BlueCross BlueShield Federal Employee Program

ICLUSIG
(ponatinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Iclusig (ponatinib) is a kinase inhibitor used to treat certain patients with either chronic myeloid leukemia (CML) or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL). Patients with either condition are classified into 3 groups that help predict outlook: chronic phase, accelerated phase or blast phase. Treatment with Iclusig medication can be used in any of these three phases but should be strictly reserved for patients whose disease is either T315I-positive, resistant or intolerant to at least two prior kinase inhibitors or for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated (1).

Regulatory Status

FDA-approved indications: Iclusig is a kinase inhibitor indicated for the treatment of adult patients with: (1)

1. Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia (Ph+ALL)
    - Newly diagnosed Ph+ALL, in combination with chemotherapy
    - As monotherapy in Ph+ALL for whom no other kinase inhibitors are indicated or T315I-positive Ph+ALL

2. Chronic Myeloid Leukemia (CML)
    - Chronic phase (CP) CML with resistance or intolerance to at least two prior kinase inhibitors
    - Accelerated phase (AP) or blast phase (BP) CML for whom no other kinase inhibitors are indicated
    - T315I-positive CML (chronic phase, accelerated phase, or blast phase)

<u>Limitations of Use:</u>

Iclusig is not indicated and is not recommended for the treatment of patients with newly diagnosed CP-CML (1).

Iclusig has a boxed warning alerting patients and healthcare professionals that arterial and venous thrombosis and occlusions have occurred in Iclusig-treated patients, including fatal myocardial infarction, stroke, stenosis of large arterial vessels of the brain, severe peripheral vascular disease, and the need for urgent revascularization procedures. 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 and interrupt or discontinue Iclusig based on severity (1).

Heart failure, including fatalities, occurred in Iclusig-treated patients. Monitor cardiac function and interrupt or discontinue Iclusig for new or worsening heart failure (1).

Hepatotoxicity, liver failure and death have occurred in Iclusig-treated patients. Monitor hepatic function and interrupt or discontinue Iclusig based on severity (1).

Iclusig can cause fetal harm. Females of reproductive potential should be advised to use effective contraception during treatment with Iclusig and for 3 weeks after the last dose (1).

The safety and efficacy of Iclusig in patients less than 18 years of age have not been established (1).

Summary

Iclusig is a kinase inhibitor that is indicated for the treatment of chronic myelogenous leukemia (CML) and Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL). Iclusig has boxed warnings addressing arterial and venous thrombosis, vascular occlusion, heart failure, and hepatotoxicity that warrant close monitoring. The safety and efficacy of Iclusig in patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Iclusig while maintaining optimal therapeutic outcomes.

References

1. Iclusig [package insert]. Lexington, MA; Takeda Pharmaceuticals America, Inc.; March 2024.
2. NCCN Drugs & Biologics Compendium® Ponatinib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 13, 2025.