VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 04/01/2020

OVERVIEW

Iclusig, a tyrosine kinase inhibitor (TKI), is indicated for the treatment of adults with T315I-positive chronic myeloid leukemia (CML) [chronic phase {CP}, accelerated phase {AP}, or blast phase {BP}] and T135I-positive Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL).[1] Iclusig is also indicated for the treatment of adults with CP, AP, or BP CML or Ph+ ALL for whom no other TKI therapy is indicated. 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. There are four other TKIs approved for the treatment of Ph+ CML: Gleevec® (imatinib tablets, generic), Sprycel® (dasatinib tablets), Tasigna® (nilotinib capsules), and Bosulif® (bosutinib tablets).[5-8] These agents are indicated for the treatment of Ph+ CML in various phases; some TKIs are indicated after resistance or intolerance to prior therapy. Sprycel and Gleevec are also indicated for use in patients with Ph+ ALL.[5,6]

Clinical Efficacy

The PACE (Ponatinib Ph+ ALL and CML Evaluation) trial was a Phase II, open-label, multinational study that assessed Iclusig in patients with CML or Ph+ ALL (n = 449) who were heavily pretreated with resistance to or unacceptable adverse effects with Sprycel® (dasatinib tablets) or Tasigna® (nilotinib capsules) or who had the BCR-ABL T315I mutation.[1,2] Benefits (e.g., major cytogenetic response, complete cytogenetic response) were noted in many patients.[2] A Phase I, dose-escalation trial (n = 81) investigated Iclusig in patients with resistant hematologic cancer including CML and Ph+ ALL.[3] Results suggest that Iclusig was highly active in heavily pretreated patients with Ph+ leukemias with resistance to TKI inhibitors, including patients with the BCR-ABL T315I mutation, other mutations, or no mutations. Other data are also available.[11,12]

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for CML (version 3.2020 – January 30, 2020) state that for patients with CP CML with a low-risk score, the primary treatment recommended includes a first-generation TKI (Gleevec or generic imatinib 400 mg QD [Category 1]), or a second-generation TKI (Bosulif 400 mg QD [Category 1], Sprycel 100 mg QD [Category 1], or Tasigna 300 mg BID [Category 1]).[9] For patients with CP CML with an intermediate- or high-risk score, a second-generation TKI is preferred (Bosulif 400 mg QD [Category 1], Sprycel 100 mg QD [Category 1], or Tasigna 300 mg BID [Category 1]). A first-generation TKI (Gleevec or generic imatinib 400 mg QD) is an alternative [Category 2A]. Iclusig is an option for patients with a T315I mutation and for with disease that has not responded to multiple TKIs or in whom another TKI is not indicated. The NCCN guidelines for ALL (adult and adolescent young adults) [version 1.2020 – January 15, 2020] recommend Iclusig as an option for patients with relapsed or refractory ALL and note its activity against T315I mutations.[10]

Safety

Iclusig has a Boxed Warning regarding arterial occlusion, venous thromboembolism, heart failure and hepatotoxicity.[1] The dosage and administration section notes that the optimal dose of Iclusig has not been identified. In clinical trials, the initial dose of Iclusig was 45 mg once daily (QD). However, many

patients (68%) required dose reductions to 30 mg to 15 mg QD during the therapy course. Consideration should be given to discontinue Iclusig if a response has not occurred by 3 months (90 days). Iclusig has a Risk Evaluation and Mitigation Strategy (REMS) program.[4]

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 the following criteria:

FDA-Approved Indications

1. **Chronic Myeloid Leukemia (CML) That is Philadelphia Chromosome Positive.** Approve for 3 years if the patient meets one of the following criteria (A or B):
   - **A)** The patient is T315I-positive, OR
   - **B)** The patient has tried at least two other tyrosine kinase inhibitors indicated for use in Philadelphia chromosome positive CML.
     Note: Examples include Gleevec® (imatinib tablets), Sprycel® (dasatinib tablets), and Tasigna® (nilotinib capsules).

2. **Acute Lymphoblastic Leukemia (ALL) That is Philadelphia Chromosome Positive (Ph+).** Approve for 3 years if the patient meets ONE of the following criteria (A or B):
   - **A)** The patient is T315I-positive; OR
   - **B)** The patient has tried at least two other tyrosine kinase inhibitors that are used for Philadelphia chromosome positive ALL.
     Note: Examples include Gleevec® (imatinib tablets), and Sprycel® (dasatinib tablets).

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]. Cambridge, MA: Takeda/ARIAD Pharmaceuticals, Inc.; January 2020.
2. Cortes JE, Kim DW, Pinilla-Ibarz J, et al, for the PACE Investigators. A phase 2 trial of ponatinib in Philadelphia chromosome-positive leukemias. *N Eng J Med*. 2013;369(19)1783-1796.
3. Cortes JE, Kantarjian H, Shah NP, et al. Ponatinib in refractory Philadelphia chromosome-positive leukemias. *N Engl J Med*. 2012;367(22):2075-2088.
4. US Food and Drug Administration. Approved Risk Evaluation and Mitigation Strategy (REMS) document. Iclusig® (ponatinib) tablets. Initial REMS Approval on 12/2013. Most recent modification on 11/2016. November 28, 2016. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/rems/Iclusig_2016-11-28_Full.pdf. Accessed on March 17, 2020.
5. Gleevec® tablets [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals, Inc.; July 2018.
6. Sprycel® tablets [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; December 2018.

7. Tasigna® capsules [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals, Inc.; September 2019.
8. Bosulif® tablets [prescribing information]. New York, NY: Pfizer Inc; October 2019.
9. The NCCN Chronic Myeloid Leukemia Clinical Practice Guidelines in Oncology (Version 3.2020 – January 30, 2020. © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 17, 2020.
10. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (Version 1.2020 – January 15, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 17, 2020.
11. Lipton JH, Chuah C, Guerci-Bresler A, et al, for the EPIC Investigators. Ponatinib versus imatinib for newly diagnosed chronic myeloid leukaemia: an international, randomized, open-label, phase 3 trial. *Lancet Oncol*. 2016;17:612-621.
12. Jain P, Kantarjian H, Jabbour E, et al. Ponatinib as first-line treatment for patients with chronic myeloid leukaemia in chronic phase: a phase 2 study. *Lancet Haematol*. 2015;2:e376-383.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual revision	Removed the criteria allowing for approval if the patient has been started on Iclusig for an indication or condition addressed as an approval in the Recommended Authorization section.	03/07/2018
Annual revision	No criteria changes.	03/20/2019
Annual revision	The following changes was made: **Chronic Myeloid Leukemia that is Ph+:** The wording that the patient has tried two other tyrosine kinase inhibitors for chronic myeloid leukemia was changed to state "at least two" and examples of tyrosine kinase inhibitors were moved from the criteria to a note. **Acute Lymphoblastic Leukemia that is Ph+:** The wording that the patient has tried two other tyrosine kinase inhibitors for acute lymphoblastic leukemia was changed to state "at least two" and examples of tyrosine kinase inhibitors were moved from the criteria to a note.	04/01/2020

Ph+ – Philadelphia chromosome positive.