Clinical Policy Title:	duvelisib
Policy Number:	RxA.360
Drug(s) Applied:	Copiktra®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Duvelisib (Copiktra®) is a kinase inhibitor. It is indicated for:

- Treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies.
- Treatment of adult patients with 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 (ORR); continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
duvelisib (Copiktra®)	CLL / SLL, FL	25 mg orally twice daily. A cycle consists of 28 days. Reduce dose to 15 mg twice daily when co-administered with strong CYP3A4 inhibitors.	50 mg/day

Dosage Forms

- Capsules: 25 mg, 15 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of relapsed or refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age 18 years of age or older;

4. Relapsed/refractory disease after at least two prior therapies (see Appendix B for examples);*
   *Prior authorization may be required.
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 50 mg (2 capsules) per day;
   b. 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
Commercial: 6 months
Medicaid: 6 months

B. Follicular and Marginal Zone Lymphomas (must meet all)**:**

1. Diagnosis is one of the following (a or b):
   a. Follicular Lymphoma;
   b. Marginal zone lymphoma (off-label) (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 18 years of age or older;
4. Relapsed/refractory disease after ≥ 2 prior therapies (see Appendix B for examples);*
   *Prior authorization may be required.
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 50 mg (2 capsules) per day;
   b. 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance, 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 or b):*
   a. New dose does not exceed 50 mg (2 capsules) per day;
   b. 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
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

CLL: Chronic Lymphocytic Leukemia
FDA: Food and Drug Administration
FL: Follicular Lymphoma
SLL: Small Lymphocytic Lymphoma

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
CLL/SLL Examples of first-line, second-line and subsequent therapies: • FCR (fludarabine, cyclophosphamide, rituximab) • HDMP (high-dose methylprednisolone) + rituximab • Single-agent examples: 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
Follicular Lymphoma Examples of first-line, second-line and subsequent therapies: • bendamustine + Gazyva® or rituximab • CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Gazyva® or rituximab • CVP (cyclophosphamide, vincristine, prednisone) + Gazyva® or rituximab • Single-agent examples: rituximab; Revlimid ± rituximab	Varies	Varies
Marginal Zone Lymphomas Examples of first-line, second-line and subsequent therapies: • bendamustine + rituximab	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
• RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) • RCVP (rituximab, cyclophosphamide, vincristine, prednisone) • Single-agent examples: rituximab; Leukeran ± rituximab; cyclophosphamide ± rituximab; Imbruvica; Revlimid ± rituximab; Copiktra®; Aliqopa® (copanlisib)		

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

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

- CYP3A inducers: Avoid co-administration with strong CYP3A inducers.

References

1. Copiktra Prescribing Information. Needham, MA: Verastem, Inc.; July 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211155s000lbl.pdf. Accessed June 01, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/. Accessed June 02, 2021.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf . Accessed June 02, 2021.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf . Accessed June 02, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Line of Business Policy Applies to was update to all lines of business. 3. Initial and Continued Approval Duration: Commercial approval duration was updated from 'length of benefit' to '6 months'.	08/02/2020	09/14/2020

Review/Revision History	Review/Revised Date	P&T Approval Date
4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. References were updated.		
Policy was reviewed. 1. Initial Approval Criteria and Continued Therapy Approval Criteria were updated to remove HIM approval duration. 2. Initial Approval Criteria IA.4 was updated from “Relapsed/refractory disease after at least one prior therapy” to “Relapsed/refractory disease after at least two prior therapies…”. 3. Appendix B verbiage was rephrased to “Below are suggested therapeutic alternatives…….”. 4. Appendix B footnote was updated to,” Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only”. 5. Appendix D was updated to include drug interaction information, ”CYP3A inducers: Avoid co-administration with strong CYP3A inducers.” 6. References were reviewed and updated.	06/02/2021	09/14/2021