

Pralsetinib (Gavreto™)

Pronounced: PRAL-se-tih-nib

Classification: Kinase inhibitor

About Pralsetinib (Gavreto[™])

Pralsetinib is a kinase inhibitor. A kinase is an enzyme that promotes cell growth. There are many types of kinases, which control different phases of cell growth. By blocking a particular enzyme from working, this medication can slow the growth of cancer cells.

Pralsetinib is a type of targeted therapy that blocks a protein called "rearranged during transfection" (RET). Pralsetinib blocks RET fusions. RET fusions lead to uncontrolled cell growth and cancer. By inhibiting RET, this medication can slow or stop tumor growth. Your oncology team will test your tumor for this abnormality, which must be present in order to receive the medication.

How to Take Pralsetinib

Pralsetinib is taken as a capsule by mouth, once a day, on an empty stomach. You should not eat 2 hours before or 1 hour after taking the medication. Do not crush, chew or open the capsules. If you miss your dose and it is still the same day, take your missed dose as soon as possible and resume your schedule as normal on the next day. Do not take an extra dose if you vomit after taking it and resume your normal schedule the next day.

It is important to make sure you are taking the correct amount of medication every time. Before every dose, check that what you are taking matches what you have been prescribed.

The blood levels of this medication can be affected by certain foods and medications, so they should be avoided. These include: grapefruit, grapefruit juice, verapamil, ketoconazole, rifampin, phenytoin, St. John's wort, and itraconazole, among others. Be sure to tell your healthcare provider about all medications and supplements you take.

Storage and Handling

Store your medication in the original, labeled container at room temperature and in a dry location (unless otherwise directed by your healthcare provider or pharmacist). This medication should not be stored in a pillbox. Keep containers out of reach of children and pets.

If a caregiver prepares your dose for you, they should consider wearing gloves or pouring the pills directly from their container into the cap, a small cup, or directly into your hand. They should avoid touching the pills. They should always wash their hands before and after giving you the medication. Pregnant or nursing women should not prepare the dose for you. Ask your oncology team where to return any unused medication for disposal. Do not flush down the toilet or throw in the trash.

Where do I get this medication?

Certain cancer medications are only available through specialty pharmacies. If you need to get this medication through a specialty pharmacy, your provider will help you start this process. Where you can fill your prescriptions may also be influenced by your prescription drug coverage. Ask your health care provider or pharmacist for assistance in identifying where you can get this medication.

Insurance Information

This medication may be covered under your prescription drug plan. Patient assistance may be available to qualifying individuals depending upon prescription drug coverage. Co-pay cards, which reduce the patient co-pay responsibility for eligible commercially (non-government sponsored) insured patients, may also be available. Your care team can help you find these resources, if they are available.

Possible Side Effects

There are a number of things you can do to manage the side effects of pralsetinib. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

Liver Toxicity

This medication can cause liver toxicity, which your oncology care team may monitor for using blood tests called liver function tests. Notify your healthcare provider if you notice yellowing of the skin or eyes, your urine appears dark or brown, or you have pain in your abdomen, as these can be signs of liver toxicity.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the red cell count is low, you may feel tired or weak. You should let your oncology care team know if you experience any shortness of breath, difficulty breathing or pain in your chest. If the count gets too low, you may receive a blood transfusion.

Low White Blood Cell Count (Leukopenia or Neutropenia)

White blood cells (WBC) are important for fighting infection. While receiving treatment, your WBC count can drop, putting you at a higher risk of getting an infection. You should let your doctor or nurse know right away if you have a fever (temperature greater than 100.4°F or 38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- Washing hands, both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bath daily and perform frequent mouth care.
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.
- Ask your oncology care team before you, or someone you live with, has any vaccinations.

Kidney Problems

This medication can cause kidney problems, including an increased creatinine level, which your oncology care team may monitor for using blood tests. Notify your healthcare provider if you notice decreased urine output, blood in the urine, swelling in the ankles, or loss of appetite.

Fatigue

Fatigue is very common during cancer treatment and is an overwhelming feeling of exhaustion that is not usually relieved by rest. While on cancer treatment, and for a period after, you may need to adjust your schedule to manage fatigue. Plan times to rest during the day and conserve energy for more important activities. Exercise can help combat fatigue; a simple daily walk with a friend can help. Talk to your healthcare team for helpful tips on dealing with this side effect.

Constipation

There are several things you can do to prevent or relieve constipation. Include fiber in your diet (fruits and vegetables), drink 8-10 glasses of non-alcoholic fluids a day, and keep active. A stool softener once or twice a day may prevent constipation. If you do not have a bowel movement for 2-3 days, you should contact your healthcare team for suggestions to relieve the constipation.

Muscle or Joint Pain/Aches

Your healthcare provider can recommend medications and other strategies to help relieve pain.

High Blood Pressure

This medication can cause high blood pressure (hypertension). Be sure to tell your provider of any history of high blood pressure before starting pralsetinib. Patients should have their blood pressure checked regularly during therapy. Any hypertension should be treated appropriately. If hypertension cannot be controlled, the medication may be stopped. Report any headaches, vision changes or dizziness to your oncology care team.

Electrolyte Abnormalities

This medication can affect the normal levels of some electrolytes (e.g. sodium, phosphate, calcium) in your body. Your levels will be monitored using blood tests. If your levels become too low, your care team may prescribe specific electrolytes to be given by IV or taken by mouth. Do not take any supplements without first consulting with your care team.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the count is low you are at a higher risk of bleeding. Let your oncology care team know if you have any excess bruising or bleeding, including nose bleeds, bleeding gums or blood in your urine or stool. If the platelet count becomes too low, you may receive a transfusion of platelets. If your platelets are low:

- Do not use a razor (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin/Advil (ibuprofen), Aleve (naproxen), Celebrex (celecoxib) etc. as these can all increase the risk of bleeding. Please consult with your healthcare team regarding use of these agents and all over the counter medications/supplements while on therapy.
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Diarrhea

Your oncology care team can recommend medications to relieve diarrhea. Also, try eating low-fiber, bland foods, such as white rice and boiled or baked chicken. Avoid raw fruits, vegetables, whole grain breads, cereals and seeds. Soluble fiber is found in some foods and absorbs fluid, which can help relieve diarrhea. Foods high in soluble fiber include: applesauce, bananas (ripe), canned fruit, orange sections, boiled potatoes, white rice, products made with white flour, oatmeal, cream of rice, cream of wheat, and farina. Drink 8-10 glasses on non-alcoholic, un-caffeinated fluid a day to prevent dehydration.

Peripheral Edema

Peripheral edema is swelling of the extremities caused by retention of fluid. It can cause swelling of the hands, arms, legs, ankles and feet. The swelling can become uncomfortable. Notify your oncology care team if you are experiencing any new or worsening swelling.

Less common, but important side effects can include:

- Lung Problems: Patients can develop an inflammation of the lungs (called pneumonitis) or interstitial lung disease that causes lung scarring while taking this medication. Notify your oncology care team right away if you develop any new or worsening symptoms, including shortness of breath, trouble breathing, cough or fever.
- **Bleeding**: This medication can lead to hemorrhagic events, also known as severe bleeding. If you have any signs of bleeding such as bright red or coffee-ground appearing vomit, red or black stool, coughing up blood, pink or brown urine, more bruising than normal, nose bleeds, drowsiness, headache, or change in speech you should call your provider right away.
- Wound healing: This medication can lead to slower or incomplete wound healing, such as a surgical wound not healing

or staying closed. Be sure to inform the team performing the surgical procedure that you are taking pralsetinib. You should also inform your oncology team that a surgical procedure is planned It is recommended that this medication be discontinued at least 5 days prior to any surgery. In addition, this medication should not be started or restarted for at least 2 weeks following major surgery and any surgical incision should be fully healed. If you have a surgical wound that has not healed or begins to have signs of infection (redness, swelling, warmth), report this to your healthcare team.

• **Tumor Lysis Syndrome:** If there are a large amount of tumor cells in your body prior to treatment, you are at risk for tumor lysis syndrome. This happens when the tumor cells die too quickly and their waste overwhelms the body. You may be given a medication (allopurinol) and IV fluids to help prevent this. If you experience nausea, vomiting, diarrhea or become lethargic (drowsy, sluggish), notify your oncology team right away. TLS can affect your kidney function. Your provider will monitor your kidney function with blood work. Notify your provider if you have little or no urine output.

Reproductive Concerns

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. Effective non-hormonal birth control is necessary for women during treatment and for at least 2 weeks after treatment. Men should use appropriate birth control while receiving the medication and for 1 week after the last dose. Even if your menstrual cycle stops or you believe you are not producing sperm, you could still be fertile and conceive. You should not breastfeed while receiving this medication or for 1 week after your last dose.

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