

Package leaflet: Information for the patient

Gavreto 100 mg hard capsules pralsetinib

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

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 used to treat adults with advanced stages of a form of lung cancer called ‘non-small cell lung cancer’ (‘NSCLC’), that presents with a specific rearrangement in a gene called rearranged during transfection (RET) if you have not been previously treated with another RET inhibitor medicine.

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 protein called a RET fusion protein, which can lead to uncontrolled cell growth and cancer. Gavreto blocks the action of RET fusion proteins and may help to slow or stop your lung 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 doctor.

2. What you need to know before you take Gavreto

Do not take Gavreto

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

Warnings and precautions

Talk to your doctor or pharmacist before taking Gavreto.

- if you have a history of lung or breathing problems other than lung cancer.
- if you have had high blood pressure
- if you have had liver problems
- if you have had bleeding problems
- if you have ever had tuberculosis or if you have been in close contact with someone who has or has had tuberculosis. Your doctor may perform tests to see if you have tuberculosis

Gavreto can cause side effects that you need to tell your doctor about straight away. These include:

- **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, or cough with or without mucous, or fever.
- **high blood pressure (hypertension).** Gavreto can increase the occurrence of high blood pressure. 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 injury (transaminase elevations).** Your doctor will take blood tests before you start treatment, then every 2 weeks for the first 3 months of your treatment and then as needed. This is to check 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 have any of these symptoms: are vomiting blood or vomit that looks like coffee-grounds, coughing up blood or blood clots, have pink or brown urine, red or black (looks like tar) stools, 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.
- **abnormal ECG.** Gavreto may result in abnormal ECGs. You will have an ECG taken before and during your treatment with Gavreto. Tell your Doctor if you feel light-headed or experience palpitations as it may be a symptom of abnormal ECG.

Look out for this while you are taking Gavreto. See ‘Side effects’ in section 4 for more information.

Children and adolescents

Gavreto has not been studied in children or adolescents. Do not give this medicine to children or adolescents under the age of 18 years.

Other medicines and Gavreto

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Gavreto may affect the way other medicines work, and certain other medicines may affect how Gavreto works.

Tell your doctor or pharmacist before taking Gavreto if you are taking any of the following medicines:

The following medicines can increase the concentration of Gavreto in the blood:

- medicines used to treat AIDS/HIV (e.g. ritonavir, saquinavir)
- medicines used to treat infections. These include medicines that treat fungal infections (antifungals such as ketoconazole, itraconazole, voriconazole, posaconazole) and medicines that treat certain types of bacterial infection (antibiotics such as telithromycin)
- nefazodone, a medicine used to treat depression

The following medicines can reduce the effectiveness of Gavreto:

- medicines used to stop seizures or fits (anti-epileptics such as phenytoin, carbamazepine, or phenobarbital)
- medicines used to treat tuberculosis (e.g. rifampicin, rifabutin)
- St. John's Wort, a herbal medicine used to treat depression

Gavreto may affect the way some other medicines work, including:

- cyclosporine
- paclitaxel
- warfarin

The medicines listed here may not be the only ones that could interact with Gavreto.

Ask your doctor or pharmacist for advice before taking any medicine.

Gavreto with food and drink

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

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Contraception in females:

You should avoid becoming pregnant while taking this medicine. If you are able to have children, you must use highly effective contraception (for example, double-barrier contraception such as condom and diaphragm) while on treatment and for at least 2 weeks after stopping treatment. Gavreto may reduce the effectiveness of hormonal contraceptive methods (for example, birth control pill); therefore, hormonal contraceptives may not be considered highly effective. If hormonal contraception is unavoidable, it must be used in combination with a condom.

Contraception in males:

Males with female partners of childbearing potential must use effective contraception, including a barrier method, during treatment and for 1 week after completion of treatment.

Talk to your doctor about the right methods of contraception for you and your partner.

Pregnancy:

This medicine is not recommended for use during pregnancy unless absolutely necessary. Avoid becoming pregnant while being treated with this medicine as it may harm your unborn baby. Your doctor will discuss with you the potential risks of taking Gavreto during pregnancy.

Your doctor may check if you are pregnant before you start treatment with this medicine.

Breast-feeding:

Tell your doctor if you are breast-feeding or planning to breast-feed. It is not known if Gavreto passes into your breast milk. You should not breast-feed during treatment with this medicine and for at least 1 week after the last dose. Talk to your doctor about the best way to feed your baby during this time.

Fertility:

It is possible that this medicine could permanently affect your ability to have children. You are encouraged to talk to a doctor about saving your sperm or eggs before using Gavreto.

Driving and using machines

Gavreto may affect your ability to drive or use machines. Gavreto may cause you to feel fatigued. If this happens, you should not drive or operate heavy machinery until your symptoms resolve. Talk to your doctor about whether it is okay for you to drive or use machines.

Gavreto contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per hard capsule, that is to say essentially “sodium-free”.

3. How to take Gavreto

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

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

If you get side-effects, your doctor may change your dose, temporarily stop, or permanently stop treatment. Do not change your dose or stop taking Gavreto unless your doctor tells you to.

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.

If you take more Gavreto than you should

If you have accidentally taken too many capsules, talk to your doctor straight away. You may require medical attention.

If you forget to take Gavreto

If you miss a dose of Gavreto, take it as soon as you remember on the same day. Take your regular dose of Gavreto the next day.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Most serious side effects

Some side effects may be serious. Tell your doctor straight away if you get the following side effect (see also section 2):

- New or worsening signs of difficulty in breathing, shortness of breath, or cough with or without mucous, or fever
- 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, bleeding or bruising more easily than normal (potential signs of liver problems).
- Bleeding with symptoms such as coughing up blood

Other side effects:

Tell your doctor or pharmacist if you notice any of the following side effects:

Very common (may affect more than 1 in 10 people):

- Lung infection
- Bladder infection
- Blood test showing decrease in red blood cells
- Blood test showing decrease in a type of white blood cells (e.g., neutrophils, lymphocytes, etc.)
- Low platelet level

- Blood tests showing increased or decreased amounts of blood mineral
- Altered taste
- Headache
- Increased blood pressure
- Bleeding
- Lung inflammation
- Cough
- Shortness of breath
- Constipation
- Diarrhoea
- Dryness affecting eyes, mouth and skin
- Abdominal (belly) pain
- Vomiting
- Yellow skin and eyes
- Rash
- Bone or muscle pain
- Lack of energy
- Swellings (e.g. feet, ankle, face, eye, joint)
- Fever
- Blood tests showing altered amounts of a substance produced by the liver (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, bilirubin)
- Blood test showing an increased level of an important substance used for assessing kidney function (creatinine)
- 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 swelling and sores in the mouth
- Prolongation of the QT interval on your ECG

Uncommon (may affect up to 1 in 100 people):

- Tuberculosis

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Gavreto

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle label and outer carton after "EXP". The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions. Store in the original package in order to protect from moisture.

Do not use this medicine if you notice that the bottle is damaged or shows signs of tampering.

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. 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:
 - The capsule content contains: hypromellose, microcrystalline cellulose, pregelatinised starch, sodium hydrogen carbonate, citric acid, and magnesium stearate (see section 2 “Gavreto contains sodium”).
 - The capsule shell contains: brilliant blue FCF (E133), hypromellose, and titanium dioxide (E171).
 - The printing ink contains: shellac, propylene glycol (E1520), potassium hydroxide, and titanium dioxide (E171).

What Gavreto looks like and contents of the pack

Gavreto 100 mg hard capsules are light blue, opaque hard capsules with “BLU-667” printed on the capsule shell body and “100 mg” on the capsule shell cap in white ink.

Gavreto is available in a plastic bottle with child-resistant closure containing 60, 90 or 120 hard capsules and a desiccant sachet. Each carton contains one bottle.

Keep the desiccant sachet in the bottle. The desiccant is a moisture absorbing material filled in a small sachet to protect the capsules from moisture. Do not swallow the desiccant.

Not all pack sizes may be marketed.

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This medicine has been given ‘conditional approval’. This means that there is more evidence to come about this medicine.