Iclusig

Description

Iclusig (ponatinib)

Background
Iclusig is an orally administered 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 and for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated (1).

Regulatory Status
FDA-approved indication: Iclusig is a kinase inhibitor indicated for: (1)

1. 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)
2. 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

Limitations of use:
Iclusig is not indicated and is not recommended for the treatment of patients with newly diagnosed chronic phase CML (1).
These indications are based upon response rate. There are no trials verifying an improvement in disease-related symptoms or increased survival with Iclusig (1).

Iclusig has a boxed warning alerting patients and healthcare professionals that arterial and venous thrombosis and occlusions have occurred in at least 27% of 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 stop Iclusig immediately for vascular occlusion (1).

Heart failure, including fatalities, occurred in 8% of Iclusig treated patients. Monitor cardiac function and interrupt or stop Iclusig for new or worsening heart failure (1).

Hepatotoxicity, liver failure and death have occurred in Iclusig treated patients. Monitor hepatic function and interrupt Iclusig if hepatotoxicity is suspected (1).

Iclusig is classified as pregnancy category D. Females of reproductive potential should be advised to avoid pregnancy while being treated with Iclusig. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus (1).

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

Related policies
Blincyto, Bosulif, Erwinaze, Iclusig, Introns A, Marqibo, Sprycel, Synribo

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 in patients who are 18 years of age or older with one of the following: T315I-positive chronic myeloid leukemia (CML), T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL), CML for whom no other tyrosine kinase inhibitor therapy is indicated, or Ph+ALL for whom no other tyrosine kinase inhibitor therapy is indicated. Patients must also be monitored for thromboembolic events, vascular occlusions, as well as monitoring cardiac and hepatic function during treatment with Iclusig.
Iclusig is considered **investigational** in patients who are less than 18 years of age and 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) at least 6 months prior to request for treatment
2. T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
3. CML for whom no other tyrosine kinase inhibitor therapy is indicated, defined as disease that was resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy
4. Ph+ALL for whom no other tyrosine kinase inhibitor therapy is indicated, defined as disease that was resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy

**AND ALL** of the following:

a. Will be monitored for evidence of thromboembolism and vascular occlusion
b. Cardiac function will be monitored
c. Hepatic function will be monitored

**Prior – Approval Renewal Requirements**

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. CML for whom no other tyrosine kinase inhibitor therapy is indicated, defined as disease that was resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy

4. Ph+ALL for whom no other tyrosine kinase inhibitor therapy is indicated, defined as disease that was resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy

**AND ALL** if the following:

a. Has not had any thromboembolic events or vascular occlusions while being treated with Iclusig
b. Has not had developed any heart failure while being treated with Iclusig
c. Has not had developed any hepatotoxicity while being treated with Iclusig

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**Policy Guidelines**

**Pre - PA Allowance**

None

**Prior - Approval Limits**

Duration 12 months

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**Prior – Approval Renewal Limits**

Duration 12 months

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**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 (1).

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

**References**

**Policy History**

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<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>December 2012</td>
<td>New addition</td>
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<tr>
<td>March 2013</td>
<td>Annual review</td>
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<tr>
<td>December 2013</td>
<td>Criteria revised with new boxed warnings and requirements for T315I-positive chronic myeloid leukemia (CML)</td>
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<tr>
<td>March 2015</td>
<td>Annual review and reference update</td>
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<tr>
<td>December 2015</td>
<td>Annual editorial review</td>
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<tr>
<td>June 2016</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td></td>
<td>Addition of at least 6 months prior to request for treatment to CML</td>
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<td>Policy code changed from 5.04.30 to 5.21.30</td>
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**Keywords**

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 24, 2016 and is effective on July 1, 2016.

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