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5.21.030

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

Last Review Date: December 8, 2023

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: (1)

1. Treatment of adult patients with chronic phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to at least two prior kinase inhibitors

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

3. Treatment of adult patients with T315I-positive chronic myeloid leukemia (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)

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 is 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 chronic myeloid leukemia (CML)
   a. At least 6 months prior to request for treatment

2. T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)

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

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

5. Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   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 chronic myeloid leukemia (CML)

2. T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)

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

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

5. Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
   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

Strength	Quantity
10 mg	270 tablets per 90 days **OR**
15 mg	270 tablets per 90 days **OR**
30 mg	90 tablets per 90 days **OR**
45 mg	90 tablets per 90 days

Maximum daily limit of any combination: 45 mg
*** Quantity limits listed above must be used to achieve dose optimization**
**Utilizing the highest strengths available to achieve the dosage is recommended to minimize dosing errors and improve compliance

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.; February 2022.
2. NCCN Drugs & Biologics Compendium® Ponatinib 2023. National Comprehensive Cancer Network, Inc. Accessed on October 13, 2023.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.