



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Iclusig (*ponatinib*)

An overview of Iclusig and why it is authorised in the EU

What is Iclusig and what is it used for?

Iclusig is a cancer medicine used to treat adults with the following types of leukaemia (cancer of white blood cells):

- chronic myeloid leukaemia (CML) at any stage of the disease (chronic, accelerated or blast phase), when treatment with dasatinib or nilotinib (cancer medicines) has not worked, or when these medicines cannot be used because of side effects and imatinib (a cancer medicine) is not suitable, or when the cancer has a change in the *BCR-ABL1* gene called T315I mutation;
- acute lymphoblastic leukaemia (ALL) when the cancer is Philadelphia chromosome-positive (Ph+). Ph+ means that some of the patient's genes have rearranged to form an abnormal chromosome that leads to the development of leukaemia. Iclusig is used when treatment with dasatinib has not worked, or when dasatinib cannot be used because of side effects and imatinib is not suitable, or when the cancer has a change in the *BCR-ABL1* gene called T315I mutation;
- newly diagnosed acute lymphoblastic leukaemia when the cancer is Ph+. Iclusig is used together with reduced-intensity chemotherapy, which is less toxic than standard chemotherapy.

Iclusig contains the active substance ponatinib.

How is Iclusig used?

Iclusig can only be obtained with a prescription, and treatment should be started by a doctor who is experienced in the diagnosis and treatment of leukaemia.

Iclusig is available as tablets to be taken by mouth once per day. Treatment is continued for as long as the patient benefits. If a patient develops certain severe side effects, the doctor may decide to reduce the dose or stop treatment temporarily or permanently. Patients with newly diagnosed Ph+ ALL first receive Iclusig together with reduced-intensity chemotherapy, and then Iclusig on its own.

Because Iclusig can cause blood clots or blockages in arteries and veins, the doctor should assess the patient's heart and blood vessels health before starting and during treatment. Treatment should be stopped immediately if a blockage develops in an artery or vein.

For more information about using Iclusig, see the package leaflet or contact your doctor or pharmacist.

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How does Iclusig work?

The active substance in Iclusig, ponatinib, belongs to a group of medicines called 'tyrosine kinase inhibitors'. These compounds act by blocking enzymes known as tyrosine kinases. Ponatinib acts by blocking a tyrosine kinase called BCR-ABL. This enzyme is found on the surface of leukaemia cells where it is involved in stimulating the cells to divide uncontrollably. By blocking BCR-ABL, Iclusig helps to control the growth and spread of leukaemia cells.

What benefits of Iclusig have been shown in studies?

Iclusig has been investigated in one main study involving 449 patients with CML or Ph+ ALL and who were intolerant or resistant to treatment with dasatinib or nilotinib, or had the T315I mutation. In the study, Iclusig was not compared with another treatment. The response to treatment was assessed by measuring the proportion of patients who had a major haematological response (when the number of white blood cells returns to normal or there is no evidence of leukaemia) or a major cytogenetic response (when the proportion of white blood cells containing the Philadelphia chromosome falls to below 35%).

The study showed that treatment with Iclusig led to clinically relevant responses in all groups of patients. Among patients with CML in the chronic phase, around 54% (144 out of 267) had a major cytogenetic response. In the accelerated phase, around 58% (48 out of 83) had a major haematological response, while in the blast phase, around 31% (19 out of 62) had a major haematological response. Among patients with Ph+ ALL, around 41% (13 out of 32) had a major haematological response.

A main study involving 245 adults showed that Iclusig in combination with reduced-intensity chemotherapy is effective in treating Ph+ ALL. In this study, participants received reduced-intensity chemotherapy with either Iclusig or imatinib (another tyrosine kinase inhibitor).

The main measure of effectiveness was the proportion of participants who had a complete response (no detectable signs of cancer) and no minimal residual disease (when a very small number of cancer cells remain in the body after treatment). At the end of induction treatment with Iclusig and reduced-intensity chemotherapy, about 34% of participants (53 out of 154) had a complete response with no minimal residual disease, compared with about 17% of participants (13 out of 78) treated with imatinib and reduced-intensity chemotherapy. Information on how long patients lived overall was not yet available.

What are the risks associated with Iclusig?

For the full list of side effects and restrictions with Iclusig, see the package leaflet.

The most common serious side effects with Iclusig (which may affect more than 2 in 100 people) include pneumonia (infection of the lungs), pancreatitis (inflammation of the pancreas), pyrexia (fever), abdominal (belly) pain, myocardial infarction (heart attack), atrial fibrillation (irregular and uncoordinated contractions of the upper chambers of the heart), peripheral arterial occlusive disease (problem with blood flow in the arteries), anaemia (low levels of red blood cells), angina pectoris (pains to the chest, jaw and back due to problems with blood flow to the heart), decreased blood levels of platelets (components that help the blood to clot), febrile neutropenia (fever with a low level of neutrophils, a type of white blood cell), hypertension (high blood pressure), coronary artery disease (heart disease caused by narrowing or blockage of blood vessels supplying the heart muscle), congestive cardiac failure (when the heart does not work as well as it should), cerebrovascular

accident (stroke), sepsis (when bacteria and their toxins circulate in the blood, leading to organ damage), cellulitis (inflammation of the deep skin tissue), acute kidney injury (kidney damage), urinary tract infection (infection of the parts of the body that collect and pass out urine) and increased levels of lipase (an enzyme).

Arterial occlusions (clots or blockages in the arteries) may affect more than 1 in 5 people, with serious arterial occlusions affecting 1 in 5 people. Serious venous occlusions (clots or blockages in the veins) may affect up to 1 in 20 people. Venous thromboembolic reactions (problems due to blood clots in the veins) may affect up to 1 in 10 people.

Why is Iclusig authorised in the EU?

The European Medicines Agency decided that Iclusig's benefits are greater than its risks and it can be authorised for use in the EU. Iclusig was shown to be an effective treatment for patients with CML or Ph+ ALL who have limited treatment options.

Regarding safety, the side effects with Iclusig were broadly similar to those of other tyrosine kinase inhibitors and mostly manageable with dose reduction or dose delay. There is a risk of problems resulting from blood clots or blockages in arteries or veins with Iclusig, including heart attacks and strokes. This risk can be reduced by identifying and treating conditions that may contribute to the risk, both before and during treatment. These conditions include high blood pressure and raised cholesterol.

What measures are being taken to ensure the safe and effective use of Iclusig?

The company that markets Iclusig must submit the final results of the study in people with newly diagnosed Ph+ ALL to confirm its safety and effectiveness.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Iclusig have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Iclusig are continuously monitored. Side effects reported with Iclusig are carefully evaluated and any necessary action taken to protect patients.

Other information about Iclusig

Iclusig received a marketing authorisation valid throughout the EU on 1 July 2013.

Further information on Iclusig can be found on the Agency's website:

<https://www.ema.europa.eu/en/medicines/human/EPAR/clusig>.

This overview was last updated in 03-2026.