PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Copiktra Prior Authorization Policy
- Copiktra® (duvelisib capsules – Verastem)

REVIEW DATE: 11/04/2020

OVERVIEW

Copiktra, a kinase inhibitor, is indicated for the treatment of adults with:[1]

- **Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma** (SLL), relapsed or refractory, after at least two prior therapies.
- **Follicular lymphoma**, relapsed or refractory, after at least two prior systemic therapies.

Disease Overview

CLL is one of the most prevalent adult leukemias in the Western world, with an age-adjusted incidence of 4 to 5 per 100,000.[2,3] In 2019, an estimated 20,720 patients were diagnosed with CLL in the US, and around 3,930 patients will die from the disease.[3] The median age at diagnosis is 72 years of age and men are more affected than women (2:1).[2] Lymphadenopathy may be a finding upon presentation, as well as symptoms such as fevers, night sweat, weight loss, or fatigue.[2,3] CLL and SLL are different manifestations of the same condition but managed similarily.[3] Both diseases are characterized by a progressive accumulation of leukemic cells, which appear as small mature lymphocytes and may be found among occasional larger or atypical cells, in the peripheral blood, bone marrow, and lymphoid tissues. One major distinction is that in CLL, a significant number of the abnormal lymphocytes are present in blood, in addition to bone marrow and lymphoid tissue. Comparably, in SLL there are few, if any, abnormal lymphocytes circulating in blood. The bulk of the disease is in the lymph nodes, bone marrow, and in other lymphoid tissue. Many patients with CLL have cytogenetic abnormalities which can serve as markers that provide prognostic information. Drug therapy for CLL is not curative and is often not necessary in uncomplicated early disease. Some patients can be monitored without therapy until they have progressive or symptomatic/active disease. Many medications and therapy regimens are used to manage CLL. Factors to consider for recommending the most optimal regimen for a patient include disease stage, patient symptoms, fitness and other concomitant illnesses of the patient, genetic factors, and the treatment scenario.

Guidelines

Copiktra is included in several guidelines published by the National Comprehensive Cancer Network (NCCN).

- **CLL/SLL:** The NCCN guidelines for CLL/SLL (version 1.2021 – September 28, 2020) address CLL.[3] Copiktra is one of several therapies for relapsed or refractory therapy (category 2A). The guidelines note that CLL and SLL are different manifestations of the same condition and are treated similarly.
- **Follicular Lymphoma:** The NCCN guidelines for B-cell Lymphomas (version 4.2020 – August 13, 2020) recommend Copiktra as second-line and subsequent therapy in patients with follicular lymphoma (Grade 1 to 2) among patients relapsed or refractory after two prior therapies (category 2A).[4]
- **Marginal Zone Lymphoma:** The NCCN guidelines for B-Cell Lymphomas (version 4.2020 – August 13, 2020) recommend Copiktra as second-line and subsequent therapy for marginal zone lymphomas that are refractory or refractory to two prior therapies.[4] Other regimens are recommended first-line including many that are rituximab-based. Many recommendations for the

different types of gastric MALT and nongastric MALT lymphoma follow those of marginal zone lymphomas.

Safety
Copiktra has a Boxed Warning regarding fatal and serious toxicities such as infections, diarrhea or colitis, cutaneous reactions, and pneumonitis.[1] Copiktra was approved with a Risk Evaluation and Mitigation Strategy (REMS) program to assist physicians in the management of these risks. Other Warnings are present regarding hepatotoxicity, neutropenia, and embryofetal toxicity.

POLICY STATEMENT
Prior Authorization is recommended for prescription benefit coverage of Copiktra. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Copiktra is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Chronic Lymphocytic Leukemia (CLL).** Approve for 3 years if the patient has tried two prior therapies.
   Note: Examples of therapies include Imbruvica® (ibrutinib capsules and tablets); Venclexta® (venetoclax tablets) with or without rituximab; Venclexta plus Gazyva® (obinutuzumab injection for intravenous use); chlorambucil plus Gazyva; chlorambucil plus rituximab; FCR (fludarabine, cyclophosphamide, and rituximab); FR (fludarabine plus rituximab); PCR (pentostatin, cyclophosphamide, and rituximab); Treanda® (bendamustine injection) with or without rituximab; high-dose methylprednisolone (HDMP) plus rituximab; Campath® (alemtuzumab injection for intravenous use) with or without rituximab; Calquence® (acalabrutinib capsules); Zydelig® (idelalisib tablets) with or without rituximab; Gazyva; Rituxan; Arzerra® (ofatumumab injection for intravenous use); or chlorambucil.

2. **Follicular Lymphoma.** Approve for 3 years if the patient has tried two prior therapies.
   Note: Examples of therapies include Treanda® (bendamustine injection) plus rituximab; Treanda plus Gazyva® (obinutuzumab injection for intravenous use); CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) plus Gazyyva; RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone); RCVP (rituximab, cyclophosphamide, vincristine, prednisone); chlorambucil with or without rixtuximab; cyclophosphamide with or without rituximab; Gazyva; Revlimid® (lenalidomide capsules); CVP plus Gazyva; Zydelig® (idelalisib tablets); chlorambucil; cyclophosphamide; or Aliqopa® (copanlisib injection for intravenous use).

3. **Small Lymphocytic Lymphoma (SLL).** Approve for 3 years if the patient has tried two prior therapies.
   Note: Examples of therapies include Imbruvica® (ibrutinib capsules and tablets); Venclexta® (venetoclax tablets) with or without rituximab; Venclexta plus Gazyva® (obinutuzumab injection for intravenous use); chlorambucil plus Gazyva® (obinutuzumab injection for intravenous use); chlorambucil plus rituximab; FCR (fludarabine, cyclophosphamide, and rituximab); FR (fludarabine plus rituximab); PCR (pentostatin, cyclophosphamide, and rituximab); Treanda® (bendamustine

injection) with or without rituximab; high-dose methylprednisolone (HDMP) plus rituximab; Campath® (alemtuzumab injection for intravenous use) with or without rituximab; Calquence® (acalabrutinib capsules); Zydelig® (idelalisib tablets) with or without rituximab; Gazyva; Rituxan; Arzerra® (ofatumumab injection for intravenous use); or chlorambucil.

Other Uses with Supportive Evidence

4. **MALT Lymphoma (Gastric and Nongastric).** Approve for 3 years if the patient has tried two other therapies.
   Note: Examples of therapies include rituximab; Treanda® (bendamustine injection for intravenous use) plus rituximab; RCHOP (rituximab, cyclophosphamide, vincristine, prednisone); RCVP (rituximab, cyclophosphamide, vincristine, prednisone); chlorambucil with or without rituximab; cyclophosphamide with or without rituximab; Imbruvica® (ibrutinib tablets and capsules); Zydelig® (idelalisib tablets); Revlimid® (lenalidomide capsules) with or without rituximab; or Aliqopa® (copanlisib injection for intravenous use).

5. **Marginal Zone Lymphoma.** Approve for 3 years if the patient has tried two other therapies.
   Note: Examples of therapies include rituximab; Treanda® (bendamustine injection for intravenous use) plus rituximab; RCHOP (rituximab, cyclophosphamide, vincristine, prednisone); RCVP (rituximab, cyclophosphamide, vincristine, prednisone); chlorambucil with or without rituximab; cyclophosphamide with or without rituximab; Imbruvica® (ibrutinib tablets and capsules); Zydelig® (idelalisib tablets); Revlimid® (lenalidomide capsules) with or without rituximab; or Aliqopa® (copanlisib injection for intravenous use).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Copiktra 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. Copiktra® capsules [prescribing information]. Needham, MA: Verastem; July 2019.
2. Hallek M, Shanafelt TD, Eichhorst B. Chronic lymphocytic leukemia. *Lancet*. 2018;391:1524-1537.
3. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (Version 1.2021 – September 28, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on October 28, 2020.
4. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 4.2020 – August 13, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on October 28, 2020.