

Patient Information Leaflet (PIL)
Iclusig 15 mg film-coated tablets
Iclusig 45 mg film-coated tablets
Ponatinib



- Have high blood pressure
- Have bleeding problems
- Plan to have any surgical procedures
- Are lactose (milk sugar) intolerant (Iclusig tablets contain lactose)
- Drink grapefruit juice
- Have any other medical conditions
- Are pregnant or plan to become pregnant. Iclusig can harm your unborn baby.
- Are you breast-feeding or do you plan to breast feed

Blood Tests and other health evaluations

Your doctor will perform:

- Evaluations of your heart function and the condition of your arteries and veins
- A complete blood count
This will be repeated every 2 weeks for the first 3 months after starting the therapy. Afterwards it is performed monthly or as indicated by the doctor
- Checks of the serum protein known as lipase
A serum protein called lipase will be checked every 2 weeks for the first 2 months, then as indicated by your doctor. A break in treatment or a decrease in dose may be required when lipase is increased
- Liver tests

Liver function tests will be performed at least monthly or as indicated by your doctor.

Children and adolescents

Do not give this medicine to children under 18 years because no data are available in children.

Taking Iclusig with other medicines, herbal or dietary supplements

Please tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. The following medicines can affect or be affected by Iclusig:

- **ketoconazole, itraconazole, voriconazole, posaconazole:** medicines to treat fungal infections
- **indinavir, nelfinavir, ritonavir, saquinavir,** medicine to treat HIV infections.
- **clarithromycin, telithromycin:** medicines to treat bacterial infections
- **nefazodone:** a medicine to treat depression.
- **St. John's wort:** a herbal product used to treat depression
- **carbamazepine:** a medicine to treat epilepsy, euphoric/depressive stages and certain pain conditions
- **phenytoin:** medicines to treat epilepsy
- **rifampicin:** medicines to treat tuberculosis or certain other infections
- **boceprevir, telaprevir:** medicines to treat hepatitis C
- **conivaptan:** a medicine to treat low sodium levels

Iclusig with food and drink

While taking Iclusig, avoid grapefruit products such as grapefruit juice.

Iclusig may be taken with or without foods.

Pregnancy and breast-feeding

If you are pregnant, or are planning to become pregnant, tell your doctor before you take Iclusig.

Verify the pregnancy status of females of reproductive potential prior to initiating Iclusig treatment.

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 doctor or pharmacist 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 doctor if this is a concern for you.

Breast-feeding:

- It is not known if Iclusig passes into your breast milk. **Do not** breastfeed during treatment and for **6 days** after your last dose of Iclusig

For men:

- Men receiving treatment with Iclusig are advised not to father a child during treatment. Effective contraception must be used during treatment.

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

Driving and using machines

You should take special care when driving and using machines as patients taking Iclusig may experience visual disturbance, dizziness, sleepiness, and tiredness.

Important information about some of the ingredients of Iclusig

Iclusig contains lactose. If you have been told by your doctor or pharmacist that you have an intolerance to milk sugar (lactose) contact your doctor or pharmacist before taking this medicine.

4. HOW TO TAKE ICLUSIG

Always take Iclusig exactly as your doctor or pharmacist has told you. You should check with your doctor or pharmacist if you are not sure.

The usual dose is

- A 45 mg film-coated tablet for the recommended dose.
- A 15 mg film-coated tablet to allow for dose adjustments

The recommended starting dose is one 45 mg film-coated tablet once daily.

Your doctor may reduce your dose or tell you to temporarily stop taking Iclusig if:

- An appropriate response to the treatment is reached
- The number of white blood cells called neutrophils is reduced
- The number of blood platelets is reduced
- A severe side effect occurs, not affecting the blood
 - Pancreas inflammation
 - Increased levels of the serum protein lipase
- You develop heart or blood vessel problems
- You have a liver disorder

Iclusig use may be resumed at the same, or a reduced dose, after the event is resolved or controlled. Your doctor may evaluate your response to the treatment at regular intervals.

Instructions for proper use:

- Swallow the tablets whole. The tablets can be taken with or without food. Do not crush or dissolve the tablets. Do not swallow the desiccant canister contained in the bottle.

Frequency of administration:

Make sure you take Iclusig daily for as long as it is prescribed. This is a long-term treatment.

If you take more Iclusig than you should

Talk to your doctor immediately if this occurs.

If you forget to take Iclusig

Do not take a double dose to make up for a forgotten dose. Take your next dose at your regular time.

If you stop taking Iclusig

Do not stop taking Iclusig without your doctor

If you have any further questions on the use of this product, ask your doctor or pharmacist.

5. POSSIBLE SIDE EFFECTS

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

Serious side effects (very common: affects more than 1 to 10 users):

- **Blood clots or blockage in your blood vessels (arteries and veins).** A blood clot or blockage in your blood vessels can prevent proper blood flow to your heart, brain or other parts of your body and may lead to tissue death, heart attack, stroke or death.
- **High blood pressure.** Your blood pressure should be checked regularly and any high blood pressure should be treated while you are taking Iclusig. Tell your doctor if you get confusion, headaches, dizziness, chest pain or shortness of breath.
- **Neuropathy.** Iclusig may cause damage to the nerves in your arms, brain, hands, legs, or feet (neuropathy). Tell your doctor if you get any of these symptoms during treatment with Iclusig:
 - Muscle weakness, tingling, burning, pain and 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, change in taste
- **Effects on the eye.** Serious eye problems that can lead to blindness or blurred vision may happen with Iclusig. Tell your doctor if you get any of the following symptoms: bleeding in the eye, perceived flashes of light, light sensitivity, floaters, dry inflamed, swollen or itchy eyes and eye pain. Your doctor will monitor your vision before and during your treatment with Iclusig
- **Low blood cell counts.** Iclusig may cause low blood cell counts. Your doctor will check your blood counts regularly during treatment with Iclusig. Tell your doctor right away if you have a fever or any signs of an infection while taking Iclusig.
 - Decreased number of red blood cells (symptoms include: weakness, dizziness, fatigue)
 - Decreased number of blood platelets (symptoms include: increased tendency to bleed or bruise)
 - Decreased number of white blood cells called neutrophils (symptoms include: increase tendency for infection).
- **Bleeding.** Iclusig can cause bleeding which can be serious and may lead to death. Tell your doctor 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
- **Liver problems.** Iclusig can cause liver problems, including liver failure. Get medical help right away if you get any of these symptoms:
 - Yellowing of your skin or the white part of your eyes (jaundice)
 - Dark "tea-colored" urine
 - Sleepiness
 - Loss of appetite
 - Bleeding or bruising

Serious side effects (common: affects 1 to 10 users in 100):

- **Inflammation of the pancreas (pancreatitis).** Symptoms include sudden stomach-area pain, nausea, and vomiting. Your doctor should do blood tests to check for pancreatitis during treatment with Iclusig.
- **Fever,** often with other signs of infection due to decreased number of white blood cells
- **Fluid retention.** Your body may hold too much fluid (fluid retention). Tell your doctor 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
- **Heart problems and irregular heartbeat.** Iclusig can cause heart problems, including heart failure. Iclusig may also cause an irregular heartbeats and heart attack. Tell your doctor right away if you experience loss of consciousness, faintness, dizziness, chest pain, palpitations.

Serious side effects (Not known: frequency cannot be estimated from the available data)

- **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
 - An abnormal heartbeat

Your doctor may do blood tests to check for TLS

- **Posterior reversible encephalopathy syndrome (PRES).** Iclusig may trigger a condition called PRES. Call your doctor right away if you get headaches, seizures, confusion, changes in vision, problems thinking.
- **Possible wound healing problems.** If you need to have a surgical procedure, tell your doctor that you are taking Iclusig. You should stop taking Iclusig at least 1 week before any planned surgery.
- **A tear in your stomach or intestinal wall (perforation).** Tell your doctor right away if you get:

- Severe pain in your stomach-area (abdomen)
- Swelling of the abdomen
- High fever

Other possible side effects that may occur with the following frequencies are:

Very common side effects (affects more than 1 per 10 users):

- Arterial ischemia
- Abdominal pain
- Constipation
- Nausea
- Diarrhea
- Vomiting
- Sores in the mouth and mouth pain
- Urinary tract infection
- Upper airway infection
- Headache
- Dizziness
- Cough
- Breathing difficulties
- Rash and related conditions
- Dry skin
- Itchy skin
- Joint pain
- Muscle pain
- Muscle spasms
- Pain in arms or legs
- Back pain
- Bone pain
- Fatigue
- Fever Pyrexia
- Common cold
- Decreased appetite
- Insomnia
- Increased blood levels of several liver enzymes called:
 - Alanine aminotransferase
 - Aspartate aminotransferase
 - Alkaline phosphatase
- Decreased blood levels of several liver enzymes called:
 - Albumin
 - bilirubin
- Anaemia
- Decreases in blood cell counts
- Increased blood levels of several pancreatic enzymes called:
 - Lipase
 - Amylase
- Changes in blood levels of:
 - Phosphorus (decreased)
 - Calcium (increased or decreased)
 - Sodium (increased or decreased)
 - Glucose (increased or decreased)
 - Potassium (increased or decreased)
 - Creatinine (increased)

Common side effects (affects more than 1 per 100 users)

- Cardiac failure
- Bacteria in the blood
- Pneumonia
- Swollen, or red area of skin that feels hot and tender
- Erythema
- Hair loss
- musculoskeletal pain
- Chills
- Weight loss
- Increased blood levels of triglycerides

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

6. HOW TO STORE ICLUSIG

Keep Iclusig out of the reach and sight of children.

Do not store Iclusig above 30°C. Store in the original container.

The bottle contains one sealed plastic canister containing a desiccant canister. Keep the canister in the bottle. Do not swallow the desiccant canister.

Do not use Iclusig after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

7. CONTENTS OF THE PACK AND OTHER INFORMATION

What Iclusig contains

The active substance is ponatinib.

Each 15 mg film-coated tablet contains 15 mg ponatinib (as ponatinib hydrochloride).

Each 45 mg film-coated tablet contains 45 mg ponatinib (as ponatinib hydrochloride).

The other ingredients are 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.

What Iclusig looks like and contents of the pack

Iclusig film-coated tablets are white and round.

Iclusig 15 mg film-coated tablets are approximately 6 mm in diameter with "A5" on one side, and plain on the other side.

Iclusig 45 mg film-coated tablets are approximately 9 mm in diameter with "AP4" on one side and plain on the other side

Iclusig is available in plastic bottles, each containing one desiccant canister and induction sealed child resistant closure.

Bottles are packed within a cardboard box.

Bottles of Iclusig 15 mg contain 30 film-coated tablets.

Bottles of Iclusig 45 mg contain 30 film-coated tablets.

Manufacturer and batch release site:

Patheon Inc.

2100 Syntex Court,

Mississauga, ON, L5N 7K9

Canada

Marketing Authorisation Holder:

ARIAD Pharmaceuticals, Inc. (A Wholly-Owned Subsidiary of Takeda Pharmaceutical Co. Ltd).

40 Landsdowne Street

Cambridge, MA, 02139

United States

Biologix FZ Co is responsible for distribution and drug safety in selected countries of the Middle East.

Biologix FZ Co

Dubai Free Zone, Road WB 21, Warehouse,

C17 PO Box 54405, Al Tawar Dubai,

United Arab Emirates

This leaflet was last approved in {12/2017}; version number 01

For any information about this medicinal product, please contact the local representative of the

Marketing Authorisation Holder:

Biologix FZ Co

Dubai Free Zone, Road WB 21, Warehouse, C17 PO Box 54405,

Al Tawar Dubai, United Arab Emirates

Telephone no.: 00971 4 299 7171

To report any side effect(s):

- **Saudi Arabia:**

- The National Pharmacovigilance and Drug Safety Center (NPC)
 - Fax: +966-11-205-7662
 - Call NPC at +966-11-2038222, Exts: 2317-2356-2340
 - Toll free phone: 8002490000
 - E-mail: npc.drug@sfda.gov.sa
 - Website: www.sfda.gov.sa/npc

- **UAE Ministry of Health**

- Pharmacovigilance and Medical Device Section
Drug Department and Prevention

UAE MOH

Hotline : 800111111

Email : pv@moh.gov.ae

P.O. Box : 1853 Dubai UAE

- **Other GCC States:**

- Please contact the relevant competent authority.

ARIAD Pharmaceuticals, Inc. (A Wholly-Owned Subsidiary of Takeda Pharmaceutical Co. Ltd).

This is a Medicament

- A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the - pharmacist who sold the medicament.

- The doctor and the pharmacist are the experts in medicines, their benefits and risks.

- Do not by yourself interrupt the period of treatment prescribed for you.

- Do not repeat the same prescription without consulting your doctor.

- Keep all medicaments out of the reach of children.

Council of Arab Health Ministers

Union of Arab Pharmacists