

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

GAVRETO® 100 mg hard capsules

Sugar free

Read all of this leaflet carefully before you start taking GAVRETO

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or healthcare provider.
- Gavreto has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What Gavreto is and what it is used for
2. What you need to know before you take Gavreto
3. How to take Gavreto
4. Possible side effects
5. How to store Gavreto
6. Contents of the pack and other information

1. What Gavreto is and what it is used for

What Gavreto is

GAVRETO is a cancer medicine that contains the active substance pralsetinib.

What Gavreto is used for

Gavreto is a prescription medicine that is used to treat certain cancers caused by an abnormal gene called rearranged during transfection (RET):

- adults with advanced stages of a form of a lung cancer called 'non-small cell lung cancer' ('NSCLC')

- adults with advanced medullary thyroid cancer (MTC) or MTC that has spread who require a medicine by mouth or injection (systemic therapy).
- adults with thyroid cancer who require a medicine by mouth or injection (systemic therapy) and who have received radioactive iodine and it did not work or is no longer working.

GAVRETO is used when a test has shown that your cancer cells have a change in the *RET* gene.

How Gavreto works

In patients whose cancer is due to an altered RET gene, the change in the gene causes the body to make an abnormal RET protein, which can lead to uncontrolled cell growth and cancer. GAVRETO blocks the action of the abnormal RET proteins and may help to slow or stop your lung or thyroid cancer from growing. It may also help to shrink your cancer.

If you have any questions about how GAVRETO works or why this medicine has been prescribed for you, please ask your healthcare provider.

2. What you need to know before you take Gavreto

Do not take Gavreto

- if you are hypersensitive (allergic) to pralsetinib or any of the other ingredients of Gavreto (listed in section 6).

Warnings and precautions

Tell your doctor or healthcare provider before taking Gavreto:

- if you have a history of lung or breathing problems other than lung cancer,
- if you have high blood pressure,
- if you have liver problems,
- if you have bleeding problems.

If you are female tell your healthcare provider:

- if you are pregnant or plan to become pregnant,
- if you are breastfeeding or plan to breastfeed.

Treatment with GAVRETO may harm your unborn baby. See “**Pregnancy**,

Breastfeeding and fertility” for detailed advice.

What you should tell your doctor or pharmacist during your treatment with GAVRETO:

Tell your healthcare provider immediately if you get any of these symptoms during treatment with GAVRETO:

- **lung inflammation (pneumonitis).** GAVRETO may cause severe, life-threatening or fatal swelling (inflammation) of the lungs during treatment. The signs may be similar to those from your lung cancer. Tell your doctor straight away if you have any new or worsening signs including difficulty in breathing, shortness of breath, cough with or without mucous, or fever.
- **high blood pressure (hypertension).** High blood pressure is common with GAVRETO and may sometimes be severe. Your doctor will monitor your blood pressure before you start treatment, then after 1 week of your treatment and then as needed. If you have high blood pressure, which is not well controlled with blood pressure medicines, please consult your doctor as it is important to make sure that your blood pressure is under control before starting GAVRETO treatment.
- **liver problems (increased liver function blood test results).** Liver problems (increased liver function blood test results) can happen during treatment with GAVRETO and may sometimes be serious. Your doctor will take blood tests before you start treatment, every 2 weeks for the first 3 months of your treatment and then as needed. This is to check that you do not have any liver problems while taking GAVRETO. Tell your doctor straight away if you get any of the following signs: yellowing of your skin or the whites of your eyes, pain on the right side of your stomach area, dark urine, itchy skin, feeling less hungry than usual, nausea or vomiting, feeling tired, bleeding or bruising more easily than normal.
- **bleeding problems.** Serious bleeding can occur during treatment with GAVRETO. Tell your doctor straight away if you are vomiting blood or vomit that 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.

Older people (≥65 years)

You can use GAVRETO if you are aged 65 years or over at the same dose as for other adults.

Children and adolescents (<18 years)

NSCLC

Do not give GAVRETO to children or adolescents under 18 years because it is not known if GAVRETO is safe and effective.

RET-Mutant Medullary Thyroid Cancer (MTC) and RET-Fusion Positive Thyroid Cancer

Do not give GAVRETO to children or adolescents under 18 years because it is not known if GAVRETO is safe and effective.

Other medicines and Gavreto

Always tell your healthcare professional if you are taking, have recently taken or might take any other medicine. (This includes complementary or traditional medicines.)

Certain other medicines may affect how GAVRETO works.

Gavreto with food and drink

You should avoid drinking grapefruit juice and eating grapefruit or Seville oranges while on treatment with GAVRETO.

Pregnancy, breastfeeding and fertility

Pregnancy

- Avoid becoming pregnant while being treated with this medicine as it may harm your unborn baby. If you are pregnant, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine. Your healthcare provider will consider the benefit of you taking GAVRETO against the risk to your baby.
- Your healthcare provider may check if you are pregnant before you start treatment with GAVRETO.
- If you do become pregnant during your treatment with GAVRETO, tell your

healthcare provider straight away. You and your healthcare provider will decide what is best for you and your unborn baby.

Contraception

For women

If you are able to have children, you must use effective non-hormonal birth control (contraception) while on treatment and for at least 2 weeks after stopping treatment. Birth control methods that contain hormones (such as birth control pills, injections or transdermal system patches) may not work as well during treatment with GAVRETO.

Talk to your healthcare provider about the birth control methods that may be right for you and your partner.

For men

If your female partner is able to have children, you need to prevent pregnancy. You should use effective birth control (contraception) during treatment and for 1 week after your final dose of GAVRETO.

Talk to your healthcare provider about the birth control methods that may be right for you and your partner.

Breastfeeding

Do not breastfeed while taking this medicine and for at least 1 week after the last dose. This is because it is not known if GAVRETO passes into breast milk. If you are breastfeeding or planning to breastfeed, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

Fertility

GAVRETO may affect your ability to have children. Talk to your healthcare provider if this is a concern for you.

Driving and using machines

GAVRETO may make you feel tired or dizzy. If this happens, do not drive or use machines.

3. How to take Gavreto

Do not share medicines prescribed for you with any other person.

Always take GAVRETO exactly as your doctor has told you. Check with your doctor or pharmacist if you are unsure.

The recommended dose is 400 mg (4 capsules) taken by mouth once daily for adults.

GAVRETO is for oral use. Swallow the capsules whole with a glass of water, on an empty stomach. Do not eat for at least two hours before and at least one hour after taking GAVRETO.

If you vomit after taking a dose of GAVRETO, do not take an extra dose. Take your regular dose of GAVRETO the next day.

Taking GAVRETO at the same time each day will help you to remember when to take your medicine.

Continue taking GAVRETO every day for as long as your healthcare provider tells you. Do not stop treatment with GAVRETO unless your healthcare provider tells you to. Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with GAVRETO if you develop side effects.

If you take more Gavreto than you should

In the event of overdose, consult your doctor or pharmacist straight away. You may require medical attention. If neither is available, contact the nearest hospital or poison control centre, and take your medicine and this leaflet with you.

If you forget to take Gavreto

If you miss a dose of GAVRETO, take it as soon as possible on the same day. Then take your next dose of GAVRETO at your regular time the next day.

4. Possible side effects

[Gavreto]GAVRETO can have side effects. Not all side effects reported for GAVRETO are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking [Gavreto]GAVRETO, please consult your healthcare provider for advice.

GAVRETO may cause serious side effects. Tell your healthcare provider right away if you get the following side effects:

- New or worsening signs of difficulty in breathing, shortness of breath, cough, or fever. GAVRETO may cause severe, life-threatening or fatal swelling (inflammation) of the lungs during treatment.
- Confusion, headaches, shortness of breath, dizziness or chest pain (high blood pressure).
- Yellowing of your skin or the whites of your eyes, pain on the right side of your stomach area, dark urine, itchy skin, feeling less hungry than usual, nausea or vomiting, feeling tired, or bleeding or bruising more easily than normal.
- Vomiting blood or vomit that 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.

The possible side effects of GAVRETO include:

Very common: may affect more than 1 in 10 people

- Inflammation or infection of the lungs (pneumonitis or pneumonia)
- Bladder infection
- Increased blood pressure (hypertension)
- Decreased red blood cells, white blood cells or platelets
- Abnormal liver or kidney function blood tests
- Constipation, Diarrhea, Nausea, Abdominal Pain, Vomiting
- Dry mouth
- Loss of taste or disturbed sense of taste
- Fatigue
- Fever
- Headache

- Dizziness
- Swelling of the face, ankles, hands, legs, or torso (oedema)
- Muscle pain (myalgia)
- Cough, shortness of breath
- Rash
- Bleeding
- Blood test showing higher amounts of an enzyme important for muscle function in your blood (creatine phosphokinase)

Common: may affect up to 1 in 10 people

- Painful sores in the mouth (stomatitis)

If you get any side effects, talk to your healthcare provider. This includes any possible side effects not listed in this leaflet.

Reporting of side effects

If you get side effects, talk to your doctor or nurse. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications:

<https://www.sahpra.org.za/Publications/Index/8>. By reporting side effects, you can help provide more information on the safety of Gavreto.

5. How to store Gavreto

Do not store above 30 °C. Keep the bottle tightly closed in order to protect from moisture.

Store out of reach of children.

This medicine should not be used after the expiry date (EXP) shown on the pack. Do not use this medicine if you notice the bottle is damaged or shows signs of tampering. Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets). These measures will help protect the environment.

6. Contents of the pack and other information

What Gavreto contains

The active substance is pralsetinib. Each hard capsule contains 100 mg of pralsetinib.

The other ingredients are:

Capsule content: hydroxypropyl methylcellulose, microcrystalline cellulose, sodium bicarbonate, citric acid (anhydrous), magnesium stearate, pregelatinised starch.

Capsule shell: hypromellose, titanium dioxide, FD&C Blue #1 (Brilliant Blue FCF).

Printing ink: shellac, dehydrated alcohol, isopropyl alcohol, butyl alcohol, propylene glycol, strong ammonia solution, purified water, potassium hydroxide, titanium dioxide.

Gavreto is sugar free.

What Gavreto looks like and contents of the pack

Gavreto 100 mg hard capsules are light blue opaque capsules with “BLU-667” printed on the body and “100 mg” on the cap in white ink, containing a white to off-white powder.

Gavreto is available in a round, white plastic bottle with white child resistant cap containing 60, 90 or 120 hard capsules and silica gel desiccant packet.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

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