Clinical Policy: Ponatinib (Iclusig)

Reference Number: CP.PHAR.112
Effective Date: 06.01.13
Last Review Date: 05.21
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Ponatinib (Iclusig®) is a kinase inhibitor.

FDA Approved Indication(s)

Iclusig is indicated for:

- Treatment of adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) or Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukemia (ALL) for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated.
- Treatment of adult patients with T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Ph+ ALL.

Limitation(s) of use: Iclusig is not indicated and is not recommended for the treatment of patients with newly diagnosed chronic phase CML.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Iclusig is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Myeloid Leukemia (must meet all):

1. Diagnosis of Ph+ (BCR-ABL1-positive) CML;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, Bosulif®, Sprycel®, Tasigna®);
   b. Member has BCR-ABL T315I mutation;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 45 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid - 6 months
Commercial - Length of Benefit

B. Acute Lymphoblastic Leukemia (must meet all):
1. Diagnosis of Ph+ (BCR-ABL1-positive) ALL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, Bosulif®, Sprycel®, Tasigna®, Iclusig®);
4. Request meets one of the following (a or b):*
   a. Dose does not exceed 45 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid - 6 months
Commercial - Length of benefit

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Iclusig for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 45 mg per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid - 12 months
Commercial - Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
CML: chronic myelogenous leukemia
FDA: Food and Drug Administration
Ph+: Philadelphia chromosome-positive

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
imatinib (Gleevec®)	Adult: • 400-600 mg/day PO for chronic phase • 600-800 mg/day PO for accelerated phase or blast crisis (800 mg given as 400 BID)	Adult: 800 mg/day
Bosulif® (bosutinib)	400 mg PO QD	600 mg/day
Sprycel® (dasatinib)	Adults: • Chronic phase: 100-140 mg/day PO • Accelerated, myeloid phase, or lymphoid blast phase: 140-180 mg/day PO	Adults: 180 mg/day
Tasigna® (nilotinib)	Adults: 300 mg PO BID	Adults: 600 mg/day
Iclusig® (ponatinib)	Starting dose 45 mg PO QD	45 mg/day

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): arterial occlusion, venous thromboembolism, heart failure, hepatotoxicity

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Ph+ CML and Ph+ ALL	Starting dose 45 mg PO QD	45 mg/day

VI. Product Availability

Tablets: 15 mg, 45 mg

VII. References

1. Iclusig Prescribing Information. Cambridge, MA: Ariad Pharmaceuticals, Inc.; December 2020. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=16d804b6-4957-43ee-b18c-3b36ec37c5ac . Accessed February 12, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 12, 2021.
3. National Comprehensive Cancer Network Guidelines. Chronic Myeloid Leukemia Version 3.2021. Available at www.nccn.org. Accessed February 12, 2021.
4. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia Version 1.2021. Available at www.nccn.org. Accessed February 12, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added background information about Ph+ ALL Modify algorithm to allow treatment for patient with T3151 mutation without requiring use of other TKIs Modified algorithm to allow for assessment of therapeutic response for patient with Ph+ ALL	05.15	05.15
Policy converted to new template. Age requirement removed. Therapeutic response criteria under continued approval is replaced by disease progression statement. FDA indication language "for which no other TKI therapy is indicated" is translated as "a contraindication to or failed trial of at least 2 other TKI therapies" which is supported by the NCCN CML/ALL guidelines. NCCN compendia use added for ALL.	05.16	06.16
CML NCCN compendial uses added. Reasons to discontinue deleted. Maximum dose added to continued therapy section.	06.17	06.17
2Q 2018 annual review: no significant changes; policies combined for Commercial and Medicaid; added age (CML), added COC statement; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; references reviewed and updated.	02.13.18	05.18
2Q 2019 annual review: Ph+ designation added to CML; hematologist added to CML/ALL criteria; references reviewed and updated.	02.19.19	05.19
2Q 2020 annual review: HIM line of business added; references reviewed and updated.	02.11.20	05.20
2Q 2021 annual review: added, Member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, bosutinib, dasatinib, nilotinib, ponatinib) for CML and ALL; allowed option for T315I mutation to bypass prior TKIs for CML; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.12.21	05.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.