

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrRETEVMO™

Selpercatinib capsules

Read this carefully before you start taking RETEVMO and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about RETEVMO.

Serious Warnings and Precautions

- Only a doctor who has experience treating cancer should treat you with this drug.
- RETEVMO can harm your unborn baby.
- RETEVMO can cause serious side effects including:
 - **Hemorrhage** (severe bleeding; blood loss): Bleeding can occur with RETEVMO treatment and can be serious. It may even cause death. If you experience bleeding, your doctor may stop your treatment.
 - **Liver problems:** Liver problems and increased liver enzymes are very common with RETEVMO and may sometimes be serious. Your healthcare professional will run blood tests to check your liver before and during treatment.
 - **Allergic reactions:** RETEVMO may cause a fever, rash, muscle or joint pain. This is common in the first month of treatment. If you experience an allergic reaction, your doctor may prescribe medicine to treat your reaction.
 - **Hypertension** (high blood pressure): High blood pressure is very common with RETEVMO and may sometimes be serious. Your blood pressure should be well controlled before you start taking RETEVMO. Your healthcare professional should check your blood pressure regularly when you take RETEVMO. If blood pressure becomes a problem, your doctor may prescribe medicine to treat your high blood pressure.
 - **QT prolongation** (a heart rhythm condition): Changes to your heart rhythm can occur with RETEVMO treatment and can be serious. Your healthcare professional will check that your heart is working properly before and during your treatment.

See the Serious side effects and what to do about them table, below, for more information on these serious side effects.

What is RETEVMO used for?

See the following boxed text:

For the following indications, RETEVMO has been approved with conditions (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

RETEVMO is used to treat certain cancers caused by abnormal *RET* genes in:

- adults with a type of lung cancer called non-small cell lung cancer (NSCLC). It is used when your cancer has spread to other parts of your body.
- adults and children 12 to 17 years old with medullary thyroid cancer. It is used when:
 - your cancer is advanced or has spread to other parts of your body, and
 - your cancer cannot be removed using surgery
- adults with differentiated thyroid cancer. It is used when:
 - your cancer is advanced or has spread to other parts of your body,
 - your cancer cannot be removed using surgery,
 - radioactive iodine therapy did not work, is no longer working or is not appropriate, and
 - you have tried treatment with sorafenib and/or lenvatinib

Your healthcare professional will perform a test to make sure that RETEVMO is right for you.

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

How does RETEVMO work?

RETEVMO works by blocking the action of RET protein kinase. Specific RET altered proteins can lead to uncontrolled cell growth and cancer. RETEVMO stops specific RET altered proteins from working. RETEVMO may slow or stop the cancer from growing. It may also help to shrink the cancer.

What are the ingredients in RETEVMO?

Medicinal ingredients: selpercatinib

Non-medicinal ingredients: Black iron oxide, colloidal silicon dioxide, FD & C Blue No. 1 (80 mg capsule only), gelatin, microcrystalline cellulose, pharmaceutical grade printing ink, titanium dioxide

RETEVMO comes in the following dosage forms:

Capsule: 40 mg and 80 mg

Do not use RETEVMO if:

- You are allergic to selpercatinib or any of the other ingredients in this medicine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take RETEVMO. Talk about any health conditions or problems you may have, including if you have:

- heart problems or have a family history of heart problems, including a condition known as QT prolongation. QT prolongation happens when there are changes in the electrical activity of the heart. This can cause heart rhythm problems.
- high blood pressure
- liver problems
- kidney problems
- diabetes
- a recent history of significant bleeding
- a history of stroke or brain injury
- a history of anorexia or other eating disorder
- persistent vomiting
- been told that you have an imbalance of electrolytes in your blood, such as potassium, magnesium or calcium
- a condition called “autonomic neuropathy” that causes problems with blood pressure, heart rate, sweating, bowel and bladder control and digestion

Other warnings you should know about:

Risk of wound healing problems: Wounds may not heal properly during treatment with RETEVMO. Tell your healthcare professional 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 healthcare professional should tell you when you may start taking RETEVMO again after surgery.

Tumor lysis syndrome: RETEVMO can cause a serious side effect known as Tumor lysis syndrome (TLS). TLS is caused by a sudden, rapid death or breakdown of cancer cells due to treatment. TLS is a condition that can cause kidney failure and abnormal heart rhythm. You may be at risk of TLS if you have:

- Tumors that are growing quickly,
- Many or large tumours,
- Problems with your kidneys or
- You do not have enough water or fluids in your body.

Your healthcare professional will check you for signs and symptoms of TLS. Drink plenty of water when taking RETEVMO to stay well hydrated.

Pregnancy and breastfeeding:

Female patients:

- If you are pregnant, able to get pregnant or think you are pregnant, there are specific risks you should discuss with your healthcare professional.
- You should not take RETEVMO if you are pregnant. It can harm your unborn baby.
- If you are able to become pregnant:
 - Your healthcare professional will do a pregnancy test before you start RETEVMO. This test must show that you are not pregnant.
 - Avoid becoming pregnant while you are taking RETEVMO. Use highly effective birth control during treatment and for at least 2 weeks after your last dose. Talk to your healthcare professional about birth control methods that may be right for you during this time.
 - Tell your healthcare professional right away if you become pregnant or think you are pregnant during treatment with RETEVMO.
- If you are breastfeeding or planning to breastfeed: it is not known if RETEVMO passes into breast milk. Do not breastfeed during treatment with RETEVMO and for at least 2 weeks after your final dose. Talk to your healthcare professional about the best way to feed your baby during this time.

Male patients with female partners who are able to become pregnant:

- Use highly effective birth control while you are on RETEVMO and for at least 2 weeks after your last dose.
- If during your treatment with RETEVMO, your sexual partner becomes pregnant or thinks she may be pregnant, tell your healthcare professional right away.

Fertility: Taking RETEVMO may affect fertility in males and females. This means that it may be difficult for you to have a child. Talk to your healthcare professional if you have questions about this.

Driving and Using Machines: Fatigue and dizziness can occur with RETEVMO. Be cautious after taking RETEVMO to see how you feel before driving a vehicle or using machinery.

Children and adolescents:

- RETEVMO is not approved for the treatment of lung cancer or thyroid cancer other than medullary thyroid cancer in patients under 18 years of age.
- For the treatment of medullary thyroid cancer, RETEVMO is not approved for use in children under 12 years of age.

- Taking RETEVMO may cause slowed growth in children 12 to 17 years of age.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with RETEVMO:

- Alfentanil – used to treat pain
- Amphotericin B – used to treat fungal infections
- Avanafil – used to treat erectile dysfunction
- Bosentan, diltiazem, verapamil – used to treat high blood pressure and heart arrhythmias
- Buprenorphine – used to treat pain and help people stop taking pain medication
- Bupropion – used to treat depression and to help people stop smoking
- Buspirone – used to treat anxiety
- Carbamazepine – used to treat seizures, nerve pain, and sometimes used to treat bipolar disorders
- Ciprofloxacin, clarithromycin – used to treat bacterial infections
- Conivaptan – used to treat low sodium levels in the blood
- Dabigatran – used to prevent blood clots
- Darifenacin – used to treat a frequent need to urinate
- Darunavir, efavirenz, ritonavir, tipranavir – used to treat human immunodeficiency virus (HIV) infection
- Dexamethasone and other corticosteroids – used to treat asthma, severe allergies, certain lung diseases, a number of skin diseases, brain and eye swelling, and certain forms of arthritis. Dexamethasone may also be used to treat certain types of cancers.
- Dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole, cimetidine, famotidine, nizatidine, aluminum hydroxide gel, subsalicylate, calcium carbonate, magnesium hydroxide, ranitidine – used to treat too much stomach acid
- Enzalutamide – used to treat prostate cancer
- Everolimus – used to treat cancer
- Fluconazole, itraconazole, ketoconazole, miconazole, posaconazole, voriconazole, rifampin, rifabutin – used to treat fungal and bacterial infections
- Ibrutinib – used to treat cancer
- Lomitapide, lovastatin, simvastatin – used to treat high cholesterol
- Midazolam – used for sedation and to treat anxiety
- Montelukast – used to treat asthma
- Naloxegol – used to treat constipation caused by some pain medications
- Paclitaxel – used to treat a number of different cancers

- Phenobarbital, phenytoin – used to prevent and control seizures
- Repaglinide, rosiglitazone, pioglitazone – used to treat diabetes
- Sorafenib – used to treat cancer
- Selexipag – used to treat pulmonary arterial hypertension
- St. John’s Wort – an herbal medicine used to treat depression
- Telithromycin – used to treat certain types of bacterial infection
- Triazolam – used to help with sleeping
- Vardenafil – used to treat erectile dysfunction
- Medicines that cause heart rhythm conditions, including QT prolongation or torsade de pointes
- Medicines that cause a decrease in electrolyte levels. This includes:
 - diuretics (used to remove water from the body)
 - laxatives (used to loosen stools and increase bowel movements)
 - enemas (used to empty the bowels)
- Medicines that cause a decrease in heart rate. This includes:
 - beta-blockers (used to lower blood pressure)
 - digitalis glycosides (such as digoxin; used to treat congestive heart failure and abnormal heart rhythms)
 - calcium channel blockers (such as diltiazem and verapamil; used to lower blood pressure)
 - cholinesterase inhibitors (used to treat Alzheimer’s and dementia symptoms)
 - alpha2-adrenoceptor agonists (used to treat high blood pressure, irregular heart rate, sedation, and the inability to feel pain)
 - I_f inhibitors (used to treat heart failure)
 - sphingosine-1 phosphate receptor modulators (used to treat multiple sclerosis)
- Products with grapefruit

Ask your doctor or pharmacist if you are not sure whether your medicine is one of the medicines listed above.

How to take RETEVMO:

- Take exactly as prescribed for you by your doctor. Do not change your dose or stop taking RETEVMO unless your doctor tells you to. Check with your doctor or pharmacist if you are not sure.
- RETEVMO is taken twice a day. Take at about the same time every day, about 12 hours apart.
- Swallow RETEVMO whole. Do not open, crush, or chew the capsule.
- Take with or without food, unless you are also taking a proton pump inhibitor (see next

bullet point).

- During treatment with RETEVMO, you should avoid taking medicines to treat stomach-acid issues called proton pump inhibitors, H2 blockers and antacids. These medicines can affect how RETEVMO works. If this cannot be avoided and you need to take:
 - a proton pump inhibitor (such as dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole sodium, and rabeprazole): then, take RETEVMO with food.
 - an H2 blocker (such as famotidine, nizatidine, and cimetidine): then, take RETEVMO 2 hours before or 10 hours after the H2 blocker.
 - an antacid (such as calcium carbonate, magnesium hydroxide, and simethicone): then, take RETEVMO 2 hours before or 2 hours after taking the antacid.

Usual dose:

The usual dose depends on your body weight. Your doctor will determine the right dose for you.

- For patients weighing less than 50 kg, the usual dose is: 120 mg twice a day. This is a total daily dose of 240 mg.
- For patients weighing 50 kg or greater, the usual dose is: 160 mg twice a day. This is a total dose of 320 mg.

Your doctor may interrupt, change, or stop your dose. This may occur:

- based on your current health,
- if you take certain other medications,
- if your disease gets worse,
- if you develop certain side effects, or
- you are having surgery.

Overdose:

If you think you, or a person you are caring for, have taken too much RETEVMO, contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

- If you miss a dose and it is more than 6 hours until your next scheduled dose, take the missed dose as soon as you remember. Then continue with your next dose at your regular time.
- If it is within 6 hours of your next dose, skip the missed dose. Wait and take your next dose at your scheduled time. Do not take an extra dose.
- If you vomit after taking a dose, do not take an extra dose. Take your next dose at your regular time.

What are possible side effects from using RETEVMO?

These are not all the possible side effects you may have when taking RETEVMO. If you experience any side effects not listed here, tell your healthcare professional.

- Dry mouth, diarrhea, constipation, nausea, abdominal pain, vomiting
- Swelling in the stomach, arms, legs, hands, feet, eyes, face or other parts of your body
- Difficulty emptying your bladder, involuntary leakage of urine
- Fatigue, tiredness
- Decreased appetite
- Body pain, bone pain
- Headache, dizziness, ringing in the ears
- Cough, difficulty swallowing, shortness of breath
- Runny and stuffed nose, itchy eyes, sneezing, flushed and hot skin
- Skin rash, dry skin, skin sores or open wounds
- Confusion
- Erectile dysfunction
- Muscle pain, stiffness, weakness, cramps
- Feeling anxious, sad mood, difficulty sleeping, decreased sexual desire

RETEVMO can cause abnormal ECG and blood test results. ECG stands for electrocardiogram. Your doctor will do some tests before and during your treatment. These include checking for heart and liver problems and electrolyte levels in your blood. The doctor will interpret the results. They will tell you if there are any abnormalities in your tests that might need treatment.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Hypertension (high blood pressure): headache, nosebleeds, shortness of breath, dizziness, chest pain, confusion.		✓	
Leukopenia, neutropenia, lymphopenia (low white blood cells): chills, fever, infection. fatigue, aches and pains, and flu-like symptoms.		✓	

<p>Liver problems and increased liver enzymes: loss of appetite, feeling sick or being sick, yellow skin, itching or pain in your liver area, yellowing of your skin and/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 stomach.</p>		✓	
<p>QT Prolongation (a heart rhythm condition): a change in the way your heart beats (palpitations), dizziness, shortness of breath, chest pain, fainting, loss of consciousness, seizures.</p>		✓	
<p>Thrombocytopenia (low blood platelets): bruising or bleeding for longer than usual if you hurt yourself, tiredness, weakness, 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.</p>		✓	
<p>Urinary tract infections: pain or burning sensation when peeing, need to pee more often than usual, pee that looks cloudy, blood in pee, feeling hot and shivery, pain in the lower stomach and back.</p>		✓	
<p>COMMON</p>			
<p>Allergic reactions: fever, rash, muscle or joint pain.</p>			✓

<p>Anemia (low red blood cells): Being short of breath, feeling very tired, loss of energy, weakness, chest pain, headache, dizziness, feeling light-headed.</p>		✓	
<p>Eye problems: dry eye, eye swelling, blurry vision.</p>		✓	
<p>Heart problems, including:</p> <ul style="list-style-type: none"> • Chest discomfort or pain • Cardiac arrhythmias/ palpitations: fast, slow or irregular heartbeat, heart racing, skipping beats, shortness of breath, weakness, inability to exercise, fluid in the legs. • Pericardial effusion (fluid around the heart): sharp, piercing chest pain over the centre or left side of the chest, which is more intense when breathing in, shortness of breath, palpitations, fever, fatigue, weakness or feeling sick, cough, swelling in the abdomen or leg. • Cardiac arrest (heart stops beating): sudden collapse, no pulse, no breathing, loss of consciousness. 			✓
<p>Hyperthyroidism (overactive thyroid gland): weight loss, rapid or irregular heartbeat, increased appetite, anxiety.</p>		✓	
<p>Hypothyroidism (underactive thyroid gland): fatigue, increased sensitivity to cold, constipation, dry skin, weight gain.</p>		✓	

<p>Infections, including of the eye, nose, tooth, mouth, sinuses, throat, lungs, air passages, skin, stomach, intestines, blood: Fever and chills, fast heartbeat, nausea and vomiting, diarrhea, fatigue or weakness, discolored skin, sweating, severe pain, cough, shortness of breath, sharp chest pain, and rapid breathing.</p>		✓	
<p>Nervous system disorders: amnesia, decreased attention, memory problems, decreased sense of taste, numbness, burning sensation, feeling light-headed, fainting, seizure, tremor.</p>		✓	
<p>Respiratory (breathing) disorders, including:</p> <ul style="list-style-type: none"> • Pleural effusion (fluid around your lungs) • Pneumonitis (inflammation of the lung tissue) • Pulmonary embolism (blood clot in the lungs) • Respiratory failure (stop breathing) <p>Symptoms include: changes in your voice, shortness of breath, chest pain, nose bleed, coughing up blood, nasal congestion and dryness, cough, sore throat, pain in ear, runny nose, bluish color around skin of fingernails and lips.</p>		✓	
<p>Skin disorders: acne, hair loss, dry or flaky skin, itching, rash, reddening of the skin, extra sensitivity to the sun, excessive sweating, redness or swelling on the palms of the hands and soles of the feet.</p>		✓	

LESS COMMON			
Chylothorax (build-up of chyle (lymphatic fluid) in the space around the lung) and chylous ascites (build-up of chyle in the space around the abdomen): shortness of breath, cough, chest discomfort, or trouble breathing.		✓	
Embolism (blockage in a blood vessel): Sudden shortness of breath, chest pain, coughing up blood, fainting, falling down, changes to your eyesight, numbness and tingling in your arms or legs, rapid breathing, rapid heart rate, muscle weakness.			✓
Gastrointestinal disorders: stomach pain, diarrhea often with blood, rectal bleeding and pain, weight loss, fatigue, nausea, vomiting, fever, difficulty swallowing, sore throat, cough, chest pain, pain in gums, mouth sores.		✓	
Hemorrhage (severe bleeding; blood loss): very low blood pressure, rapid heart rate, cold clammy skin, weakened pulse, fatigue, tingling or numbness in arms or legs, changes to vision, changes to balance, fainting, sudden severe headache, difficulty speaking, nausea, vomiting.		✓	
Hypotension (low blood pressure): dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up).		✓	
Kidney failure/Acute kidney injury: Pee less, swelling in your legs, ankles or feet, short of breath, chest pain, muscle cramps, confusion, nausea,			✓

weakness, skin rashes, irregular heartbeat.			
Tumor lysis syndrome (the sudden, rapid death or breakdown of cancer cells due to treatment): nausea, shortness of breath, irregular heartbeat, heart rhythm disturbances, pee less, cloudy pee, muscle spasms or twitching, tiredness, joint pain, severe muscle weakness, seizures.			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on [Adverse Reaction Reporting \(https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html\)](https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store RETEVMO at room temperature (15°C to 30°C).
- Do not use this medicine after the expiry date (EXP) shown on the bottle.
- Keep out of reach and sight of children.

If you want more information about RETEVMO:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website \(https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html\)](https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); or by calling 1-888-545-5972.

This leaflet was prepared by Loxo Oncology, Inc.

Last Revised: MAR 02, 2023

RETEVMO is a trademark owned by or licensed to Eli Lilly and Company, its subsidiaries or affiliates.

RET-0003-CA-PM-20230302