Clinical Policy: Ponatinib (Iclusig)

Reference Number: ERX.SPA.17
Effective Date: 07.01.16
Last Review Date: 05.22
Line of Business: Commercial, 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 the treatment of adult patients with:

- Chronic phase chronic myeloid leukemia (CML) with resistance or intolerance to at least two prior kinase inhibitors.
- 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.
- 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Iclusig is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Myeloiod 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, b, or c):
   a. Request is for chronic phase CML and member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, Bosulif®, Sprycel®, Tasigna®, Iclusig®);
   b. Request is for accelerated or blast phase CML for members whom no other TKI therapy is indicated;
   c. 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:
Commercial – Length of Benefit
Medicaid – 6 months

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 meets one of the following (a or b):
   a. Member has BCR-ABL T315I mutation;
   b. No other TKI therapy is indicated (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:
Commercial – Length of Benefit
Medicaid – 6 months

C. Myeloid/Lymphoid Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and FGFR1 or ABL1 rearrangement in blast or chronic phase;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. If disease is ABL1 rearrangement positive, one of the following (a or b):
   a. Member has contraindication, intolerance, or disease progression on imatinib;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see Appendix D);
5. Dose is within FDA maximum limit for any FDA-approved indication or 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:
Commercial – Length of Benefit
Medicaid – 6 months

D. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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:
Commercial – Length of Benefit
Medicaid – 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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®)	ALL: Adult: 600 mg/day PO for relapsed / refractory Ph+ ALL Pediatric: 340 mg/m^2/day PO in combination with chemotherapy for newly diagnosed Ph+ ALL CML: 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) Pediatric: 340 mg/m^2/day PO for chronic phase • MLNE: 100-400 mg PO QD [NCCN]	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

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

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

Appendix D: States with Regulations against Redirections in Certain Oncology Settings

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.

State	Step Therapy Prohibited?	Notes
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial requests only** For stage 4 metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Accelerated or blast phase CML and Ph+ ALL	Starting dose 45 mg PO QD. Consider reducing the dose of Iclusig for patients with accelerated phase (AP) CML who have achieved a major cytogenetic response.	45 mg/day
Chronic phase CML	Starting dosage is 45 mg PO QD with a reduction to 15 mg PO QD upon achievement of ≤1% BCR-ABL1. Patients with loss of response can re-escalate the dose of Iclusig to a previously tolerated dosage of 30 mg or 45 mg PO QD.	45 mg/day

VI. Product Availability

Tablets: 10 mg, 15 mg, 30 mg, 45 mg

VII. References

1. Iclusig Prescribing Information. Cambridge, MA: Ariad Pharmaceuticals, Inc.; February 2022. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/203469s035lbl.pdf. Accessed April 18, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed January 31, 2022.
3. National Comprehensive Cancer Network Guidelines. Chronic Myeloid Leukemia Version 2.2022. Available at www.nccn.org. Accessed January 31, 2022.
4. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia Version 4.2021. Available at www.nccn.org. Accessed January 31, 2022.
5. National Comprehensive Cancer Network Guidelines. Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf. Accessed January 27, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: specialist involvement in care added; age (CML) added, COC statement added; NCCN and FDA approved uses summarized for improved clarity; approval durations increased to length of benefit; references 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: no significant changes; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	02.11.20	05.20
2Q 2021 annual review: added requirement that member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, bosutinib, dasatinib, nilotinib, ponatinib) for CML; allowed	02.12.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
option for T315I mutation to bypass prior TKIs for CML; added TKI alternatives dosing; references reviewed and updated.		
2Q 2022 annual review: per NCCN for CML clarified 2TKI requirement is for chronic phase CML and added additional option for accelerated or blast phase CML for members whom no other TKI therapy is indicated, for ALL removed 2 TKI requirement and replaced with requirement that either member has BCR-ABL T315I mutation or no other TKI therapy is indicated, added off-label criteria set for lymphoid, myeloid or mixed lineage neoplasms with redirection to imatinib for ABL1 rearrangement positive unless state regulations do not allow step therapy in certain oncology settings; added additional 10 mg and 30 mg strengths to Section VI; references reviewed and updated.	01.31.22	05.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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