Corporate Medical Policy

Copanlisib (Aliqopa™)

File Name:	copanlisib_aliqopa
Origination:	7/2018
Last CAP Review:	11/2020
Next CAP Review:	11/2021
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Description of Procedure or Service

Aliqopa™ (copanlisib) is a kinase inhibitor indicated for the treatment of adults with relapsed follicular lymphoma who have received at least two prior systemic therapies.

Follicular lymphoma is a mostly indolent, B-cell lymphoma and one of the most common types of non-Hodgkin lymphoma. Per the National Cancer Institute, approximately 72,240 patients in the U.S. were diagnosed with some type of NHL in 2017 with roughly 20,140 of NHL patients dying from the disease. Most patients with follicular lymphoma present with disseminated disease, and treatment depends upon tumor stage. Observation may be recommended for patients with advanced disease, with treatment reserved for development of systemic symptoms. Chemoimmunotherapy is the most common first-line treatment strategy; however, conventional therapy is not curative and most patients with follicular lymphoma develop progressive disease or are refractory to initial therapy.

In general, the indications for treatment of relapsed follicular lymphoma are similar to that of initial therapy; however, there is no standardized approach and participation in a clinical trial is encouraged. A preferred order of treatment has not been established, although a risk-stratified approach may identify which patients with more aggressive disease may benefit from more intensive therapies. The main treatment options for patients with first relapse may include chemoimmunotherapy, high dose chemotherapy with hematopoietic stem cell transplant or radioimmunotherapy. Most patients experience multiple relapses and will be treated with many different agents at some point during the disease course. Aliqopa (copanlisib) has been studied in patients with multiply relapsed disease.

Copanlisib inhibits phosphatidylinositol-3-kinase (PI3K) with primary activity against isoforms PI3K-α and PI3K-δ, which are expressed in malignant B cells. This activity has been shown to cause tumor cell death by apoptosis and inhibition of proliferation of primary malignant B cell lines. Additionally, copanlisib inhibits several essential cell-signaling pathways, including B-cell receptor (BCR) signaling, CXCR12 mediated chemotaxis of malignant B cells, and NFκB signaling in lymphoma cell lines.

Related Policies:
Monoclonal Antibodies for Non-Hodgkin Lymphoma and Acute Myeloid Leukemia In the Non-Hematopoietic Stem Cell Transplant Setting
Hematopoietic Stem-Cell Transplant for Non-Hodgkin Lymphomas

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Copanlisib (Aliqopa™)

Policy

BCBSNC will provide coverage for copanlisib (Aliqopa) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Copanlisib (Aliqopa) is covered

Copanlisib (Aliqopa) is considered medically necessary for adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic therapies. (See Policy Guidelines)

Use of copanlisib (Aliqopa) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); **OR**

- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Copanlisib (Aliqopa) is not covered

Copanlisib (Aliqopa) is considered **investigational** and therefore not covered when the above criteria are not met.

Copanlisib (Aliqopa) is considered investigational when used for:

1. Non-cancer indications; **OR**

2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under "When Copanlisib (Aliqopa) is covered."

Policy Guidelines

In the CHRONOS-1 clinical trial evaluating use of copanlisib in patients with relapsed follicular lymphoma, the majority of patients had received prior chemotherapy with an alkylating agent with or without immunotherapy, or immunotherapy monotherapy.

Dosing and Administration

Aliqopa (copanlisib) is administered by intravenous (IV) infusion and is intended to be used as a single agent.

The recommended dosing regimen for Aliqopa is 60 mg given as a 1-hour IV infusion on days 1, 8, and 15 of a 28-day treatment cycle using an intermittent schedule of three weeks on and one week off. Treatment is to be continued until disease progression or unacceptable toxicity.

Adverse Reactions

Serious side effects or toxicities may include infection, hyperglycemia, hypertension, non-infectious pneumonitis (NIP), neutropenia, severe cutaneous reactions, and thrombocytopenia. Toxicity to Aliqopa should be managed with dose reduction, delay in treatment, or discontinuation of therapy.

Safety and effectiveness have not been established in pediatric patients.

Evidence

On September 14, 2017, copanlisib received accelerated approval by the U.S. Food and Drug Administration (FDA) for the treatment of adults with relapsed follicular lymphoma who have received at least two prior systemic therapies. This approval was based on overall response rate demonstrated in the CHRONOS-1 trial. This phase 2, single-arm, multicenter clinical trial included 104 patients with follicular B-cell non-Hodgkin lymphoma who had relapsed disease following at least two prior treatments that included rituximab and an alkylating agent (median age, 62 years; median number of prior therapies, 3). Patients received 60 mg of copanlisib administered as a 1-hour IV infusion on days 1, 8, and 15 of a 28-day treatment cycle with continued treatment until disease progression or unacceptable toxicity. The primary endpoint was overall response rate, which was 59% (95% confidence interval [CI], 49-68) with a median duration of response of 12.2 months (range, 0 to 22.6 months; 95% CI, 6.9 to 22.6 months). The complete response rate was 14% and partial response rate was 44%. Median time to response was 1.7 months (range 1.3 to 9.7 months).

Clinical Trials

There are several ongoing Phase III randomized clinical trials to evaluate the efficacy and safety of copanlisib in patients with indolent lymphoma. The CHRONOS-2 trial currently in progress is a study assessing the safety of copanlisib versus placebo in patients with rituximab-refractory indolent non-Hodgkin's lymphoma (iNHL). The CHRONOS-3 trial is planned to analyze efficacy and safety of copanlisib in combination with rituximab as compared to placebo with rituximab in patients with relapsed iNHL. Lastly, the CHRONOS-4 trial also planned will evaluate efficacy and safety of copanlisib in combination with standard immunochemotherapy as compared to placebo with standard immunochemotherapy in patients with relapsed iNHL. Further clinical data are needed to determine additional benefit and place in therapy for copanlisib.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), "Investigational (Experimental) Services."

Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J9057*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

U.S. Food and Drug Administration (FDA). Aliqopa (copanlisib). Highlights of prescribing information. September 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209936s000lbl.pdf. Accessed July 2018.

U.S. Food and Drug Administration. FDA approves new treatment for adults with relapsed follicular lymphoma. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm576129.htm. Accessed July 11, 2018.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. B-Cell Lymphomas, version 4.2018. Revised May 15, 2018. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 2018.

Dreyling M, Santoro A, Mollica L, et al. Phosphatidylinositol 3-kinase inhibition by copanlisib in relapsed or refractory indolent lymphoma. J Clin Oncol 2017;35:3898-3905.

Medical Director review 7/2018

Specialty Matched Consultant Advisory Panel 11/2018

Specialty Matched Consultant Advisory Panel 11/2019

Specialty Matched Consultant Advisory Panel 11/2020

Policy Implementation/Update Information

8/10/18	New policy developed. Aliqopa is considered medically necessary for adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic therapies. Added HCPCS code C9030 to "Billing/Coding" section. References added. Medical Director review 7/2018. (krc)
12/14/18	Specialty Matched Consultant Advisory Panel review 11/28/2018. No change to policy intent. (krc)
12/31/18	Updated title formatting to "Copanlisib (Aliqopa)." Added HCPCS code J9057 to Billing/Coding section and deleted code C9030 effective 1/1/19. (krc)
12/10/19	Minor typographical edits made throughout policy for consistency. No change to policy intent. Specialty Matched Consultant Advisory Panel review 11/20/2019. (krc)
1/12/21	Specialty Matched Consultant Advisory Panel review 11/18/2020. No change to policy intent. (krc)