VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Iclusig® (ponatinib tablets – Ariad Pharmaceuticals)

DATE REVIEWED: 03/20/2019

OVERVIEW

Iclusig, a tyrosine kinase inhibitor (TKI), is indicated for the treatment of adult patients 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 adult patients 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 1.2019 – August 1, 2018) 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 (version 1.2018 – March 12, 2018) 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 3 years in duration.

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 two other tyrosine kinase inhibitors indicated for use in Philadelphia chromosome positive CML (e.g., Gleevec® [imatinib tablets], Sprycel® [dasatinib tablets], 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 two other tyrosine kinase inhibitors that are used for Philadelphia chromosome positive ALL (e.g., Gleevec® [imatinib tablets], Sprycel® [dasatinib tablets]).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Iclusig has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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: ARIAD Pharmaceuticals, Inc.; October 2018.
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 12, 2019.

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.; July 2018.
8. Bosulif® tablets [prescribing information]. New York, NY: Pfizer Inc; October 2018.
9. The NCCN Chronic Myeloid Leukemia Clinical Practice Guidelines in Oncology (Version 1.2019 – August 1, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 12, 2019.
10. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (Version 1.2018 – March 12, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 12, 2019.
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*	TAC Approval Date
Annual revision	No criteria changes.	03/01/2017
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

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee; CML – Chronic myeloid leukemia; Ph+ – Philadelphia chromosome positive; Acute ALL – Acute lymphoblastic leukemia; TKIs – Tyrosine kinase inhibitors.