PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

PrGAVRETO™
pralsetinib capsules
Capsules, 100 mg pralsetinib, Oral
Protein Kinase Inhibitor (L01EX)

GAVRETO, indicated for:

- the treatment of adult patients with rearranged during transfection (RET) fusion-positive locally advanced unresectable or metastatic non-small cell lung cancer (NSCLC).

has been issued market authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for GAVRETO please refer to Health Canada’s Notice of Compliance with conditions - drug products web site: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/notice-compliance/conditions.html”

Hoffmann-La Roche Limited
7070 Mississauga Road
Mississauga, Ontario, Canada
L5N 5M8

Date of Initial Authorization:
June 30, 2021

Date of Revision:
July 12, 2021

Submission Control Number: pra.12.jl.21

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PATIENT MEDICATION INFORMATION
READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrGAVRETO™
pralsetinib capsules

Read this carefully before you start taking GAVRETO 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 GAVRETO.

Serious Warnings and Precautions

• GAVRETO should only be prescribed by doctors who are experienced in the use of drugs to treat cancer.
• GAVRETO may harm your unborn baby.
• Wounds may not heal well during treatment with GAVRETO. GAVRETO should not be taken for at least 5 days before surgery and for at least 14 days after surgery and until the wound is fully healed.

GAVRETO may cause the following serious side effects:

• **Lung problems: Interstitial lung disease/Pneumonitis** (inflammation of lungs) can occur while taking GAVRETO. They may cause death.
• **Hypertension** (high blood pressure): Treatment with GAVRETO can cause high blood pressure. Your healthcare professional will ensure your blood pressure is normal before treatment. They will monitor your blood pressure levels after one week of treatment and at least monthly after. They might give you medicine to treat your high blood pressure.
• **Liver problems**: Treatment with GAVRETO can cause liver problems like increased levels of liver enzymes (ALT, AST) in the blood. You will have regular blood tests done before starting your treatment and then every two weeks during the first three months, then monthly after, while you are taking GAVRETO. These blood tests will tell your healthcare professional how your liver is working.
• **Hemorrhage** (bleeding problems): Treatment with GAVRETO can cause bleeding problems. These bleeding problems can cause death.

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

What is GAVRETO used for?

Please see the boxed text below.

For the following indication GAVRETO 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.
GAVRETO is used to treat adults with a type of lung cancer called non-small cell lung cancer (NSCLC). The non-small cell lung cancer:

- Is caused by abnormal Rearranged During Transfection (RET) gene(s) and
- Cannot be removed by surgery or has spread to other parts of the body.

A test will be done to determine if the non-small cell lung cancer is caused by RET genes.

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 GAVRETO work?

GAVRETO is a type of drug that targets and blocks abnormal RET genes. These RET genes encourage cancer cells to grow. GAVRETO might help slow down the growth or spread of cancer tumour cells.

What are the ingredients in GAVRETO?

Medicinal ingredients: pralsetinib

Non-medicinal ingredients: citric acid, FD&C blue #1 (Brilliant Blue FCF), hydroxypropyl methylcellulose (HPMC, hypromellose), magnesium stearate, microcrystalline cellulose (MCC), pharmaceutical grade printing ink, pregelatinized starch, sodium bicarbonate, and titanium dioxide.

GAVRETO comes in the following dosage forms:

- Capsules, 100mg pralsetinib

Do not use GAVRETO if:

- You are allergic to pralsetinib or any of the other ingredients in GAVRETO or the bottle.

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

- Have a history of lung or breathing problems other than lung cancer.
- Have or had high blood pressure.
- Have or had liver problems.
- Are pregnant or plan to become pregnant.
- Are breastfeeding or plan to breastfeed.
- Are younger than 18 years of age.
- Are 65 years or older. This is because you maybe more likely to experience side effects. These side effects can be serious.
- Had or plan to have surgery.
Other warnings you should know about:

**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 GAVRETO if you are pregnant. It may harm your unborn baby.
- If you are able to become pregnant:
  - Your healthcare professional will do a pregnancy test before you start taking GAVRETO. This test must show that you are not pregnant.
  - Avoid becoming pregnant while you are taking GAVRETO.
  - Use effective birth control during your treatment and for at least 2 weeks after your last dose. The birth control methods you use must not contain hormones. Hormonal birth control methods (like birth control pills) might not work with GAVRETO. Ask your healthcare professional about methods of birth control available to you.
  - Tell your healthcare professional right away if you become pregnant or think you may be pregnant during your treatment with GAVRETO.
- Do not breastfeed while you are taking GAVRETO and for at least one week after your last dose.

*Male patients*
- Use highly effective birth control if your partner can get pregnant while you are on GAVRETO and for at least 1 week after your last dose.

**Fertility in female and male patients:**
- GAVRETO may affect your fertility. Talk to your healthcare practitioner if you are planning on having children.

**Driving and using machines:**
- Before you do tasks that require special attention, wait until you know how you respond to GAVRETO.

**Check-ups and testing:** You will have regular visits with your healthcare professional during your treatment. These visits might include the following to monitor your health:
  - physical exams with a blood pressure check
  - blood tests
  - diagnostic imaging like a CT scan

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 GAVRETO:**
- **Serious drug-drug interactions include:**
  - Medicines for fungal infections such as itraconazole and ketoconazole.
  - Medicines for bacterial infections such as rifampin and clarithromycin.
  - Medicines for HIV infection, such as indinavir and ritonavir.
How to take GAVRETO:

- Take GAVRETO exactly as your healthcare professional tells you to.
- Take GAVRETO on an empty stomach. Do not eat for at least 2 hours before and at least 1 hour after taking GAVRETO.
- Do not change your dose or stop taking GAVRETO unless your healthcare professional tells you to.
- Your healthcare professional will monitor your health. They may interrupt, reduce or stop your dose. This may occur based on your current health, if you take certain other medications or if you have certain side effects.

Usual dose:

Adults:
- Take 400 mg (four 100 mg tablets) once daily by mouth.
- Your healthcare professional will monitor your health. They may interrupt, reduce or stop your dose. This may occur based on your current health, if you take certain other medications or if you have certain side effects.

Overdose:

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

Missed Dose:

If a dose of GAVRETO is missed:
- Take the missed dose as soon as you remember on the same day. Take the next dose at your regular time on the next day.
- If you do not remember on the same day, do not take an extra dose the next day.
- If you vomit after taking a dose of GAVRETO, do not take another dose on that same day. Take your next dose at your regular time on the next day.

What are possible side effects from using GAVRETO?

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

Side effects may include:

- Constipation
- Diarrhea
- Dry mouth
- Bleeding from your nose, gums, vagina
- Change in taste
- Cough
- Fever
- Headache
- Dizziness
- Dry eyes, blurred vision
• Tiredness
• Stomach pain
• Pain in your muscles, joints, neck, bones, nerves, chest, back, arms and/or legs
• Muscle weakness and spasms
• Nausea, vomiting
• Swelling: eyelids, face, hands, feet
• Bruising
• Rash

Your healthcare professional will do some tests before, during and after your treatment. These include blood tests to check your blood cell count and liver health. More frequent tests might be needed. They will tell you if your test results are abnormal and if you need treatment.

### Serious side effects and what to do about them

<table>
<thead>
<tr>
<th>Symptom / effect</th>
<th>Talk to your healthcare professional</th>
<th>Stop taking drug and get immediate medical help</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VERY COMMON</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia (decreased number of red blood cells): fatigue, loss of energy, irregular heartbeats, pale complexion, shortness of breath, weakness</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Hypertension (high blood pressure): shortness of breath, fatigue, headaches, vision problems, confusion, dizziness or fainting, nosebleeds, chest pain or pressure, and/or swelling in your ankles and legs; OR sometimes there are no symptoms.</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Liver problems (Increased levels of liver enzymes (ALT, AST) in the blood): dark urine, fatigue, loss of appetite, nausea or vomiting, sleepiness, bleeding or bruising, yellowing of the skin or eyes, pain on the upper right side of the stomach area</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Leukopenia, Lymphopenia, Neutropenia (decreased white blood cells): infections, fatigue, fever, aches, pains and flu-like symptoms</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Pneumonia (infection in the lungs): chest pain when you breath or cough, confusion, cough which</td>
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<td>✓</td>
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<td></td>
<td>Only if severe</td>
<td>In all cases</td>
</tr>
<tr>
<td>may produce phlegm, fatigue, fever, sweating and shaking chills, nausea, vomiting or diarrhea, shortness of breath</td>
<td></td>
<td></td>
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<tr>
<td><strong>Interstitial Lung Disease (ILD) / Pneumonitis</strong> (inflammation of the lung tissue): shortness of breath, cough, fatigue, loss of appetite, unintentional weight loss</td>
<td></td>
<td>✔</td>
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<tr>
<td><strong>Thrombocytopenia</strong> (low blood platelets): bruising or bleeding for longer than usual if you hurt yourself, fatigue and weakness</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td><strong>Urinary tract infection</strong> (infection in urinary system including kidneys, ureters, bladder and urethra): Pain or burning sensation while urinating, frequent urination, blood or pus in urine, pain in the pelvis or lower back, strong or foul smelling urine, cloudy urine, fever or chills, nausea or vomiting.</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td><strong>COMMON</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>Hemorrhage (bleeding problems):</strong> unusual bleeding or bruising of the skin, pink or brown urine, blood in urine, menstrual bleeding that is heavier than normal, unusual vaginal bleeding, frequent nosebleeds</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Colitis</strong> (bowel inflammation): severe or persistent diarrhea, abdominal pain, nausea and vomiting, fever</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal (GI) bleeding</strong> (bleeding anywhere along the GI tract between mouth and anus): (bleeding in esophagus, stomach or first part of small intestines): blood in vomit or vomit looks like coffee-grounds, black tarry stool, bright red blood in your stool or</td>
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<td>coming from rectum, rapid pulse, low blood pressure, low urine flow, confusion, weakness, dizziness; (bleeding from large intestine, rectum): bright red blood in your stool or coming from rectum, rapid pulse, low blood pressure, low urine flow, confusion, weakness, dizziness</td>
<td>Only if severe</td>
<td>In all cases</td>
</tr>
<tr>
<td>Hemoptysis: coughing up blood or blood clots</td>
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<tr>
<td>Intracerebral, Intracranial hemorrhage (bleeding in the brain/skull): sudden, severe headache; confusion; drowsiness or difficulty being awakened; change in speech; nausea and vomiting; seizures; loss of consciousness</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Nervous system disorders: difficulty walking, trouble with balance, falls, dizziness, light headedness, double vision, nausea, weakness, numbness or paralysis of limbs or face, difficulty speaking, severe headache, difficulty seeing, loss of consciousness, confusion, disorientation</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Pancytopenia (decreased red and white blood cells and platelets): low red blood cell count: paleness of the skin, fatigue, rapid heart rate, shortness of breath; low white blood cell count: fever, and symptoms of infection such as cough; low platelet count: bruising easily and heavy bleeding</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Sepsis (Infection of the blood): fever or dizziness, chills, high or very low body temperature, little or no urine, low blood pressure,</td>
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<td>palpitations, rapid breathing, rapid heartbeat.</td>
<td>Only if severe</td>
<td></td>
</tr>
<tr>
<td>Stomatitis (inflammation and ulceration of the mouth and lips):</td>
<td>In all cases</td>
<td></td>
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<tr>
<td>painful, red, shiny or swollen gums, tongue, mouth or throat sores, blood in</td>
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<tr>
<td>the mouth, difficult or painful swallowing or talking, dry mouth, mild burning,</td>
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<tr>
<td>or pain when eating food</td>
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</table>

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 15-30°C in original bottle.
- Protect from moisture.
- Keep out of reach and sight of children.
- Ask your pharmacist how to throw away drugs you no longer use.

If you want more information about GAVRETO:

- Talk to your healthcare professional