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5.21.030

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	January 1, 2013
Subject:	Iclusig	**Page:**	1 of 6

Last Review Date: June 13, 2024

Iclusig

Description

Iclusig (ponatinib)

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)

Limitations of Use:
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).

Related policies
Bosulif, Gleevec, Scemblix, Sprycel, Tasigna

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Iclusig may be considered **medically necessary** if the conditions indicated below are met.

Iclusig may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   a. Used as monotherapy

2. Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   a. No other tyrosine kinase (TKI) therapy is indicated
   b. Used as monotherapy

3. Newly-diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   a. Used in combination with chemotherapy

4. T315I-positive chronic myeloid leukemia (CML)
   a. At least 6 months prior to request for treatment

5. Chronic phase (CP) chronic myeloid leukemia (CML)
   a. Resistant or intolerant to at least two prior tyrosine kinase inhibitors

6. Accelerated phase (AP) or blast phase (BP) chronic myeloid leukemia (CML)
   a. No other tyrosine kinase (TKI) therapy is indicated

AND ALL of the following:

a. Prescriber agrees to monitor for evidence of thromboembolism and vascular occlusion
b. Cardiac function will be monitored
c. Hepatic function will be monitored
d. Complete blood count will be monitored
e. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Iclusig and for 3 weeks after the final dose

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   a. Used as monotherapy

2. Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   a. No other tyrosine kinase (TKI) therapy is indicated
   b. Used as monotherapy

3. Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   a. Used in combination with chemotherapy

4. T315I-positive chronic myeloid leukemia (CML)

5. Chronic phase (CP) chronic myeloid leukemia (CML)
   a. Resistant or intolerant to at least two prior tyrosine kinase inhibitors

6. Accelerated phase (AP) or blast phase (BP) chronic myeloid leukemia (CML)
   a. No other tyrosine kinase (TKI) therapy is indicated

AND NONE of the following:
   a. Thromboembolic events or vascular occlusions while being treated with Iclusig
   b. Heart failure while being treated with Iclusig
   c. Hepatotoxicity while being treated with Iclusig

AND ALL of the following:
   a. Complete blood count will be monitored
   b. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Iclusig and for 3 weeks after the final dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 45 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

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 2024. National Comprehensive Cancer Network, Inc. Accessed on May 14, 2024.

Policy History

Date	Action
December 2012	New addition
March 2013	Annual review
December 2013	Criteria revised with new boxed warnings and requirements for T315I-positive chronic myeloid leukemia (CML)

March 2015	Annual review and reference update
December 2015	Annual editorial review
June 2016	Annual editorial review and reference update Addition of at least 6 months prior to request for treatment to CML Policy code changed from 5.04.30 to 5.21.30
March 2017	Annual editorial review and reference update Addition of no dual therapy with another tyrosine kinase inhibitor and addition of the age requirement in the renewal section
June 2018	Annual editorial review and reference update Addition of quantity limits to criteria
June 2019	Annual review and reference update
June 2020	Annual editorial review and reference update. Removed no dual therapy with another TKI requirement
January 2021	Updated chronic phase CML requirement to include resistance to at least two prior TKI. Clarified requirement for AP-CML, BP-CML and Ph+ ALL specifying that it is to be used when no other TKI is indicated. Added CBC monitoring requirement. Updated pregnancy requirement. Added 10 mg tablets to PA quantity limit table
March 2021	Annual review
March 2022	Annual editorial review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.21.030
June 2023	Annual review and reference update
December 2023	Annual review and reference update
April 2024	Per PI update, added indication of newly diagnosed Ph+ ALL, and monotherapy for Ph+ ALL for whom no other kinase inhibitors are indicated or T315I-positive Ph+ALL
June 2024	Annual editorial review and reference update. Changed quantity limit to MDDL dosing at 45 mg per day

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.