PHARMACY COVERAGE GUIDELINE

COPIKTRA™ (duvelisib) oral capsule
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary y as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Copiktra (duvelisib) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

  2. Individual is 18 years of age or older

  3. Individual has a confirmed diagnosis of **ONE** of the following:
     a. Relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies

   b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. Individual is on prophylaxis for *Pneumocystis jiroveci* during treatment

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. Negative pregnancy test in a woman of reproductive potential
   b. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-1

7. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as use with strong CYP3A4 inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, others)

8. Requested agent will not be used with another PI3-kinase inhibitor (e.g. alpelisib, copanlisib, idelalisib, inavolisib)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Copiktra (duvelisib) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual's condition has responded while on therapy with response defined as there is no evidence of disease progression or unacceptable toxicity

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Requested dose is at least 15 mg twice daily

6. Individual is on prophylaxis for *Pneumocystis jiroveci* during treatment

7. Individual has not developed any significant adverse drug effects that may exclude continued use, if clinically appropriate withhold, reduce dose, or permanently discontinue based on severity, recurrence, persistence, or duration of adverse reaction as follows:

a. Recurrent or severe or life-threatening diarrhea
b. Recurrent or severe or life-threatening colitis
c. Recurrent, worsening, or nonresponsive severe cutaneous reactions or first occurrence of life-threatening cutaneous reactions
d. First occurrence of Stevens-Johnson Syndrome, toxic epidermal necrolysis, or drug rash with eosinophilia and systemic symptoms (DRESS)
e. Recurrent or nonresponsive symptomatic moderate pneumonitis or first occurrence of severe or life-threatening pneumonitis
f. *Pneumocystis jiroveci* infection
g. ALT/AST elevation greater than 20 times ULN

8. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as use with strong CYP3A4 inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, others)

9. Requested agent will not be used with another PI3-kinase inhibitor (e.g. alpelisib, copanlisib, idelalisib, inavolisib)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Copiktra (duvelisib) indicated for the treatment of adult patients with a) relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies and b) relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials

Copiktra (duvelisib) is a dual inhibitor of phosphatidylinositol 3-kinases PI3K-δ and PI3K-γ. Duvelisib induced growth inhibition and reduced viability in cell lines derived from malignant B-cells and in primary CLL tumor cells. Duvelisib inhibits several key cell-signaling pathways, including B-cell receptor signaling and CXCR12-mediated chemotaxis of malignant B-cells.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Eastern Co-operative Oncology Group (ECGO) Performance Status:

Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physical strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled, cannot carry on any self-care, totally confined to bed or chair
5	Dead
Oken, MM, Creech, RH, Tormey, DC, et al.: Toxicity and Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

PI3-kinase inhibitors:

- Piqray (alpelisib)
- Copiktra (duvelisib)
- Aliqopa (copanlisib)
- Zydelig (idelalisib)
- Itovebi (inavolisib)

Resources:

Copiktra (duvelisib) product information, revised by Secura Bio, Inc. 07-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 04, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2025 – Updated October 01, 2024. Available at https://www.nccn.org. Accessed February 03, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.