Clinical Policy: Copanlisib (Aliqopa)

Reference Number: PA.CP.PHAR.357
Effective Date: 10/2017
Last Review Date: 10/2024

Description
Copanlisib (Aliqopa®) is a phosphatidylinositol-3-kinase inhibitor.

FDA Approved Indication(s)
Aliqopa is indicated for the treatment of adult patients with relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies.*

**Accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.*

***Bayer, the manufacturer of Aliqopa, announced the voluntary withdrawal of its application for adult patients with relapsed FL who have received at least two prior systemic therapies** (*see Appendix D*)**.**

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of PA Health & Wellness that Aliqopa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Follicular and Other B-Cell Lymphomas (must meet all)**:**

1. Authorization is not permitted. Member may not initiate therapy with Aliqopa. If member is currently using Aliqopa proceed to section II.A. Follicular and Other B-Cell Lymphomas for continued therapy (*see Appendix D*).
   Approval duration: Not applicable

B. Other diagnoses/indications

1. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Follicular and Other B-Cell Lymphomas (must meet all)**:**

1. Currently receiving medication via PA Health &Wellness benefit or member is currently receiving the medication for the treatment of follicular or other B-cell lymphomas or the Continuity of Care Policy (PA.PHARM.01) applies;
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 60 mg (1 vial) per week for 3 out of 4 weeks;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health &Wellness benefit or the Continuity of Care Policy (PA.PHARM.01) applies;
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
FL: follicular lymphoma
NCCN: National Comprehensive Cancer Network

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Follicular Lymphoma *Examples of first-line, second-line and subsequent therapies:* • bendamustine + Gazyva® (obinutuzumab) or rituximab • CHOP (cyclophosphamide, doxorubicin, vincristine, predenisone) + Gazyva or rituximab • CVP (cyclophosphamide, vincristine, prednisone) + Gazyva or rituximab • Single-agent examples: rituximab; Revlimid® (lenalidomide) ± rituximab	Varies	Varies
Marginal Zone Lymphomas *Examples of first-line, second-line and subsequent therapies:* • bendamustine + rituximab, bendamustine + Gazyva® • RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) • RCVP (rituximab, cyclophosphamide, vincristine, prednisone) • Single-agent examples: rituximab; Leukeran® (chlorambucil) ± rituximab; cyclophosphamide ± rituximab; Imbruvica® (ibrutinib); Revlimid ± rituximab	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
None reported

Appendix D: Aliqopa Market Withdrawal

- Aliqopa received accelerated approval from the FDA in September 2017 based on CHRONOS-1, an open-label, single-arm phase 2 study. The FDA required clinical benefit to be confirmed through the CHRONOS-4 study. In the study, the addition of Aliqopa to standard immunochemotherapy regimens did not meet the primary endpoint of progression-free survival benefit versus the standard immunochemotherapy control arm in patients with relapsed FL.
- Bayer announced the voluntary withdrawal of its new drug application for Aliqopa on November 13, 2023. Bayer stated it was exploring access options for patients currently receiving Aliqopa who have experienced a favorable response to treatment, whose treating physician supports continuing treatment with Aliqopa, and for whom there may be no suitable alternative treatments available. No new patients should be prescribed Aliqopa per Bayer's press release. Approval was withdrawn as of March 18, 2024.
- The NCCN also removed Aliqopa as a treatment option for both FL and marginal zone lymphoma (NCCN guideline B-cell lymphomas version 2.2024).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
FL	60 mg IV on Days 1, 8, and 15 of a 28-day treatment cycle on an intermittent schedule (3 weeks on/1 week off)	60 mg/dose/week

VI. Product Availability

Single-dose vial: 60 mg

VII. References

1. Aliqopa Prescribing Information. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; September 2023. Available at: https://www.hcp.aliqopa-us.com/. Accessed July 17, 2024.
2. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. August 7, 2024.
3. Bayer press release. Bayer provides update on Aliqopa. Available at: https://www.bayer.com/en/us/news-stories/update-on-aliqopar. Accessed August 7, 2024.
4. Federal Register. Bayer HealthCare Pharmaceuticals Inc.; withdrawal of approval of new drug application for Aliqopa (copanlisib) for injection, 60 milligrams per vial, a notice by the FDA on 03/18/2024. Available at: https://www.federalregister.gov/documents/2024/03/18/2024-05619/bayer-healthcare-pharmaceuticals-inc-withdrawal-of-approval-of-new-drug-application-for-aliqopa. Accessed August 7, 2024.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9057	Injection, copanlisib, 1 mg

Reviews, Revisions, and Approvals	Date
New policy created.	07/2018
3Q 2019 annual review: No changes per Statewide PDL implementation 01/01/2020	07/2019
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: NCCN recommended B-cell lymphoma subtypes added - Appendix B required therapy examples expanded accordingly; relapsed or refractory disease added; dosing detail - 3 out of 4 weeks - added per PI; FDA/NCCN dosing limitation added; references reviewed and updated.	10/2020
4Q 2021 annual review: no significant changes; references reviewed and updated.	10/2021
4Q 2022 annual review: no significant changes; references reviewed and updated.	10/2022
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023
4Q 2024 annual review: removed initial approval criteria due to manufacturer withdrawal; added information regarding the market withdrawal to Appendix D; references reviewed and updated.	10/2024