Clinical Pharmacy Program Guidelines for Iclusig

<table>
<thead>
<tr>
<th>Program</th>
<th>Prior Authorization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication</td>
<td>Iclusig® (ponatinib)</td>
</tr>
<tr>
<td>Markets in Scope</td>
<td>Arizona, California, Florida-CHIP, Hawaii, Maryland, Nevada, New York, New York EPP, Ohio, Rhode Island, Pennsylvania, New Jersey</td>
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<tr>
<td>Issue Date</td>
<td>3/2014</td>
</tr>
<tr>
<td>Pharmacy and Therapeutics Approval Date</td>
<td>11/2018</td>
</tr>
<tr>
<td>Effective Date</td>
<td>1/2019</td>
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</tbody>
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1. **Background:**

   Iclusig® (ponatinib) is a kinase inhibitor FDA-labeled for the treatment of adult patients with T315I-positive chronic myeloid leukemia (CML) (chronic phase, accelerated phase, or blast phase) and T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL). It is also indicated for 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.¹ The National Comprehensive Cancer Network (NCCN) also recommends Iclusig for treatment of Ph+ALL patients when used in combination with an induction regimen not previously used and as induction/consolidation therapy for Ph+ALL patients as a component of HyperCVAD (hyper-fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternating with high-dose methotrexate and cytarabine). In addition, NCCN recommends Iclusig for Ph+ ALL as maintenance therapy in combination with vincristine and prednisone with or without methotrexate and mercaptopurine and post-hematopoietic stem cell transplant.²

2. **Coverage Criteria:**

   **A. Chronic Myelogenous / Myeloid Leukemia (CML)**

   1. **Initial Authorization**

      a. **Iclusig** will be approved based on **both** of the following criteria:

         (1) Diagnosis of chronic myelogenous/ myeloid leukemia (CML)

         **-AND-**

         (2) **One** of the following:

            (a) Patient is unable to take or has failed treatment with **two** or more tyrosine kinase inhibitor (TKI) therapies [e.g., imatinib mesylate,
Sprycel (dasatinib), or Tasigna (nilotinib)]

-OR-

(b) Confirmed documentation of T315I mutation

Authorization will be issued for 12 months.

2. Reauthorization

a. Iclusig will be approved based on the following criterion:

   (1) Patient does not show evidence of progressive disease while on Iclusig therapy

Authorization will be issued for 12 months.

B. Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia (Ph+ALL)

1. Initial Authorization

   Iclusig will be approved based on both of the following criteria:

   a. Diagnosis of Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL)

   -AND-

   b. One of the following:

      (1) Patient is unable to take or has failed treatment with two or more tyrosine kinase inhibitor (TKI) therapies [e.g., imatinib mesylate, Sprycel (dasatinib), or Tasigna (nilotinib)]

      -OR-

      (2) Confirmed documentation of T315I mutation

      -OR-

      (3) Used in combination with an induction regimen not previously used

      -OR-

      (4) Used as a component of HyperCVAD (hyper-fractionated
cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternating with high-dose methotrexate and cytarabine) induction or consolidation.

-OR-

(5) Used as maintenance therapy in combination with vincretine and prednisone with or without methotrexate and mercaptopurine

-OR-

(6) Used as maintenance therapy post-hematopoietic stem cell transplant

**Authorization will be issued for 12 months.**

2. **Reauthorization**
   a. **Iclusig** will be approved based on the following criterion:
      
      (1) Patient does not show evidence of progressive disease while on Iclusig therapy

      **Authorization will be issued for 12 months.**

C. **NCCN Recommended Regimens**

1. **Initial Authorization**
   a. **Iclusig** will be approved for uses not outlined above if supported by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium.

   **Authorization will be issued for 12 months.**

2. **Reauthorization**
   a. **Iclusig** will be approved based on the following criterion:
      
      (1) Documentation of positive clinical response to Iclusig therapy

      **Authorization will be issued for 12 months.**

3. **References:**

<table>
<thead>
<tr>
<th>Program</th>
<th>Prior Authorization –Iclusig (ponatinib)</th>
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<tbody>
<tr>
<td><strong>Change Control</strong></td>
<td></td>
</tr>
<tr>
<td>Date</td>
<td>Change</td>
</tr>
<tr>
<td>3/2014</td>
<td>New drug policy –FDA approval</td>
</tr>
<tr>
<td>12/2015</td>
<td>Annual Review, no change</td>
</tr>
<tr>
<td>10/2016</td>
<td>Removed “chronic phase, accelerated phase, or blast phase” from CML diagnosis requirement</td>
</tr>
<tr>
<td></td>
<td>Changed prerequisite therapy from “all” to “two” alternative tyrosine kinase inhibitors</td>
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<tr>
<td></td>
<td>Added ‘used in combination with an induction regimen not previously used’ to Ph+ALL.</td>
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<tr>
<td></td>
<td>Removed prescriber requirement</td>
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<tr>
<td></td>
<td>Increased authorization from 10 months to 12 month.</td>
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<tr>
<td>12/2016</td>
<td>Changed Gleevec to imatinib mesylate. Updated formatting and references.</td>
</tr>
<tr>
<td>11/2017</td>
<td>Removed acute lymphoblastic lymphoma based on NCCN recommendations. Updated references.</td>
</tr>
<tr>
<td>11/2018</td>
<td>Added use with HyperCVAD (hyper-fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternating with high-dose methotrexate and cytarabine) induction or consolidation and as maintenance therapy in combination with vincristine and prednisone with or without methotrexate and mercaptopurine and post-hematopoietic stem cell transplant. Added NCCN Recommended Regimen review criteria. Updated background and criteria.</td>
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