

Aliqopa™ (copanlisib) (Intravenous)

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Document Number: IC-0492

Last Review Date: 12/01/2020**Date of Origin: 06/03/2019****Dates Reviewed: 06/2019, 12/2019, 12/2020**

I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Aliqopa 60 mg vial: 3 vials per 28 day supply

B. Max Units (per dose and over time) [HCPCS Unit]:

- 60 billable units on Days 1, 8, & 15 of a 28-day cycle

III. Initial Approval Criteria ^{1-3,8}

Coverage is provided in the following conditions:

- Patient aged 18 years or older; **AND**

Universal Criteria

- Must be used as a single agent; **AND**
- Patient does not have an active infection, including clinically important localized infections; **AND**

B-Cell Lymphoma

- Patient has relapsed, refractory or progressive disease; **AND**
- Used as subsequent therapy after at least two (2) prior therapies including rituximab and an alkylating agent; **AND**
- Patient has one of the following diagnoses:
 - Follicular Lymphoma (FL) † **OR**
 - Nongastric MALT Lymphoma (Noncutaneous) ‡ **OR**
 - Gastric MALT Lymphoma ‡ **OR**
 - Nodal Marginal Zone Lymphoma ‡ **OR**
 - Splenic Marginal Zone Lymphoma ‡

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA-labeled indication(s); ‡ Compendia recommended indication(s); Ⓢ Orphan Drug

IV. **Renewal Criteria**¹⁻³

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: ≥ Grade 3 infections, pneumocystis jiroveci pneumonia (PJP) of any grade, uncontrolled hyperglycemia, uncontrolled hypertension, non-infectious pneumonitis, ANC < 0.5 x 10³ cells/mm³, severe cutaneous reactions (Grade 3 or life-threatening), thrombocytopenia, etc.; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

V. **Dosage/Administration**¹

Indication	Dose
B-cell lymphoma	60 mg administered as an intravenous infusion on Days 1, 8, and 15 of a 28-day cycle

VI. **Billing Code/Availability Information**

HCPCS Code:

- J9057 – Injection, copanlisib, 1 mg: 1 billable unit = 1 mg

NDC:

- Aliqopa 60 mg single-use vial: 50419-0385-xx

VII. **References (STANDARD)**

1. Aliqopa [package insert]. Whippany, NJ; Bayer HealthCare Pharmaceuticals Inc.; February 2020. Accessed October 2020.
2. Dreyling, M., Santoro, A., Mollica, L., et al. (2017) COPANLISIB IN PATIENTS WITH RELAPSED OR REFRACTORY INDOLENT B-CELL LYMPHOMA (CHRONOS-1). Hematological Oncology, 35(S2): 119–120. doi: 10.1002/hon.2437_107.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Copanlisib. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most

recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2020.

4. Dreyling, M., Santoro, A., Mollica, L., et al. Updated Safety and Efficacy from the Copanlisib CHRONOS-1 Trial in Patients with Relapsed or Refractory Indolent B-Cell Lymphoma: Low Incidence of Late-Onset Severe Toxicities. *Blood*, 130(Suppl 1), 2777.
5. Martin Dreyling, Armando Santoro, Luigina Mollica, et al. Phosphatidylinositol 3-Kinase Inhibition by Copanlisib in Relapsed or Refractory Indolent Lymphoma. *J Clin Oncol* 2017; 35: 3898-3905.
6. Dreyling, M., Panayiotidis P., Egyed M., et al. Efficacy of Copanlisib Monotherapy in Patients with Relapsed or Refractory Marginal Zone Lymphoma: Subset Analysis from the CHRONOS-1 Trial [abstract]. *Blood* 2017;130:Abstract 4053.
7. Palmetto GBA, LLC. Local Coverage Article: Billing and Coding: Chemotherapy (A56141). Centers for Medicare & Medicaid Services, Inc. Updated on 05/26/2020 with effective date 04/30/2020. Accessed October 2020.

VIII. References (ENHANCED)

- 1e. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) B-Cell Lymphomas, Version 4.2020. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2020.
- 2e. McLaughlin P, Grillo-López AJ, Link BK, et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. *J Clin Oncol*. 1998 Aug;16(8):2825-33.
- 3e. Sehn LH, Chua N, Mayer J, et al. Obinutuzumab plus bendamustine versus bendamustine monotherapy in patients with rituximab-refractory indolent non-Hodgkin lymphoma (GADOLIN): a randomised, controlled, open-label, multicentre, phase 3 trial. *Lancet Oncol*. 2016 Aug;17(8):1081-1093.
- 4e. Dreyling, M., Santoro, A., Mollica, L., et al. Long-Term Efficacy and Safety from the Copanlisib CHRONOS-1 Study in Patients with Relapsed or Refractory Indolent B-Cell Lymphoma. *Blood*. 2018;132:1595.
- 5e. Czuczman MS, Fayad L, Delwail V, et al. Ofatumumab monotherapy in rituximab-refractory follicular lymphoma: results from a multicenter study. *Blood*. 2012 Apr 19;119(16):3698-704.
- 6e. Sehn LH, Goy A, Offner FC, et al. Randomized Phase II Trial Comparing Obinutuzumab (GA101) With Rituximab in Patients With Relapsed CD20+ Indolent B-Cell Non-Hodgkin Lymphoma: Final Analysis of the GAUSS Study. *J Clin Oncol*. 2015;33(30):3467–3474.
- 7e. Magellan Health, Magellan Rx Management. Aliqopa Clinical Literature Review Analysis. Last updated October 2020. Accessed October 2020.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C82.00	Follicular lymphoma grade I, unspecified site
C82.01	Follicular lymphoma grade I, lymph nodes of head, face and neck
C82.02	Follicular lymphoma, grade I, intrathoracic lymph nodes
C82.03	Follicular lymphoma grade I, intra-abdominal lymph nodes
C82.04	Follicular lymphoma grade I, lymph nodes of axilla and upper limb
C82.05	Follicular lymphoma grade I, lymph nodes of inguinal regional and lower limb
C82.06	Follicular lymphoma grade I, intrapelvic lymph nodes
C82.07	Follicular lymphoma grade I, spleen
C82.08	Follicular lymphoma grade I, lymph nodes of multiple sites
C82.09	Follicular lymphoma grade I, extranodal and solid organ sites
C82.10	Follicular lymphoma grade II, unspecified site
C82.11	Follicular lymphoma grade II, lymph nodes of head, face and neck
C82.12	Follicular lymphoma, grade II, intrathoracic lymph nodes
C82.13	Follicular lymphoma grade II, intra-abdominal lymph nodes
C82.14	Follicular lymphoma grade II, lymph nodes of axilla and upper limb
C82.15	Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb
C82.16	Follicular lymphoma grade II, intrapelvic lymph nodes
C82.17	Follicular lymphoma grade II, spleen
C82.18	Follicular lymphoma grade II, lymph nodes of multiple sites
C82.19	Follicular lymphoma grade II, extranodal and solid organ sites
C82.20	Follicular lymphoma grade III, unspecified, unspecified site
C82.21	Follicular lymphoma grade III, unspecified, lymph nodes of head, face and neck
C82.22	Follicular lymphoma, grade III, unspecified, intrathoracic lymph nodes
C82.23	Follicular lymphoma grade III, unspecified, intra-abdominal lymph nodes
C82.24	Follicular lymphoma grade III, unspecified, lymph nodes of axilla and upper limb
C82.25	Follicular lymphoma grade III, unspecified, lymph nodes of inguinal region and lower limb
C82.26	Follicular lymphoma grade III, unspecified, intrapelvic lymph nodes
C82.27	Follicular lymphoma grade III, unspecified, spleen
C82.28	Follicular lymphoma grade III, unspecified, lymph nodes of multiple sites
C82.29	Follicular lymphoma grade III, unspecified, extranodal and solid organ sites
C82.30	Follicular lymphoma grade IIIa, unspecified site
C82.31	Follicular lymphoma grade IIIa, lymph nodes of head, face and neck
C82.32	Follicular lymphoma, grade IIIa, intrathoracic lymph nodes
C82.33	Follicular lymphoma grade IIIa, intra-abdominal lymph nodes
C82.34	Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb
C82.35	Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb
C82.36	Follicular lymphoma grade IIIa, intrapelvic lymph nodes
C82.37	Follicular lymphoma grade IIIa, spleen

C82.38	Follicular lymphoma grade IIIa, lymph nodes of multiple sites
C82.39	Follicular lymphoma grade IIIa, extranodal and solid organ sites
C82.40	Follicular lymphoma grade IIIb, unspecified site
C82.41	Follicular lymphoma grade IIIb, lymph nodes of head, face and neck
C82.42	Follicular lymphoma, grade IIIb, intrathoracic lymph nodes
C82.43	Follicular lymphoma grade IIIb, intra-abdominal lymph nodes
C82.44	Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb
C82.45	Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb
C82.46	Follicular lymphoma grade IIIb, intrapelvic lymph nodes
C82.47	Follicular lymphoma grade IIIb, spleen
C82.48	Follicular lymphoma grade IIIb, lymph nodes of multiple sites
C82.49	Follicular lymphoma grade IIIb, extranodal and solid organ sites
C82.50	Diffuse follicle center lymphoma, unspecified site
C82.51	Diffuse follicle center lymphoma, lymph nodes of head, face, and neck
C82.52	Diffuse follicle center lymphoma, intrathoracic lymph nodes
C82.53	Diffuse follicle center lymphoma, intra-abdominal lymph nodes
C82.54	Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb
C82.55	Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.56	Diffuse follicle center lymphoma, intrapelvic lymph nodes
C82.57	Diffuse follicle center lymphoma, spleen
C82.58	Diffuse follicle center lymphoma, lymph nodes of multiple sites
C82.59	Diffuse follicle center lymphoma, extranodal and solid organ sites
C82.60	Cutaneous follicle center lymphoma, unspecified site
C82.61	Cutaneous follicle center lymphoma, lymph nodes of head, face, and neck
C82.62	Cutaneous follicle center lymphoma, intrathoracic lymph nodes
C82.63	Cutaneous follicle center lymphoma, intra-abdominal lymph nodes
C82.64	Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb
C82.65	Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.66	Cutaneous follicle center lymphoma, intrapelvic lymph nodes
C82.67	Cutaneous follicle center lymphoma, spleen
C82.68	Cutaneous follicle center lymphoma, lymph nodes of multiple sites
C82.69	Cutaneous follicle center lymphoma, extranodal and solid organ sites
C82.80	Other types of follicular lymphoma, unspecified site
C82.81	Other types of follicular lymphoma, lymph nodes of head, face, and neck
C82.82	Other types of follicular lymphoma, intrathoracic lymph nodes
C82.83	Other types of follicular lymphoma, intra-abdominal lymph nodes
C82.84	Other types of follicular lymphoma, lymph nodes of axilla and upper limb
C82.85	Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb
C82.86	Other types of follicular lymphoma, intrapelvic lymph nodes
C82.87	Other types of follicular lymphoma, spleen

C82.88	Other types of follicular lymphoma, lymph nodes of multiple sites
C82.89	Other types of follicular lymphoma, extranodal and solid organ sites
C82.90	Follicular lymphoma, unspecified, unspecified site
C82.91	Follicular lymphoma, unspecified, lymph nodes of head, face and neck
C82.92	Follicular lymphoma, unspecified, intrathoracic lymph nodes
C82.93	Follicular lymphoma, unspecified, intra-abdominal lymph nodes
C82.94	Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb
C82.95	Follicular lymphoma, unspecified lymph nodes of inguinal region and lower limb
C82.96	Follicular lymphoma, unspecified, intrapelvic lymph nodes
C82.97	Follicular lymphoma, unspecified, spleen
C82.98	Follicular lymphoma, unspecified, lymph nodes of multiple sites
C82.99	Follicular lymphoma, unspecified, extranodal and solid organ sites
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site
C83.81	Other non-follicular lymphoma, lymph nodes of head, face and neck
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes
C83.83	Other non-follicular lymphoma, intra-abdominal lymph nodes
C83.84	Other non-follicular lymphoma, lymph nodes of axilla and upper limb
C83.85	Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
C83.86	Other non-follicular lymphoma, intrapelvic lymph nodes
C83.87	Other non-follicular lymphoma, spleen
C83.88	Other non-follicular lymphoma, lymph nodes of multiple sites
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C85.80	Other specified types of non-Hodgkin lymphoma, unspecified site
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face and neck
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region of lower limb
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87	Other specified types of non-Hodgkin lymphoma, spleen

C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma)

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at:

<http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): J & M	NCD/LCD/Article Document (s): A56141
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56141&bc=gAAAAAAAAAAAAAAAA	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; DLBCL = diffuse large B-cell lymphoma; MRD = minimal residual disease; TLS = tumor lysis syndrome; IPI = International Prognostic Index; ASCT = autologous stem-cell transplantation; TTF = time to treatment failure; DFS = disease free survival

B-Cell Lymphoma

Second line or subsequent therapy							
Regimen	NCCN Category	FDA Approved	Trial Design	Comparator	Primary End-Point	Line of Therapy	Conclusion
Rituximab (weekly x4)	2A	Yes	Single-arm, multi-center	N/A	-----	Relapsed disease	<ul style="list-style-type: none"> The response rate of 48% with rituximab is comparable to results with single-agent cytotoxic chemotherapy. Toxicity was mild.
Bendamustine + obinutuzumab (BO), followed by maintenance obinutuzumab in non-progressing patients	2A preferred (in patients refractory to rituximab)	Yes	Phase 3 (GADOLIN) , randomized, controlled, open-label, multi-center	Bendamustine (B)	PFS	Refractory to rituximab	<ul style="list-style-type: none"> Obinutuzumab plus bendamustine followed by obinutuzumab maintenance has improved efficacy over bendamustine monotherapy in rituximab-refractory patients with indolent non-Hodgkin lymphoma, with manageable toxicity
Copanlisib	2A	Yes	Phase 2 (CHRONOS-1)	N/A	ORR	Relapsed or refractory indolent B-cell NHL after ≥ 2 prior lines of therapy (including	<ul style="list-style-type: none"> Copanlisib demonstrated significant efficacy with an ORR of 61% and a manageable safety profile in heavily pretreated patients with relapsed or refractory indolent lymphoma.

						rituximab and an alkylating agent/regimen)	
Ofatumumab	2A	No	Phase 2	N/A	ORR	Refractory to rituximab	<ul style="list-style-type: none"> • Ofatumumab is modestly active with an ORR of 22% in patients refractory to rituximab
Obinutuzumab	None	No	Phase 2 (GAUSS study). randomized	Rituximab	ORR	Relapsed or refractory	<ul style="list-style-type: none"> • Obinutuzumab failed to demonstrate a PFS or OS benefit when compared with rituximab.