Ponatinib (Iclusig®)

**Pronounced:** poe-na-ti-nib

**Classification:** Tyrosine Kinase Inhibitor

**About Ponatinib (Iclusig®)**

Ponatinib is a tyrosine 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.

**How to Take Ponatinib**

Ponatinib comes as a tablet to take by mouth. It is usually taken once a day, with or without food. Take ponatinib at around the same time every day. Swallow the tablets whole, do not crush, chew, or break ponatinib tablets. If you miss a dose, take the next dose at the regular time and do not take 2 doses to make up for the missed dose.

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 modafinil. 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?**

Certain cancer medications, including ponatinib, 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 of Ponatinib

There are a number of things you can do to manage the side effects of ponatinib. 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:

**Blood Clots, Stroke and Heart Attack**

Ponatinib can increase the risk of blood clots, stroke, and heart attack. It can also cause blockages or clots in your blood vessels. If you have symptoms of these problems, you should contact your healthcare provider immediately or go to an emergency room. Symptoms can include: swelling, redness or pain in an extremity, chest pain or pressure, pain in your arm, back, neck or jaw, shortness of breath, numbness or weakness on one side of the body, trouble talking, confusion or mental status changes. Let your care team know if you have a history of previous blood clots, as you may require preventive medication.

**Heart Problems**

This medication can cause or worsen pre-existing heart problems including congestive heart failure, restrictive cardiomyopathy, decreased heart function and heart attack. Notify your healthcare provider if you have sudden weight gain or swelling in the ankles or legs. If you develop chest pain or pressure, pain in the left arm, back, or jaw, sweating, shortness of breath, clammy skin, nausea, dizziness or lightheadedness, call 911 or go to the nearest emergency room.

**Liver Toxicity**

This medication can cause liver toxicity, which your doctor may monitor for using blood tests, called liver function tests. If you develop elevations in your liver function tests, your healthcare provider may need to lower your dose or stop the medication. Notify your care team if you notice yellowing of the skin or eyes, your urine appears dark or brown or pain in your abdomen, as these can be signs of liver toxicity.

**High Blood Pressure**

This medication can cause high blood pressure (hypertension). 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.

**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.

**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 the 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.

**Rash and Dry Skin**
Some patients may develop a rash, scaly skin, or red itchy bumps. Use an alcohol-free moisturizer on your skin and lips; avoid moisturizers with perfumes or scents. Your oncology care team can recommend a topical medication if itching is bothersome. If your skin does crack or bleed, be sure to keep the area clean to avoid infection. Be sure to notify your oncology care team of any rash that develops, as this can be a reaction. They can give you more tips on caring for your skin.

**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.

**Nausea and 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.

**Peripheral Neuropathy (Numbness or Tingling in the Hands and/or Feet)**
Peripheral neuropathy is a toxicity that affects the nerves. It causes a numbness or tingling feeling in the hands and 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 your healthcare provider know if you experience numbness or tingling in the hands and feet, as they may need to adjust the doses of your medication.

**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.
Muscle or Joint Pain/Aches and Headache

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

Less common, but important side effects can include:

- **Other Heart Problems:** This medication can cause slow or abnormal heartbeats or an abnormal heart rhythm called QT prolongation. Notify your oncology care team right away if you feel abnormal heartbeats or if you feel dizzy or faint.

- **Fluid Retention:** Ponatinib can cause fluid retention. This may result in swelling of the arms or legs, fluid in the lungs (pleural effusion), or heart (pericardial effusion). Notify your care team if you develop swelling in your arms, legs, feet, or abdomen, have an unexpected weight gain, racing heartbeat, shortness of breath, or difficulty breathing, or if you develop a dry cough.

- **Effects on the Pancreas:** This medication can affect your pancreas and your oncology provider will monitor for this problem with blood tests. Let your provider know if you have a history of pancreatitis or excessive alcohol use, or if you develop abdominal pain or nausea and vomiting.

- **Wound healing:** This medication can lead to slower or incomplete wound healing, such as a surgical wound not healing or staying closed. Therefore, it is recommended that the medication be discontinued 1 week prior to any surgery. Your clinician will monitor wound healing before restarting this medication. 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. You should inform the team performing the procedure and your oncology team of the upcoming procedure in advance of scheduling your procedure.

- **GI Tear:** This medication can cause a tear in the intestinal wall, also called a gastrointestinal perforation. Signs of this can include: new or worsening pain in the abdomen, new abdominal swelling, chills, fever, constipation, nausea, or vomiting. If you experience any of these, contact your healthcare provider immediately or go to the emergency room.

- **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.

- **Effects on the Eyes:** This medication can cause eye problems. Your provider may have your eyes examined before and/or during treatment. Be sure to report any symptoms of eye problems to your oncology provider, including blurred vision, changes in vision, dry eye, eye pain, yellowing of colors or seeing "floaters" or spots in your field of vision.

- **Posterior Reversible Encephalopathy Syndrome (PRES):** In rare cases, this medication has caused a neurological disorder called posterior reversible encephalopathy syndrome (PRES), also called reversible posterior leukoencephalopathy (RPLS). Symptoms of PRES/RPLS include headache, seizure, lethargy, confusion, blindness, and other visual and neurological disturbances. Report any of these symptoms to your healthcare team immediately.

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 birth control is necessary during treatment and for 3 weeks after treatment ends. 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 taking this medication or for 6 days after your last dose.