Chronic Myelogenous Leukemia (CML) Agents
Iclusig (ponatinib)
Bosulif (bosutinib)
Effective 9/01/2022

Plan	☒ MassHealth ☐ MassHealth (PUF) ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☒ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☐ Medical Benefit (NLX)		
Specialty Limitations	This medication has been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	**Specialty Medications**		
	All Plans	Phone: 866-814-5506	Fax: 866-249-6155
	Non-Specialty Medications		
	MassHealth	Phone: 877-433-7643	Fax: 866-255-7569
	Commercial	Phone: 800-294-5979	Fax: 888-836-0730
	Exchange	Phone: 855-582-2022	Fax: 855-245-2134
	Medical Specialty Medications (NLX)		
	All Plans	Phone: 844-345-2803	Fax: 844-851-0882
Exceptions	N/A		

Overview

Iclusig (ponatinib) is a kinase inhibitor indicated for the:

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

Bosulif (bosutinib) is indicated for the treatment of:

- Newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML)
- Chronic phase, accelerated phase (AP), or blast phase (BP) Ph+ CML with resistance or intolerance to prior therapy

No PA	Drugs that require PA
Gleevec® # (imatinib)	Bosulif® (bosutinib)[PD]
Sprycel® (dasatinib)	Iclusig® (ponatinib)
Tasigna® (nilotinib)	

This is a brand-name drug with FDA "A"-rated generic equivalents. Prior authorization is required for the brand, unless a particular form of that drug (for example, tablet, capsule, or liquid) does not have an FDA "A"-rated generic equivalent.

PD Preferred Drug. In general, a trial of the preferred drug or clinical rationale for prescribing a non-preferred drug within a therapeutic class. **Please note, for CML agents, a trial with a preferred agent is not required prior to approval of a non-preferred agent.**

Coverage Guidelines

Authorization may be reviewed on a case by case basis for members new to the plan who are currently receiving treatment with requested medication, excluding when the product is obtained as samples or via manufacturer's patient assistance programs

OR

Authorization may be granted if the member meets **ALL** following criteria and documentation has been submitted:

Iclusig® (ponatinib)

Chronic Myelogenous Leukemia

Prescriber provides documentation of **ALL** of the following:

1. Appropriate diagnosis
2. Prescriber is a hematologist or oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. Paid claim or physician documentation of inadequate response or adverse reaction to **TWO** of the following or a contraindication to **ALL** of the following:
        a. Bosulif® (bosutinib)
        b. imatinib
        c. Sprycel® (dasatinib)
        d. Tasigna® (nilotinib)
    b. Confirmed T315I mutation

Acute Lymphoblastic Leukemia

Prescriber provides documentation of **ALL** of the following:

1. Appropriate diagnosis
2. Prescriber is a hematologist or oncologist
3. Appropriate dosing
4. Paid claim or physician documentation of inadequate response or adverse reaction to **ONE** of the following or a contraindication to **ALL** of the following*:
    a. imatinib
    b. Sprycel® (dasatinib)
    c. Tasigna® (nilotinib)

**Documentation of contraindication to imatinib and dasatinib is sufficient for approval if request notes ponatinib to be used with hyper-CVAD regimen (nilotinib trial is not required)*

Bosulif® (bosutinib)

Chronic Myelogenous Leukemia

1. Appropriate diagnosis
2. Prescriber is a hematologist or oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. Member has chronic phase Philadelphia chromosome-positive (Ph+) CML
    b. Paid claims or physician documentation of inadequate response or adverse reaction to **ONE** prior therapy for CML or contraindication to **ALL** other therapies for CML (see Appendix for examples of recommended agents for the treatment of CML)

Continuation of Therapy
Reauthorization requires physician attestation of continuation of therapy and positive response to therapy.

Limitations
1. Initial approvals and reauthorizations will be granted for 6 months
2. The following quantity limits apply:

Iclusig 15mg tablets	60 tablets per 30 days
Iclusig 45mg tablets	30 tablets per 30 days

Appendix
Appendix I: First-line therapy for CML
The NCCN Guidelines for the treatment of CML breaks down recommendations for first-line therapy based on three different phases, chronic, accelerated, and blast. Recommendations for each category are listed below. Please note these lists may not be all inclusive.

Chronic phase-low-risk, intermediate-risk or high-risk score
- a. bosutinib
- b. dasatinib
- c. imatinib
- d. nilotinib

Accelerated phase
- a. bosutinib
- b. dasatinib
- c. imatinib
- d. nilotinib
- e. omacetaxine
- f. ponatinib

Blast phase-lymphoid
- a. ALL-type induction chemotherapy plus a TKI
    - i. Examples of ALL-type induction chemotherapy:
        - a) EsPhALL and backbone of the Frankfurt-Munster regimen (cyclophopsamide, vincristine, daunorubicin, dexamethasone, cytarabine, methotrexate, pegaspargase and prednisone)
        - b) Hyper-CVAD (hyperfractionated cyclophosphamide, vincristine, doxirubinin, and dexamethasone) alternating with high-dose methotrexate and cytarabine
        - c) Multiagent chemotherapy (daunorubicin, vincristine, prednisone, and cyclophosphamide)
        - d) Vincristine and dexamethasone
        - e) CALGB 10701 chemotherapy regimen (dexamethasone, vincristine, daunorubicin, methotrexate, etoposide, and cytarabine)
        - f) Blinatumomab

    - ii. Examples of TKIs
        - a) bosutinib
        - b) dasatinib

c) imatinib
d) nilotinib
e) ponatinib

b. TKI plus steroids
   i. Examples of TKIs
      a) bosutinib
      b) dasatinib
      c) imatinib
      d) nilotinib
      e) ponatinib

Blast phase-myeloid

a. Acute myeloid leukemia (AML)-type induction chemotherapy plus a TKI
   i. Examples of AML-type induction chemotherapy
      a) Cytarabine plus idarubicin or daunorubicin
      b) Cytarabine plus daunorubicin and gemtuzumab ozogamicin
      c) Cytarabine plus daunorubicin and midostaurin
      d) Liposomal daunorubicin plus cytarabine
      e) Cytarabine plus daunorubicin and cladribine
      f) High-dose cytarabine plus idarubicin or daunorubicin
      g) High-dose cytarabine, fludarabine, idarubicin, and granulocyte colony stimulating factor (GCSF)
   ii. Examples of TKIs
      a) bosutinib
      b) dasatinib
      c) imatinib
      d) nilotinib
      e) ponatinib

b. TKI
   i. Examples of TKIs
      a) bosutinib
      b) dasatinib
      c) imatinib
      d) nilotinib
      e) ponatinib

Treatment recommendations based on BCR-ABL1 mutation profile

Drug	Contraindicated Mutations
Bosutinib	T315I, V299L, G250E, or F317L
Dasatinib	T315I/A, F317L/V/I/C, or V299L
Nilotinib	T315I, Y253H, E255K/V, or F359V/C/I
Asciminib, ponatinib, omacetaxine	None

Members may receive other lines of therapy not indicated in the latest update of the NCCN guidelines and those will be reviewed on a case-by-case basis.

References

i. Iclusig (ponatinib) [prescribing information]. Lexington, MA: Takeda Pharmaceuticals America Inc; February 2022.
ii. Bosulif (bosutinib) [prescribing information]. New York, NY: Pfizer; October 2021.
iii. Cortes JE, Kim D-W, Pinilla-Ibarz J, et al. Ponatinib efficacy and safety in Philadelphia chromosome-positive leukemia: final 5-year results of the phase 2 PACE trial. *Blood*. 2018;132(4):393-404.

Review History

10/9/2020: Created criteria to be in compliance with the Masshealth partial unified formulary requirements effective 1/1/21.
05/18/2022: Reviewed and Updated for May P&T; renamed criteria Chronic Myelogenous Leukemia (CML) Agents; added Bosulif to program with PA as preferred drug; added reference table; added Appendix for First line therapy for CML. Effective 6/1/2022
07/20/2022 – Reviewed and Updated for July P&T. First-line therapy for CML appendix updated to reflect latest NCCN guideline. Effective 9/1/2022.

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