



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EPAR summary for the public

Iclusig

ponatinib

This is a summary of the European public assessment report (EPAR) for Iclusig. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Iclusig.

For practical information about using Iclusig, patients should read the package leaflet or contact their doctor or pharmacist.

What is Iclusig and what is it used for?

Iclusig is a cancer medicine that contains the active substance ponatinib. It is used to treat adults with the following types of leukaemia (cancer of the white blood cells):

- chronic myeloid leukaemia (CML) in its different stages known as chronic, accelerated and blast phases;
- acute lymphoblastic leukaemia (ALL) in patients who are 'Philadelphia-chromosome positive' (Ph+). Ph+ means that some of the patient's genes have rearranged themselves to form a special chromosome called the Philadelphia chromosome that leads to the development of leukaemia. The Philadelphia-chromosome is found in some ALL patients and is present in most patients with CML.

Iclusig is used in patients who cannot tolerate or do not respond to dasatinib or (for patients with CML) nilotinib, which are other cancer medicines of the same class, and in whom subsequent treatment with imatinib (a third such medicine) is not considered appropriate. It is also used in patients who have a genetic mutation called 'T315I mutation' which makes them resistant to treatment with imatinib, dasatinib or nilotinib.

Because the numbers of patients with CML and ALL are low, the diseases are considered 'rare', and Iclusig was designated an 'orphan medicine' (a medicine used in rare diseases) on 2 February 2010.



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 (15 mg, 30 mg and 45 mg). The recommended starting dose is 45 mg once per day. Treatment is continued until either the disease gets worse or until the patient cannot tolerate the medicine any longer. The doctor should consider stopping treatment if a complete haematological response (a return to normal of the number of white cells in the blood) is not obtained within three months.

Iclusig can lead to clots or blockages in arteries and veins and patients should have the condition of their heart and circulation considered before starting and during treatment, and be treated appropriately for any problems. The dose may need to be reduced or interrupted if the patient experiences certain side effects; it should be interrupted immediately if a blockage develops in an artery or vein. For further information, see the summary of product characteristics (also part of the EPAR).

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 in some receptors 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 results of the study showed that treatment with Iclusig led to clinically relevant responses in all groups of patients:

- among the patients with CML in the chronic phase, around 54% (144 out of 267) had a major cytogenetic response;
- among the patients with CML in the accelerated phase, around 58% (48 out of 83) had a major haematological response;
- among the patients with CML in the blast phase, around 31% (19 out of 62) had a major haematological response;
- among the patients with with Ph+ ALL, around 41% (13 out of 32) had a major haematological response.

What are the risks associated with Iclusig?

The most common serious side effects with Iclusig (which may affect more than 1 in 100 people) are pneumonia (infection of the lungs), pancreatitis (inflammation of the pancreas), pyrexia (fever), abdominal pain (stomach ache), myocardial infarction (heart attack), atrial fibrillation (irregular rapid contractions of the upper chambers of the heart), anaemia (low red blood cell counts), decreased blood levels of platelets (components that help the blood to clot), febrile neutropenia (low white blood cell counts with fever), cardiac failure (when the heart does not work as well as it should), increased levels of lipase (an enzyme), dyspnoea (difficulty breathing), diarrhoea, decreased levels of neutrophils (a type of white blood cell), pancytopenia (low overall blood cell counts) and pericardial effusion (fluid around the heart). In clinical studies, after over 3 years (40 months) of treatment arterial and venous occlusive adverse events (clots or blockages in the arteries or veins) occurred in 23% of patients, with serious adverse events occurring in 18% of patients.

The most common side effects of any kind (which may affect more than 2 in 10 people) are decreased levels of platelets, rash, dry skin and abdominal pain. For the full list of all side effects and restrictions with Iclusig, see the package leaflet.

Why is Iclusig approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Iclusig's benefits are greater than its risks and recommended that it be approved for use in the EU. The CHMP noted that Iclusig was shown to be an effective treatment for those patients with CML or Ph+ ALL who have limited treatment options. Regarding its safety, the side effects with Iclusig were largely similar to other tyrosine kinase inhibitors and mostly manageable with dose reduction or dose delay. The risk of problems (including heart attacks and strokes) resulting from blood clots or blockages in arteries or veins could be reduced by checking for and treating contributory conditions such as high blood pressure and raised cholesterol both before and during treatment.

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

A risk management plan has been developed to ensure that Iclusig is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Iclusig, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that markets Iclusig will provide educational material for all doctors who are expected to prescribe this medicine highlighting important risks for which monitoring and dose adjustments are recommended. Also, the company will conduct a study in order to determine the best starting dose of Iclusig and to assess the safety and effectiveness of Iclusig following dose reduction in patients with chronic phase CML who achieve major cytogenetic response.

Other information about Iclusig

The European Commission granted a marketing authorisation valid throughout the European Union for Iclusig on 1 July 2013.

The full EPAR for Iclusig can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_public_assessment_reports. For more information about treatment with Iclusig, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summaries of the opinion of the Committee for Orphan Medicinal Products for Iclusig can be found on the Agency's website:

- [CML](#);
- [ALL](#).

This summary was last updated in 11-2015.