PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Pr **ROZLYTREK®**

entrectinib capsules

Capsules, 100 mg and 200 mg, Oral

Antineoplastic agent

ROZLYTREK, indicated for:

- the treatment of adult patients with unresectable locally advanced or metastatic extracranial solid tumours, including brain metastases, that have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation, and with no satisfactory treatment options

has been issued marketing authorization with conditions, pending the results of new information to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for ROZLYTREK please refer to Health Canada's Notice of Compliance with conditions - drug products web site.

*ROZLYTREK has also been issued **marketing authorization without conditions** for the treatment of patients with ROS1-positive, locally advanced or metastatic non-small cell lung cancer (NSCLC).*

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Date of Revision:
07-JAN-2021

Submission Control No: 242028

This product has been authorized under the Notice of Compliance with Conditions (NOC/c) for one or all of its indicated uses.

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

A NOC/c is a form of market approval granted to a product on the basis of **promising** evidence of clinical effectiveness following review of the submission by Health Canada.

Products authorized under Health Canada's NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame.

What will be different about this Product Monograph?

The following Product Monograph will contain boxed text at the beginning of each major section clearly stating the nature of the market authorization. Sections for which NOC/c status holds particular significance will be identified in the left margin by the symbol NOC/c. These sections may include, but are not limited to, the following:

- Indications;
- Action and Clinical Pharmacology;
- Warnings and Precautions;
- Adverse Reactions;
- Dosage and Administration; and
- Clinical Trials.

Adverse Drug Reaction Reporting and Re-Issuance of the Product Monograph

Health care providers are encouraged to report Adverse Drug Reactions associated with normal use of these and all drug products to Health Canada's Canada Vigilance Program at 1-866-234-2345. The Product Monograph will be re-issued in the event of serious safety concerns previously unidentified or at such time as the sponsor provides the additional data in support of the product's clinical benefit. Once the latter has occurred, and in accordance with the NOC/c policy, the conditions associated with market authorization will be removed.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

Pr **ROZLYTREK®**
entrectinib capsules

Read this carefully before you start taking **ROZLYTREK** 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 **ROZLYTREK**.

What is ROZLYTREK used for?

For the following indication ROZLYTREK 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 studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

Solid Tumours

ROZLYTREK is used to treat adults with solid tumours that have a Neurotrophic Tyrosine Receptor Kinase (*NTRK*) gene fusion without a known resistance mutation. ROZLYTREK can treat cancers that have spread to different parts of the body. It is for patients without other treatment options.

To benefit from ROZLYTREK, the patient must have a tumour that has an *NTRK* gene fusion. This can be checked by a test that is done before you start ROZLYTREK.

For the following indication ROZLYTREK has been approved ***without conditions***. This means it has passed Health Canada's review and can be bought and sold in Canada.

Lung Cancer

ROZLYTREK is used to treat adults with a kind of lung cancer called non-small cell lung cancer (NSCLC). The non-small cell lung cancer:

- is "ROS1-positive" (this means that your cancer cells have a fault in a gene called 'ROS1'), and
- may have spread to other parts of your body, and
- has not been treated with another drug called crizotinib.

To benefit from ROZLYTREK, the patient must have non-small cell lung cancer (NSCLC) that is ROS1-positive. This can be checked by a test that is done before you start ROZLYTREK.

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 a 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 a 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.

Serious Warnings and Precautions

- ROZYLTREK may harm your unborn baby.
- ROZYLTREK may cause congestive heart failure. This occurs when your heart muscle does not pump blood as well as it should.

How does ROZLYTREK work?
ROZLYTREK works by blocking the action of enzymes which have a fault in them. This fault is in the *NTRK* genes that make the enzymes. The faulty enzymes encourage the cancer cells to grow. ROZLYTREK may slow down or stop the cancer from growing. It may also help to shrink your cancer.

What are the ingredients in ROZLYTREK?
Medicinal ingredient: entrectinib
Non-medicinal ingredients: Colloidal silicon dioxide, crospovidone, FD&C blue #2 aluminum lake, hypromellose, lactose anhydrous, magnesium stearate, microcrystalline cellulose, propylene glycol, shellac, strong ammonia solution, tartaric acid, titanium dioxide.

Capsules also contain:
- 100 mg: yellow iron oxide
- 200 mg: FD&C yellow #6

ROZLYTREK comes in the following dosage forms:
Capsule: 100 mg and 200 mg

Do not use ROZLYTREK if:
- You are allergic to any ingredients in this drug or the bottle.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ROZLYTREK. Talk about any health conditions or problems you may have, including if you:
- Have or had any heart problems such as:
  - Congestive heart failure (your heart does not pump blood as well as it should).
  - Long QT syndrome. This is a heart rhythm condition. ROZLYTREK and certain other drugs can cause heart rhythm problems. Avoid taking these other drugs with ROZLYTREK. Taking these drugs together with ROZLYTREK might make your heath rhythm problems worse.
- Have excess uric acid in your blood.
- Have liver or kidney problems.
- Have bone fractures.
- Have nervous system or cognitive problems.
- Have problems like fainting or passing out.
- Have or have had eye or vision problems.

Other warnings you should know about:

- Only a doctor who has experience treating cancer should treat you with this drug.

Female Patients:
- Avoid becoming pregnant while taking ROZLYTREK. It may harm your unborn baby.
- Use highly effective birth control if you can get pregnant while taking ROZLYTREK and for 5 weeks after your last dose.
- Tell your healthcare professional right away if you become pregnant or think you are pregnant during treatment with ROZLYTREK.
- You should not be pregnant at the beginning of treatment with ROZLYTREK. The doctor should do a pregnancy test before you start ROZLYTREK.
- It is not known if ROZLYTREK passes into breast milk. Do not breastfeed during treatment with ROZLYTREK and for 14 days after the final dose. Talk to your healthcare professional about the best way to feed your baby during this time.

Male Patients:
- Use highly effective birth control if your partner can get pregnant while you are on ROZLYTREK and for 3 months after your last dose.

Children less than 18 years of age:
- ROZLYTREK is not recommended for use in children less than 18 years of age. There is a higher risk of bone fractures in children compared to adults when using ROZLYTREK.

Driving and using machines:
- Before you do tasks which require attention wait until you know how you respond to ROZLYTREK. It can cause you to feel faint, dizzy, or tired. It can give you blurred vision, mental status changes, confusion, and hallucinations. Do not drive or operate machines until you feel well.

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 ROZLYTREK:
- Telithromycin – used to treat certain types of bacterial infection
- St. John's Wort (*hypericum perforatum*) – a herbal medicine, used to treat depression
- Ritonavir, saquinavir - used to treat AIDS/HIV infection
- Itraconazole, ketoconazole, posaconazole and voriconazole - used to treat fungal and bacterial infections
- Phenytoin, carbamazepine, phenobarbital - used to treat seizures
- Rifampin, rifabutin – used to treat lung disease
- Grapefruit and grapefruit juice

How to take ROZLYTREK:
- Take exactly as prescribed for you by your healthcare provider. Continue to take ROZLYTREK unless your healthcare provider tells you to stop. Treatment may continue until the cancer gets worse or you get side effects that could prevent treatment continuation.
- Take with or without food.
- Swallow whole. Do not open or dissolve the capsules.

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

Recommended dose:
Adults
- Recommended Dose: 600 mg once a day.
- Your healthcare professional will monitor your health. Your doctor may interrupt, reduce, or stop your dose. This may occur based on your current health, if you take certain other medications, if your disease gets worse, or if you have too many side effects.

Overdose:

If you think you have taken too much ROZLYTREK, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
- If you are less than 12 hours late, take the missed dose as soon as you remember. Take the next dose at your regular time.
- If you are more than 12 hours late, do NOT take the missed dose. Wait until the regular time for your next dose.
- Do not take a double dose to make up for a missed dose.

What are possible side effects from using ROZLYTREK?

These are not all the possible side effects you may feel when taking ROZLYTREK. If you experience any side effects not listed here, contact your healthcare professional.

The most common side effects of ROZLYTREK include:
- tiredness, difficulty sleeping
- constipation, diarrhea, nausea, vomiting, abdominal pain
- change in sense of taste and touch
- swelling
- dizziness, headaches
- abnormal touch sensation (tingling, pain or numbness in hands, fingers and toes)
- pain in joints, bones, muscles or nerves
- weakness of muscles
- weight gain, loss of appetite, difficulty swallowing
- cough
- fever
- rash

ROZLYTREK can cause abnormal exam and blood test results. Your doctor will do some tests before and during your treatment. These include checking for heart and liver problems. 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			
Anemia (reduction in the number of red blood cells): Feel tired, looking pale and you may feel your heart pumping		✓	
Decreased Neutrophils (a kind of white blood cells): Fever, fatigue, mouth ulcer, sore throat, or infections.		✓	
Dehydration (when there is not enough water in the body): Thirst, reduced sweating and urine, dry mouth, dizziness	✓		
Eye problems: blurred vision, loss of vision in eye, double vision, increased sensitivity of the eyes to light, clouding of lens in eye, spots in vision that appear as specks or strings of floating material; spots that move with eye movement.		✓	
Liver Problems and increased liver enzymes: Loss of appetite, feeling sick or being sick, yellow skin, itching or pain in your liver area.		✓	
Lung problems/infections: difficult and painful breathing, shortness of breath, sore throat, cough, sinus congestion, wheezing, fever, runny or stuffy nose, chest pain when you breath or cough, sweating and shaking chills		✓	
Nervous System / Cognitive Disorders: feeling confused, mental status change, anxiety, persistent sad mood, decreased attention and awareness. Disorientation, agitation. Having memory problems. See or hear things that are not there (hallucinations).		✓	

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	
Urinary tract infection: blood in urine, pain when you go pee.		✓	
COMMON			
Ataxia (lack of muscle coordination): difficulty with fine motor tasks such as eating, writing or buttoning shirt; difficulty walking; loss of balance; Slurring speech.		✓	
Congestive Heart Failure (heartdoes not pump blood as well as it should): cough, shortness of breath, swelling in your legs, arms, ankles and feet, fluid retention, lack of appetite, rapid or irregular heart beat.			✓
Hypotension (low blood pressure): dizziness, fainting, lightheadedness.		✓	
Hyperuricemia (high levels of uric acid in the blood): severe pain in joints, joint stiffness, redness and swelling in joints.		✓	
Syncope (fainting)		✓	
Pulmonary embolism (blood clot in the lung): severe chest pain, coughing up blood, shortness of breath.			✓
Prolongation of QT interval (a heart rhythm condition): Irregular heartbeat, fainting, loss of consciousness, seizures.			✓
Urinary retention (difficulty emptying bladder)		✓	
NOT COMMON			
Bone fractures (broken bone): Area around break will be painful and swollen, bulge or bump at site of break, broken bone may push through skin.		✓	
Sepsis (serious infection due to bacteria in your blood): fever, shaking, chills, weakness, fast heart rate, rapid breathing.			✓

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	
Tumour lysis syndrome (the sudden, rapid death of cancer cells due to the treatment): nausea, shortness of breath, irregular heartbeat, heart rhythm disturbances, lack of urination, clouding of urine, muscle spasms or twitching, tiredness and/or joint pain, severe muscle weakness, and seizures. Metabolic disorders (kidney failure, abnormal heartbeat) and abnormal blood tests due to rapid breakdown of cancer cells.			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to 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/adverse-reaction-reporting.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 ROZLYTREK at room temperature (15°C to 30°C).
- Do not use this medicine after the expiry date (EXP) shown on the pack.
- Keep out of reach and sight of children.

If you want more information about ROZLYTREK:

- 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://health-products.canada.ca/dpd-bdpp/index-eng.jsp); the manufacturer's website www.rochecanada.com, or by calling 1-888-762-4388.

This leaflet was prepared by Hoffmann-La Roche Limited.

Last Revised: 07-JAN-2021