UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

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| Program Number | 2023 P 1043-13 |
| Program | Prior Authorization/Notification |
| Medication | Iclusig® (ponatinib) |
| P&T Approval Date | 2/2013, 7/2013, 8/2013, 2/2014, 2/2015, 2/2016, 12/2016, 11/2017, 11/2018, 11/2019, 11/2020, 11/2021, 11/2022, 11/2023 |
| Effective Date | 2/1/2024 |

**1. Background:**

Iclusig (ponatinib) is a kinase inhibitor indicated for the treatment of patients with T315I-positive chronic myeloid leukemia (CML) (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL). It is also indicated for treatment of patients with chronic phase CML with resistance or intolerance to at least two prior kinase inhibitors and accelerated phase or blast phase CML or Ph+ ALL for whom no other tyrosine kinase inhibitors (TKI) are indicated. The National Comprehensive Cancer Network (NCCN) also recommends Iclusig for the treatment of myeloid, lymphoid, or mixed lineage neoplasms with eosinophilia and FGFR1 or ABL1 rearrangements.

**Coverage Information:**

Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

**2. Coverage Criteria[a]:**

**A. <u>Patients less than 19 years of age</u>**

1. **Iclusig** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

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

**B. <u>Chronic Myelogenous / Myeloid Leukemia (CML)</u>**

1. **<u>Initial Authorization</u>**

   a. **Iclusig** will be approved based on **<u>both</u>** of the following criteria:

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

**-AND-**

      (2) **<u>One</u>** of the following:

(a) **Both** of the following:

i. Disease is in the chronic phase
ii. Patient with resistance or intolerance to **two** or more tyrosine kinase inhibitor (TKI) therapies [e.g., imatinib mesylate, Sprycel (dasatinib), or Tasigna (nilotinib)]

**-OR-**

(b) Confirmed documentation of T315I mutation

**-OR-**

(c) **Both** of the following:

i. Disease is in the accelerated or blast phase
ii. No other kinase inhibitors are indicated

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

1. **Iclusig** will be approved based on the following criterion:

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

**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.**

**D. Myeloid/Lymphoid Neoplasms**

1. **Initial Authorization**

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

(1) Diagnosis of lymphoid, myeloid, or mixed lineage neoplasms with eosinophilia

**-AND-**

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

(a) Patient has a FGFR1 rearrangement
(b) Patient has an ABL1 rearrangement

**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.**

**E. Gastrointestinal Stromal Tumors (GIST)**

1. **Initial Authorization**

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

(1) Diagnosis of gastrointestinal stromal tumor (GIST)

**-AND-**

(2) Disease is **one** of the following:

(a) Gross residual disease (R2 resection)

(b) Unresectable primary disease

(c) Tumor rupture

(d) Recurrent/metastatic disease after progression on approved therapies (e.g. imatinib, sunitinib, regorafenib, and standard dose ripretinib)

**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.**

**F. NCCN Recommended Regimens**

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B

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

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

**3. Additional Clinical Rules:**

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

**4. References:**


1. Iclusig [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; February 2022.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed September 25, 2023.


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| **Change Control** | |
| 2/2014 | Updated coverage criteria with new FDA labeling indications. |
| 9/2014 | Administrative change - Tried/Failed exemption for State of New Jersey removed. |
| 2/2015 | Added 'or has failed treatment with' and 'at least two or more' to TKI requirement. Updated references. |
| 2/2016 | Annual review. Increased authorization from 10 months to 12 month. Added 'used in combination with an induction regimen not previously used' to Ph+ALL. Formatting revision. Updated background and references. |
| 12/2016 | Annual review. Changed Gleevec to imatinib mesylate. Updated formatting and references. |
| 11/2017 | Annual review. Removed Acute Lymphoblastic Lymphoma based on |

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| | NCCN recommendations. Updated references. |
| 11/2018 | Annual review. 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. Updated references based on NCCN recommendations. |
| 11/2019 | Annual review. Updated references. |
| 11/2020 | Annual review. Updated background to reflect package insert. Updated clinical criteria for Ph+ ALL removing specific drug regimens. Updated NCCN guidelines for Myeloid/Lymphoid Neoplasms in background and criteria. Updated references. |
| 11/2021 | Annual review. Updated Ph+ALL and CML criteria to reflect package insert and NCCN recommendations. Updated background and references. |
| 11/2022 | Annual review. Updated CML and ALL criteria based on NCCN recommendations. Added state mandate footnote. Updated references. |
| 11/2023 | Annual review. Updated ALL criteria based on NCCN recommendations. Added criteria for GIST based on NCCN recommendations. Updated background and references. |