Lorlatinib (Lorbrena®)

Pronounced: lor-la-ti-nib

Classification: Tyrosine Kinase Inhibitor

About Lorlatinib (Lorbrena®)

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.

Lorlatinib works by targeting and blocking receptors found on the cancer cells called an anaplastic lymphoma kinase (ALK). In some cancers, this receptor is overactive, causing cells to grow and divide too fast. By inhibiting ALK, this medication can slow or stop cell growth of cancer cells. This medication is also used in cancer cells that work against ROS1, another type of mutation. Your oncology team will test your tumor for this abnormality, which must be present in order to receive the medication.

How to Take Lorlatinib

Lorlatinib is taken by mouth, in tablet form. Lorlatinib can be taken with or without food. The tablet should be swallowed whole. You should not chew, crush or split tablets. Try to take this medication at the same time every day. If a dose is missed, take it as soon as you remember unless it is less than 4 hours until the next scheduled dose. Skip the dose if it is less than 4 hours before the next dose. Do not take two doses at the same time to make up for a missed dose. If vomiting occurs after you take your dose, take the next dose at the regularly scheduled time.

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 (but are not limited to): grapefruit, grapefruit juice, ketoconazole, rifampin, phenytoin, St. John's wort, and fentanyl. 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 pour 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?

Lorlatinib is available through select specialty pharmacies. Your oncology team will work with your prescription drug plan to identify an in-network specialty pharmacy for distribution of this medication and shipment directly to your home.

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 lorlatinib. 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:

**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 provider if you are experiencing any new or worsening swelling.

**Peripheral Neuropathy (Numbness or Tingling in the Hands and/or Feet)**

Peripheral neuropathy is a toxicity that affects the nerves. It causes numbness or a tingling feeling in the hands and/or feet, often in the pattern of a stocking or glove. This can get progressively worse with additional doses of the medication. In some people, the symptoms slowly resolve after the medication is stopped, but for some it never goes away completely. You should let oncology care team know if you experience numbness or tingling in the hands and/or feet, as they may need to adjust the doses of your medication.

**Central Nervous System Changes**

This medication can impact the function of the central nervous system. This includes changes to mood, speech, mental status, cognition of thought, sleep, seizures and hallucinations. Additionally, this medication can lead to suicidal ideation. If you experience changes in mood (mania, sadness, hopelessness, obsessive-compulsive behaviors), changes in your sleep patterns (sleeping more or less), changes in your ability to speak, or any thoughts of harming yourself, contact your healthcare team immediately.

**Increased Cholesterol and Triglycerides**

Lorlatinib can increase the cholesterol and triglyceride (lipid) levels in your blood. Your healthcare providers will monitor your lipid levels before, during and after and may prescribe medication to help manage increased lipid levels.

**High Blood Sugar**

This medication can cause elevated blood sugar levels in patients with and without diabetes. Your oncology care team will monitor your blood sugar. If you develop increased thirst, urination or hunger, blurry vision, headaches or your breath smells like fruit, notify your healthcare team. Diabetics should monitor their blood sugar closely and report elevations to the healthcare team.

**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.

**Muscle or Joint Pain/Aches and Headache**

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

**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. Nausea and/or Vomiting

Talk to your doctor or nurse so they can prescribe medications to help you manage nausea and vomiting. In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try antacids, (e.g. milk of magnesia, calcium tablets such as Tums), saltines, or ginger ale to lessen symptoms.

Call your doctor or nurse if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

**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 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.

- 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.

**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/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.

**Changes in Appetite, Weight Gain or Taste Changes**
Nutrition is an important part of your care. Cancer treatment can affect your appetite and, in some cases, the side effects of treatment can make eating difficult. Ask your oncology care team about nutritional counseling services at your treatment center to help with food choices.

- Try to eat five or six small meals or snacks throughout the day, instead of 3 larger meals.
If you are not eating enough, nutritional supplements may help.

You may experience a metallic taste or find that food has no taste at all. You may dislike foods or beverages that you liked before receiving cancer treatment. These symptoms can last for several months or longer after treatment ends.

Avoid any food that you think smells or tastes bad. If red meat is a problem, eat chicken, turkey, eggs, dairy products and fish without a strong smell. Sometimes cold food has less of an odor.

Add extra flavor to meat or fish by marinating it in sweet juices, sweet and sour sauce or dressings. Use seasonings like basil, oregano or rosemary to add flavor. Bacon, ham and onion can add flavor to vegetables.

**Electrolyte Abnormalities**

This medication can affect the normal levels of electrolytes (potassium, magnesium, phosphorus, etc.) in your body. Your levels will be monitored using blood tests. Do not take any supplements without first consulting with your care team.

**Less common, but important side effects can include:**

- **Heart Problems**: This medication can cause slow or abnormal heart beats and/or a type of heart block called atrioventricular block (AV block). Notify your healthcare provider right away if you experience fainting, dizziness, lightheadedness, shortness of breath or chest pain.

- **Lung Problems**: Patients can develop an inflammation of the lungs (called pneumonitis) while taking this medication. Another lung problem called interstitial lung disease (ILD) is also a possible side effect. Notify your healthcare provider right away if you develop any new or worsening symptoms, including shortness of breath, trouble breathing, cough or fever.

**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. Even if your menstrual cycle stops or you believe you are not producing sperm, you could still be fertile and conceive. Effective birth control with a non-hormonal birth control method (condoms, sponge, cervical cap, spermicide) is necessary during treatment and for at least 6 months after treatment. Lorlatinib can make hormonal methods of birth control ineffective. Males with female partners of reproductive potential should use condoms during treatment for at least 3 months days after the final dose of lortatinib. You should not breastfeed while taking this medication and for one week after the last dose.