

New Labeling and Safety Information for Iclusig[®] (ponatinib)

Iclusig[®] (ponatinib)

- Revised indications
- New safety information about risk of vascular occlusion
- New dosing considerations

REVISED INDICATIONS

The indications have been limited to:

- Treatment of adult patients with T315I-positive chronic myeloid leukemia (CML) (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
- Treatment of adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia or Ph+ ALL for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated

UPDATED SERIOUS RISK OF VASCULAR OCCLUSION IN BOXED WARNING

Arterial and venous thrombosis and occlusions have occurred in at least **27%** of all Iclusig clinical trial patients, including:

- Fatal myocardial infarction
- Stroke
- Stenosis of large arterial vessels of the brain
- Severe peripheral vascular disease, and
- Need for urgent revascularization procedures

Iclusig can cause fatal and life-threatening vascular occlusion within 2 weeks of starting treatment. Patients with and without cardiovascular risk factors, including patients less than 50 years old, experienced these events. Monitor for evidence of thromboembolism and vascular occlusion. Interrupt or stop Iclusig immediately for vascular occlusion (see Table 1).

Table 1: Vascular Occlusion Incidence in Iclusig-Treated Patients in Phase 2 Trial According to Risk Categories

	Prior history of ischemia, hypertension, diabetes, or hyperlipidemia	No history of ischemia, hypertension, diabetes, or hyperlipidemia
Age: 49 or younger	18% (6/33)	12% (13/112)
Age: 50 to 74 years	33% (50/152)	18% (20/114)
Age: 75 and older	56% (14/25)	46% (6/13)
All age groups	33% (70/210)	16% (39/239)
Total	24% (109/449)	

DOSING CONSIDERATIONS

Optimal dosing has not been identified.

In clinical trials, the starting dose of Iclusig was 45 mg administered orally once daily. However, 59% of the patients required dose reductions to 30 mg or 15 mg once daily during the course of therapy.

Start dosing with 45 mg once daily. Consider reducing the dose of Iclusig for chronic phase CML (CP-CML) and accelerated phase CML (AP-CML) patients who have achieved a major cytogenetic response.

Consider discontinuing Iclusig if response has not occurred by 3 months (90 days).

Do not restart Iclusig in patients with arterial or venous occlusive reactions unless the potential benefit outweighs the risk of recurrent arterial or venous occlusions and the patient has no other treatment options.

OTHER SERIOUS RISKS INCLUDED IN THE BOXED WARNING

- **Heart failure**, including fatalities, occurred in 8% of Iclusig-treated patients.
Monitor cardiac function. Interrupt or stop Iclusig for new or worsening heart failure
- **Hepatotoxicity**, liver failure and death have occurred in Iclusig-treated patients.
Monitor hepatic function. Interrupt Iclusig if hepatotoxicity is suspected

WHAT IS THE ICLUSIG REMS?

A REMS (**R**isk **E**valuation and **M**itigation **S**trategy) is a program required by the FDA to manage known or potential serious risks associated with a drug product. The purpose of the Iclusig REMS is to inform Healthcare Providers of new important safety information in the revised Iclusig label, including serious risks of Iclusig. This fact sheet is required by the FDA as part of the Iclusig REMS program.

Please visit www.iclusigREMS.com for further information.

This fact sheet does not contain the complete safety profile for Iclusig. Please see the Prescribing Information, including Boxed Warning and Medication Guide.

REPORTING ADVERSE EVENTS

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088. Healthcare Providers should report all suspected adverse events associated with Iclusig to the FDA or to ARIAD at 1-855-552-7423 or send the information to ARIAD at medinfo@ariad.com.



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