in children for the treatment of any other cancers.

Tests and follow-up
The doctor will perform tests to make sure that Retevmo is right for you:
- Your doctor will perform blood tests before and during treatment with Retevmo in order to check for liver problems.
- Retevmo may affect your blood pressure. Your blood pressure will be measured before and during treatment with Retevmo.
- Retevmo may affect your heart rate. Your doctor will perform tests before and during treatment with Retevmo to check your heart activity and the levels of salts in your body (electrolytes) and the thyroid-stimulating hormone (TSH) in your blood.
- Your doctor will perform blood tests in order to check you for tumor lysis syndrome (TLS).
- Your doctor will perform blood tests to check your thyroid function before and during treatment with Retevmo.
- Your doctor will perform a pregnancy test before you start treatment with Retevmo.

Drug interactions
If you are taking or have recently taken any other medicines, including nonprescription medications and nutritional supplements, tell your doctor or pharmacist. Retevmo may affect the way other medicines work, and other medicines may affect how Retevmo works, and may increase your risk of side effects.

During treatment with Retevmo, you should avoid taking:
- St. John’s wort
- proton pump inhibitors (PPIs), such as dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole sodium and rabeprazole
- H_2 blockers, such as famotidine, nizatidine and cimetidine
- antacids that contain aluminum, magnesium, calcium, simethicone, or buffered medicines

If you cannot avoid taking PPIs, H_2 blockers, or antacids, see Chapter 3 “**How to use this medicine?**” for more information on how to take Retevmo with these medicines.
Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

Use of this medicine and food
You can take Retevmo with or without food.

Pregnancy, breastfeeding and fertility
Pregnancy
Tell your doctor if you are pregnant or plan to become pregnant. Retevmo can harm your unborn baby. You should not become pregnant during treatment with Retevmo.
If you are able to become pregnant, your doctor will do a pregnancy test before you start treatment with Retevmo.
Women who are able to become pregnant should use effective birth control (contraception) during treatment and for **1 week** after your last dose of Retevmo. Talk to your doctor about birth control methods that may be right for you.
Tell your doctor right away if you become pregnant or think you might be pregnant during treatment with Retevmo.
Men with female partners who are able to become pregnant should use effective birth control during treatment with Retevmo and for **1 week** after your last dose of Retevmo.

Breastfeeding
Tell your doctor if you are breastfeeding or plan to breastfeed. It is not known if Retevmo passes into your breast milk. Do not breastfeed during treatment with Retevmo and for 1 week after your last dose.

Fertility
Retevmo may affect fertility in women and men, which may affect your ability to have children. Talk to your doctor if this is a concern for you.

Driving and using machines
You should take special care when driving and using machines as you may feel tired or dizzy while taking Retevmo.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor's instructions. You should 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 the doctor.

Your doctor may change your dose, temporarily stop, or permanently stop treatment with Retevmo if you have side effects. Do not change your dose or stop taking Retevmo unless your doctor tells you.

- Retevmo is taken by mouth, usually twice daily 12 hours apart.
- If you take a proton-pump inhibitor (PPIs), such as dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole sodium, and rabeprazole, take Retevmo with food.
- If you take an H_2 blocker (such as famotidine, nizatidine, and cimetidine), take Retevmo 2 hours before or 10 hours after taking the H_2 blocker.
- If you take an antacid that contains aluminum, magnesium, calcium, simethicone, or buffered medicines, take Retevmo 2 hours before or 2 hours after taking the antacid.
- If you vomit after taking a dose of Retevmo, do not take an extra dose. Take the next dose of Retevmo at your scheduled time.

Do not exceed the recommended dose.

Swallow Retevmo capsules whole. Do not crush or chew the capsules.

If you have accidentally taken a higher dose
If you have taken an overdose or if a child accidentally swallowed the medicine, contact your doctor or go to the nearest hospital Emergency Room right away and bring the medicine pack with you.

If you forgot to take the medicine
If you forgot to take the medicine at the specified time, do not take a missed dose of Retevmo unless it is more than 6 hours until your next scheduled dose.

Treatment should be continued as recommended by the doctor.
Even if there is an improvement in your health, do not stop treatment with this medicine 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 any further questions regarding the use of this medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

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

Retevmo may cause serious side effects, including:

- **Liver problems.** Liver problems (increased liver enzymes) can happen during treatment with Retevmo and may sometimes be serious. Your doctor will do blood tests before and during treatment with Retevmo to check for liver problems. Contact your doctor right away if you get any of the following symptoms of liver problems during treatment:
    - yellowing of your skin or the white part of your eyes (jaundice)
    - dark “tea-colored” urine
    - sleepiness
    - bleeding or bruising
    - loss of appetite
    - nausea or vomiting
    - pain on the upper right side of your stomach area
- **Lung problems.** Retevmo may cause severe or life-threatening inflammation of the lungs during treatment, that can lead to death. Contact your doctor right away if you have any new or worsening lung symptoms, including:
    - shortness of breath
    - cough
    - fever
- **High blood pressure (hypertension).** High blood pressure is common with Retevmo and may sometimes be severe. You should check your blood pressure regularly during treatment with Retevmo. If you develop blood pressure problems, your doctor may prescribe medicine to treat your high blood pressure. Contact your doctor if you have increased blood pressure readings or get any symptoms of high blood pressure, including:
    - confusion
    - headaches
    - shortness of breath
    - dizziness
    - chest pain
- **Heart rhythm changes (QT interval prolongation).** Retevmo may cause very slow, very fast or irregular heartbeats. Your doctor may perform tests before and during treatment with Retevmo to check the activity of your heart and the levels of body salts (electrolytes) and

thyroid-stimulating hormone (TSH) in your blood. Contact your doctor right away if you get any of the following symptoms:

- loss of consciousness
- fainting
- dizziness
- a change in the way your heart beats (heart palpitations)

- **Bleeding problems.** Retevmo can cause bleeding which can be serious and may lead to death. Contact your doctor if you have any signs of bleeding during treatment with Retevmo, including:
  - vomiting blood or if your vomit looks like coffee-grounds
  - pink or brown urine
  - red or black (looks like tar) stools
  - coughing up blood or blood clots
  - unusual bleeding or bruising of your skin
  - menstrual bleeding that is heavier than normal
  - unusual vaginal bleeding
  - nose bleeds that happen often
  - drowsiness or difficulty being awakened
  - confusion
  - headache
  - change in speech
- **Allergic reactions.** Retevmo can cause a fever, rash, muscle or joint pain, especially during the first month of treatment. Contact your doctor if you get any of these symptoms.
- **Tumor lysis syndrome (TLS).** TLS is caused by a fast breakdown of cancer cells. TLS can cause kidney failure, the need for dialysis treatment, and an abnormal heartbeat. TLS can lead to hospitalization. Your doctor may do blood tests to check you for TLS. You should stay well hydrated during treatment with Retevmo. Contact your doctor or get emergency medical help right away if you develop any of these symptoms during treatment with Retevmo:
  - nausea
  - vomiting
  - weakness
  - swelling
  - shortness of breath
  - muscle cramps
  - seizures
- **Risk of wound healing problems.** Wounds may not heal properly during treatment with Retevmo. Contact your doctor if you plan to have any surgery before or during treatment with Retevmo.
  - You should stop taking Retevmo at least 7 days before planned surgery.
  - Your doctor should tell you when you may start taking Retevmo again after surgery.
- **Low thyroid hormone levels in your blood (hypothyroidism).** Your doctor will do blood tests to check your thyroid function before and during treatment with Retevmo. Contact your doctor right away if you develop signs or symptoms of low thyroid hormone levels, including:
  - weight gain
  - feeling cold
  - tiredness that worsens or that does not go away
  - constipation
- **Hip joint problems (slipped capital femoral epiphysis or slipped upper femoral epiphysis) in children.** Contact your doctor right away if you develop signs and symptoms of hip problems, including hip or knee pain or a painless limp.

Additional side effects

The most common side effects (effects that occur in more than 1 in 10 users) of Retevmo in adults with solid tumors include:

- swelling of your arms, legs, hands, and feet (edema)
- diarrhea
- tiredness
- dry mouth
- stomach-area (abdominal) pain
- constipation
- rash
- nausea
- headache

The most common side effects (effects that occur in more than 1 in 10 users) of Retevmo in children 12 years and older with solid tumors include:

- muscle and bone pain
- diarrhea
- headache
- nausea
- vomiting
- cough
- upper respiratory tract infection
- coronavirus infection
- stomach-area (abdominal) pain
- tiredness
- fever
- bleeding
- rash
- swelling

The most common severe abnormal laboratory test results with Retevmo in adults with solid tumors include decreased white blood cell count, increased liver enzymes, decreased levels of sodium in the blood, and decreased levels of calcium in the blood.

The most common severe abnormal laboratory test results with Retevmo in children 12 years and older with solid tumors include decreased white blood cell count, decreased levels of calcium in the blood, decreased red blood cell count, increased liver enzymes, decreased levels of magnesium in the blood, and decreased levels of potassium in the blood.

Side effects reported postmarketing:
The following side effect has been identified during post-approval use of Retevmo. Because such reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- **Skin and subcutaneous tissue disorders:** Stevens-Johnson Syndrome

If a side effect occurs, if one of the side effects worsens or if you have a side effect not mentioned in the leaflet, consult your doctor.

Reporting 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 located on the Home Page of the Ministry of Health’s website (www.health.gov.il), which directs to the online form for reporting side effects, or via the following link: https://sideeffects.health.gov.il

5. HOW TO STORE THIS MEDICINE?

Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
Do not use the medicine after the expiry date (exp. date) which is stated on the label.

Storage conditions:
Store below 30°C.
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 protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, the medicine also contains:
microcrystalline cellulose, colloidal silicon dioxide

The 40 mg capsule shell contains: gelatin, titanium dioxide, ferric oxide.
The 80 mg capsule shell contains: gelatin, titanium dioxide, FD&C blue #1.

The black ink contains: shellac, alcohol (ethanol 96%), ferric oxide, purified water, propylene glycol, strong ammonia solution, isopropyl alcohol, butyl alcohol, potassium hydroxide.

What does the medicine look like and contents of the pack:
Retevmo 40 mg are gray opaque capsules imprinted with “Lilly”, “3977” and “40 mg” in black ink.
Retevmo 80 mg are blue opaque capsules imprinted with “Lilly”, “2980” and “80 mg” in black ink.

Retevmo 40 mg is supplied in a bottle with a child-resistance cap containing 60 capsules.
Retevmo 80 mg is supplied in a bottle with a child-resistance cap containing 60 or 120 capsules.

Not all pack sizes may be marketed.

Registration holder name and address:
Eli Lilly Israel Ltd., 4 HaSheizaf Street, P.O.Box 4246, Ra’anana 4366411

Manufacturer name and address:
Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana (IN) 46285, USA

Revised in December 2025.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
Retevmo 40 mg: 171-67-37212-99
Retevmo 80 mg: 171-68-37213-99

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