PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Iclusig Prior Authorization Policy
- Iclusig® (ponatinib tablets – ARIAD/Takeda)

REVIEW DATE: 03/26/2025

OVERVIEW

Iclusig, a tyrosine kinase inhibitor (TKI), is indicated for the following uses in adults:[1]

- **Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukemia (ALL):**
  - Newly diagnosed, in combination with chemotherapy.
  - For whom no other TKIs are indicated as monotherapy.
  - T315I-positive, as monotherapy.
- **Chronic myeloid leukemia (CML):**
  - Chronic phase, with resistance or intolerance to at least two prior TKIs.
  - Accelerated phase or blast phase for whom no other kinase inhibitors are indicated.
  - T315I-positive (chronic phase, accelerated phase, or blast phase).

A limitation of use is that Iclusig is not indicated and is not recommended for the treatment of patients with newly diagnosed chronic phase CML.[1]

The indication of Ph+ ALL in newly diagnosed patients in combination with chemotherapy is approved under accelerated approval based on minimal residual disease (MRD)-negative complete remission (CR) at the end of induction. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial(s).[1]

Guidelines

Iclusig is addressed in guidelines from National Comprehensive Cancer Network (NCCN):[2-4]

- **ALL:** NCCN guidelines (version 3.2024 – December 20, 2024) [adults and adolescent young adults] recommend Iclusig as a treatment option for patients with the T315I mutation and/or for patients for whom no other TKI is indicated (category 2A).[2] Iclusig is also recommended in combination with various regimens used for induction or consolidation therapy for Ph+ ALL during frontline therapy or for relapsed/refractory therapy if not previously given (category 2A). NCCN guidelines for pediatric ALL (version 3.2025 – March 17, 2024) recommend Iclusig for relapsed or refractory *BCR:: ABL1*-positive ALL (category 2B) and for relapsed/refractory T-ALL with *ABL*-class translocation (category 2A).[3]
- **CML:** NCCN guidelines (version 3.2025 – November 27, 2024) recommend Iclusig as an option for patients with Ph+ or *BCR::ABL1*-positive disease and a T315I mutation and/or chronic phase CML with resistance or intolerance to at least two prior TKIs. Iclusig is also recommended for patients with accelerated-phase CML or blast-phase CML for whom no other TKI is indicated (category 2A).[4]
- **Gastrointestinal Stromal Tumor (GIST)**: NCCN guidelines (version 2.2024 – July 31, 2024) recommend Iclusig as "Useful in Certain Circumstances" after progression on approved therapies (category 2A); the guidelines state that Iclusig has demonstrated activity in advanced GIST, particularly in patients with *KIT* exon 11 mutant disease.[5] Imatinib is a preferred regimen for first-line therapy (category 1) for sensitive mutations (excluding platelet-derived growth factor receptor alpha [*PDGFRA]* exon 18 mutations that are insensitive to imatinib including D842V mutation). Ayvakit® (avapritinib tablets) is also a preferred regimen (category 2A) for GIST with *PDGFRA*

exon 18 mutations that are insensitive to imatinib, including the *PDGFRA* D842V mutation. Second-line therapies include sunitinib as "preferred" (category 1) and dasatinib as "other recommended regimen" (category 2A). Stivarga® (regorafenib tablets) is a "preferred" third-line therapy (category 1). Qinlock® (ripretinib tablets) is a "preferred" fourth-line therapy (category 1).

- **Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions:** NCCN guidelines (version 1.2025 – February 21, 2025) recommend Iclusig for *ABL1* and *FGFR1* rearrangements in chronic phase or blast phase as "Other Recommended Regimens" (category 2A).[6] It is also recommended as treatment in combination with ALL- or acute myeloid leukemia-type induction chemotherapy followed by allogeneic hematopoietic stem cell transplantation (HSCT) [if eligible] for lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and *ABL1* and *FGFR1* rearrangements in blast phase (category 2A).

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Iclusig. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Iclusig is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Acute Lymphoblastic Leukemia.** Approve for 1 year if the patient meets BOTH of the following (A, and B):
   - **A)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has Philadelphia chromosome-positive acute lymphoblastic leukemia; OR
     - **ii.** Patient has *ABL*-class translocation; AND
   - **B)** Patient meets ONE of the following (i, ii, or iii):
     - **i.** The medication will be used in combination with chemotherapy; OR
     - **ii.** The acute lymphoblastic leukemia is T315I-positive; OR
     - **iii.** Patient has tried at least one other tyrosine kinase inhibitor.
       Note: Examples include imatinib and dasatinib.

2. **Chronic Myeloid Leukemia (CML).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has Philadelphia chromosome-positive chronic myeloid leukemia; OR
     - **ii.** Patient has *BCR::ABL1*- positive chronic myeloid leukemia; AND
   - **C)** Patient meets ONE of the following (i, ii or iii):
     - **i.** The chronic myeloid leukemia is T315I-positive, OR
     - **ii.** Patient has tried at least two other tyrosine kinase inhibitors; OR
       Note: Examples of tyrosine kinase inhibitors include imatinib, dasatinib, Danziten (nilotinib tablets), Tasigna (nilotinib capsules), and Nilotinib capsules.
     - **iii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has accelerated-phase CML or blast-phase CML; AND
       - **b)** No other tyrosine kinase inhibitor is indicated.

Other Uses with Supportive Evidence

3. **Gastrointestinal Stromal Tumor.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has tried each of the following (i, ii, iii, and iv):
     - **i.** One of imatinib or Ayvakit (avapritinib tablets); AND
     - **ii.** One of sunitinib or dasatinib; AND
     - **iii.** Stivarga (regorafenib tablets); AND
     - **iv.** Qinlock (ripretinib tablets).

4. **Myeloid/Lymphoid Neoplasms with Eosinophilia.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** The tumor has an *ABL1* rearrangement; OR
     - **ii.** The tumor has an *FGFR1* rearrangement.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Iclusig is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Iclusig® tablets [prescribing information]. Lexington, MA: ARIAD/Takeda; March 2024.
2. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 3.2024 – December 20, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 17, 2025.
3. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 3.2025 – March 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 17, 2025.
4. The NCCN Chronic Myeloid Leukemia Clinical Practice Guidelines in Oncology (version 3.2025 – November 27, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 17, 2025.
5. The NCCN Gastrointestinal Stromal Tumors Guidelines in Oncology (version 2.2024 – July 31, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 17, 2025.
6. The NCCN Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions Clinical Practice Guidelines in Oncology (version 1.2025 – February 21, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 17, 2025.