

Clinical Policy: Duvelisib (Copiktra)

Reference Number: CP.PHAR.400

Effective Date: 10.16.18

Last Review Date: 02.22

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Duvelisib (Copiktra[®]) is a kinase inhibitor.

FDA Approved Indication(s)

Copiktra is indicated for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Copiktra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all):

1. Diagnosis of CLL or SLL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age \geq 18 years;
4. Relapsed/refractory disease after at least one prior therapy (*see Appendix B for examples*);*
**Prior authorization may be required.*
5. Prescribed as a single agent;
6. Request meets one of the following (a, b, or c):*
 - a. Dose does not exceed 50 mg (2 capsules) per day;
 - b. Dose does not exceed 80 mg per day if co-administered with a moderate CYP3A4 inducer;
 - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 12 months or duration of request, whichever is less

B. Follicular and Marginal Zone Lymphomas (off-label) (must meet all):

1. Diagnosis of one of the following (a or b):
 - a. Follicular lymphoma (FL);
 - b. Marginal zone lymphoma (i, ii, or iii):
 - i. Splenic marginal zone lymphoma;
 - ii. Nodal marginal zone lymphoma;
 - iii. Extranodal marginal zone lymphoma (a or b):
 - a) Gastric MALT lymphoma;
 - b) Nongastric MALT lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age \geq 18 years;
4. Relapsed/refractory disease after \geq 2 prior therapies (*see Appendix B for examples*);*
**Prior authorization may be required.*
5. Request meets one of the following (a, b, or c):*
 - a. Dose does not exceed 50 mg (2 capsules) per day;
 - b. Dose does not exceed 80 mg per day if co-administered with a moderate CYP3A4 inducer;
 - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 12 months or duration of request, whichever is less

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Copiktra for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):*
 - a. New dose does not exceed 50 mg (2 capsules) per day;
 - b. New dose does not exceed 80 mg per day if co-administered with a moderate CYP3A4 inducer;
 - c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 12 months

Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia	NCCN: National Comprehensive Cancer Network
FDA: Food and Drug Administration	SLL: small lymphocytic lymphoma
FL: follicular lymphoma	

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<p>CLL/SLL <i>Examples of first-line, second-line and subsequent therapies:</i></p> <ul style="list-style-type: none"> • FCR (fludarabine, cyclophosphamide, rituximab) • HDMP (high-dose methylprednisolone) + rituximab • <u>Single-agent examples:</u> Imbruvica[®] (ibrutinib); Venclexta[®] (venetoclax) ± Gazyva[®] (obinutuzumab) or rituximab; Campath[®] (alemtuzumab) ± rituximab; Gazyva; Copiktra[®] (duvelisib); Calquence[®] (acalabrutinib); Revlimid[®] (lenalidomide) ± rituximab; Arzerra[®] (ofatumumab) ± FC (fludarabine, cyclophosphamide); Leukeran[®] (chlorambucil) + rituximab 	Varies	Varies
<p>Follicular Lymphoma <i>Examples of first-line, second-line and subsequent therapies:</i></p> <ul style="list-style-type: none"> • bendamustine + Gazyva or rituximab • CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Gazyva or rituximab 	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<ul style="list-style-type: none"> CVP (cyclophosphamide, vincristine, prednisone) + Gazyva or rituximab <u>Single-agent examples:</u> rituximab; Revlimid ± rituximab 		
<p>Marginal Zone Lymphomas <i>Examples of first-line, second-line and subsequent therapies:</i></p> <ul style="list-style-type: none"> bendamustine + rituximab RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) RCVP (rituximab, cyclophosphamide, vincristine, prednisone) <u>Single-agent examples:</u> rituximab; Leukeran ± rituximab; cyclophosphamide ± rituximab; Imbruvica; Revlimid ± rituximab; Copiktra; Aliqopa[®] (copanlisib) 	Varies	Varies

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): fatal and serious toxicities: infections, diarrhea or colitis, cutaneous reactions, and pneumonitis

Appendix D: General Information

- In December 2021, the manufacturer of Copiktra announced voluntary withdrawal of the previously FDA-approved indication for FL, stating that “the current treatment landscape for FL patients in the U.S. and the logistics, cost and timing of the post-marketing requirements for Copiktra in FL was no longer merited... This is a business decision and is not related to any changes in either the efficacy or safety associated with Copiktra.” As of January 2022, the NCCN continues to recommend use of Copiktra in FL as well as other B-cell lymphomas.
- Examples of moderate CYP3A4 inducers include, but are not limited to: bosentan, efavirenz, etravirine, phenobarbital, and primidone.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CLL/SLL	<p>25 mg PO BID (may reduce to 15 mg PO BID for adverse reactions). A cycle consists of 28 days</p> <p>If co-administered with a moderate CYP3A4 inducer: 40 mg PO BID if the initial Copiktra dose is 25 mg PO BID (25 mg PO BID if the initial Copiktra dose is 15 mg PO BID). After the inducer has been discontinued for at least 14 days, resume Copiktra at the dose taken prior to initiating the moderate CYP3A4 inducer</p>	<p>50 mg/day</p> <p>If co-administered with a moderate CYP3A4 inducer: 80 mg/day</p>

VI. Product Availability

Capsules: 25 mg, 15 mg

VII. References

1. Copiktra Prescribing Information. Needham, MA: Verastem, Inc.; December 2021. Available at <https://copiktra.com>. Accessed January 5, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: www.nccn.org. Accessed January 5, 2022.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 4.2021. Available at www.nccn.org. Accessed July 13, 2021.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 5.2021. Available at www.nccn.org. Accessed January 5, 2022.
5. Secura Bio Inc. Secura Bio announces Copiktra (duvelisib) strategic focus on T-cell lymphoma and voluntary U.S. withdrawal of the relapsed or refractory follicular lymphoma indication. Press release. Published December 3, 2021. Available at: <https://www.prnewswire.com/news-releases/secura-bio-announces-copiktra-duvelisib-strategic-focus-on-t-cell-lymphoma-and-voluntary-us-withdrawal-of-the-relapsed-or-refractory-follicular-lymphoma-indication-301436834.html>. Accessed January 5, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	10.16.18	11.18
No significant changes; added HIM line of business per SDC.	02.01.19	
4Q 2019 annual review: FDA/NCCN dosing limitation added; marginal zone lymphomas added per NCCN; references reviewed and updated.	08.27.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: for CLL/SLL, added requirement for use as a single agent; modified HIM/Medicaid continued approval duration from 6 months to 12 months per standard approach; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	06.28.21	11.21
RT4: updated FDA Approved Indication(s) section to remove FL indication (criteria set is retained and designated as off-label as such use continues to be supported by NCCN); updated dosing requirements to reflect modified dosing recommendations in PI for co-administration with a moderate CYP3A4 inducer.	01.05.22	
Revised Commercial approval durations from Length of Benefit to 12 months or duration of request, whichever is less.	01.10.22	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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