MEDICATION GUIDE
ICLUSIG® (eye-CLUE-sig)
(ponatinib)
tablets

What is the most important information I should know about ICLUSIG?

ICLUSIG can cause serious side effects, including:

Blood clots or blockage in your blood vessels (arteries and veins). Blood clots or blockage in your blood vessels may lead to heart attack, stroke, or death. A blood clot or blockage in your blood vessels can prevent proper blood flow to your heart, brain, bowels (intestines), legs, eyes, and other parts of your body. You may need emergency surgery or treatment in a hospital. Get medical help right away if you get any of the following symptoms:

- chest pain or pressure
- pain in your arms, legs, back, neck or jaw
- shortness of breath
- numbness or weakness on one side of your body
- leg swelling
- trouble talking
- headache
- dizziness
- severe stomach area pain
- decreased vision or loss of vision

Blood clots or blockage in your blood vessels can happen in people with or without risk factors for heart and blood vessel disease, including people 50 years of age or younger. The most common risk factors for these problems are a history of high blood pressure (hypertension), high cholesterol, and heart disease. Blood clots or blockages in your blood vessels happen more often in people as they get older, and in people with a history of decreased blood flow, high blood pressure, diabetes, or high cholesterol.

Heart problems. ICLUSIG can cause heart problems, including heart failure which can be serious and may lead to death. Heart failure means your heart does not pump blood well enough. ICLUSIG can also cause irregular, slow, or fast heartbeats and heart attack. Your healthcare provider will check you for heart problems during your treatment with ICLUSIG. Get medical help right away if you get any of the following symptoms: shortness of breath, chest pain, fast or irregular heartbeats, dizziness, or feel faint.

Liver problems. ICLUSIG can cause liver problems, including liver failure, which can be severe and may lead to death. Your healthcare provider will do blood tests before and during your treatment with ICLUSIG to check for liver problems. Get medical help right away if you get any of these symptoms of liver problems during treatment:

- yellowing of your skin or the white part of your eyes
- dark “tea-colored” urine
- sleepiness
- loss of appetite
- bleeding or bruising

See **“What are the possible side effects of ICLUSIG?”** for information about side effects.

What is ICLUSIG?

ICLUSIG is a prescription medicine used to treat adults who have:

- **Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia (Ph+ ALL)**
  - in combination with chemotherapy in newly diagnosed Ph+ ALL
  - alone in adults with Ph+ ALL who cannot receive any other kinase inhibitor medicines or who have a specific type of abnormal gene (T315I-positive) Ph+ ALL
- **Chronic Myeloid Leukemia (CML)**
  - chronic phase CML who did not tolerate or no longer benefit from treatment with at least 2 prior kinase inhibitor medicines
  - accelerated phase or blast phase CML who cannot receive any other kinase inhibitor medicines
  - a specific type of abnormal gene (T315I-positive) chronic phase, accelerated phase, or blast phase CML

  ICLUSIG is not for use to treat people with newly diagnosed chronic phase CML.

It is not known if ICLUSIG is safe and effective in children.

Before you take ICLUSIG, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of blood clots in your blood vessels (arteries or veins)
- have heart problems, including heart failure, irregular heartbeats, and QT prolongation
- have diabetes
- have a history of high cholesterol
- have liver problems
- have had inflammation of your pancreas (pancreatitis)
- have high blood pressure
- have bleeding problems
- plan to have surgery or have had a recent surgery. You should stop taking ICLUSIG at least 1 week before planned surgery. See **"What are the possible side effects of ICLUSIG?"**
- are lactose (milk sugar) intolerant. ICLUSIG tablets contain lactose.
- eat grapefruit or drink grapefruit juice. See "**How should I take ICLUSIG?"**
- are pregnant or plan to become pregnant. ICLUSIG can harm your unborn baby.
  - Your healthcare provider will do a pregnancy test before you start taking ICLUSIG.
  - **For females who can become pregnant:**
    - Use an effective form of birth control during treatment and for **3 weeks** after your last dose of ICLUSIG.
    - Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with ICLUSIG.
    - ICLUSIG may affect your ability to have children. Tell your healthcare provider if this is a concern for you.
- are breastfeeding or plan to breastfeed. It is not known if ICLUSIG passes into your breast milk. **Do not** breastfeed during treatment and for **1 week** after your last dose of ICLUSIG.

Tell your healthcare provider about all the medicines you take, including prescription medicines and over-the-counter medicines, vitamins, and herbal supplements. ICLUSIG and other medicines may affect each other causing side effects.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take ICLUSIG?

- Take ICLUSIG exactly as your healthcare provider tells you to take it.
- Do not change your dose or stop taking ICLUSIG unless your healthcare provider tells you.
- Swallow ICLUSIG tablets whole. Do not crush, break, cut, chew or dissolve ICLUSIG tablets.
- Take ICLUSIG with or without food.
- Do not eat grapefruit or drink grapefruit juice during treatment with ICLUSIG.
- If you miss a dose of ICLUSIG, take your next dose at your regularly scheduled time the next day. Do not take 2 doses at the same time to make up for a missed dose.
- If you take too much ICLUSIG, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of ICLUSIG?
ICLUSIG may cause serious side effects, including:

- See **"What is the most important information I should know about ICLUSIG?"**
- **High blood pressure (hypertension).** High blood pressure is common during treatment with ICLUSIG and can also be serious or severe. ICLUSIG can cause new or worsening high blood pressure. Your blood pressure should be checked regularly, and any high blood pressure should be treated during treatment with ICLUSIG. Tell your healthcare provider right away if you get confusion, headaches, dizziness, chest pain or shortness of breath.
- **Inflammation of the pancreas (pancreatitis).** Pancreatitis is common during treatment with ICLUSIG and can also be serious or severe. Tell your healthcare provider right away if you get any of the following symptoms: sudden stomach-area pain or discomfort, nausea, and vomiting. Your healthcare provider should do blood tests to check for pancreatitis during treatment with ICLUSIG.
- **Neuropathy.** ICLUSIG may cause damage to the nerves in your arms, brain, hands, legs, or feet (neuropathy). Tell your healthcare provider right away if you get any of these symptoms during treatment with ICLUSIG:
  - muscle weakness, tingling, burning, pain, discomfort or loss of feeling in your hands and feet

- double vision and other problems with eyesight, trouble moving the eye, drooping of part of the face, sagging or drooping eyelids, or change in taste

- **Eye problems.** Serious eye problems that can lead to blindness or blurred vision may happen with ICLUSIG. Tell your healthcare provider right away if you get any of the following symptoms: bleeding in the eye, perceived flashes of light, light sensitivity, floaters, blurred vision, dry, inflamed, swollen, or itchy eyes, or eye pain. Your healthcare provider will monitor your vision before and during your treatment with ICLUSIG.
- **Bleeding.** Bleeding is common during treatment with ICLUSIG and can also be serious and may lead to death. Tell your healthcare provider right away if you get any signs of bleeding during treatment with ICLUSIG including:
  - vomiting blood or if your vomit 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
  - confusion
  - headache
  - change in speech
- **Fluid retention.** Your body may hold too much fluid (fluid retention) which can be serious and may lead to death. Tell your healthcare provider right away if you get any of these symptoms during treatment with ICLUSIG:
  - swelling of your hands, ankles, feet, face, or all over your body
  - weight gain
  - shortness of breath and cough
- **Irregular heartbeat.** ICLUSIG may cause an irregular heartbeat. Tell your healthcare provider right away if you experience loss of consciousness, fainting, dizziness, chest pain or palpitations.
- **Low blood cell counts.** ICLUSIG may cause low blood cell counts, which can be severe. Your healthcare provider will check your blood counts regularly during treatment with ICLUSIG. Tell your healthcare provider right away if you have a fever or any signs of an infection while taking ICLUSIG.
- **Tumor Lysis Syndrome (TLS).** TLS is caused by a fast breakdown of cancer cells. TLS can cause you to have kidney failure and the need for dialysis treatment, and an abnormal heartbeat. Your healthcare provider may do blood tests to check for TLS. Drink plenty of water during treatment with ICLUSIG to help reduce your risk of getting TLS. Call your healthcare provider or get emergency help right away if you get any of the following symptoms during treatment with ICLUSIG:
  - nausea and vomiting
  - weakness
  - swelling
  - shortness of breath
  - muscle cramps
  - seizures
- **Reversible Posterior Leukoencephalopathy Syndrome (RPLS – also known as Posterior Reversible Encephalopathy Syndrome).** ICLUSIG may trigger a condition called RPLS. Call your healthcare provider right away if you get headaches, seizures, confusion, changes in vision or problems thinking.
- **Wound healing problems.** Wound healing problems have happened in some people who take ICLUSIG. Tell your healthcare provider if you plan to have any surgery before or during treatment with ICLUSIG.
  - You should stop taking ICLUSIG at least 1 week before planned surgery.
  - Your healthcare provider should tell you when you may start taking ICLUSIG again after surgery.
- **A tear in your stomach or intestinal wall (perforation).** Tell your healthcare provider right away if you get:
  - severe pain in your stomach-area (abdomen)
  - swelling of the abdomen
  - high fever

The most common side effects of ICLUSIG when given alone include:

- skin rash
- joint pain
- stomach-area (abdomen) pain
- tiredness
- headache
- liver problems
- swelling of your hands, ankles, feet, face, or all over your body (fluid retention and edema)
- fever
- increase in lipase levels (a blood test done to check your pancreas)
- low hemoglobin in the blood (anemia)
- blood clots or blockage in blood vessels (arteries)
- irregular heartbeat
- low blood platelet counts

- constipation
- high blood pressure
- dry skin
- nausea
- bleeding
- low blood levels of white blood cells

The most common side effects of ICLUSIG when given with chemotherapy include:

- liver problems
- joint pain
- skin rash
- headache
- fever
- stomach-area (abdomen) pain
- constipation
- tiredness
- nausea
- mouth sores
- high blood pressure
- increase in lipase levels (a blood test done to check your pancreas)
- numbness or tingling (pins and needles), pain, or weakness in the hands or feet
- bleeding
- fever due to low white blood cell counts (febrile neutropenia)
- swelling of your hands, ankles, feet, face, or all over your body (fluid retention and edema)
- vomiting
- irregular heartbeat
- low blood levels of white blood cells
- low blood platelet counts
- low hemoglobin in the blood (anemia)
- changes in liver function tests

Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with ICLUSIG if you have certain side effects.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of ICLUSIG. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ICLUSIG?
Store ICLUSIG at room temperature between 68°F to 77°F (20°C to 25°C).

Keep ICLUSIG and all medicines out of the reach of children.

General information about the safe and effective use of ICLUSIG
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ICLUSIG for a condition for which it was not prescribed. Do not give ICLUSIG to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for information about ICLUSIG that is written for health professionals.

What are the ingredients in ICLUSIG?

Active ingredient: ponatinib

Inactive ingredients: lactose monohydrate, microcrystalline cellulose, sodium starch glycolate (type B), colloidal silicon dioxide and magnesium stearate. The tablet coating consists of talc, polyethylene glycol, polyvinyl alcohol and titanium dioxide.

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