POLICY NUMBER UM_1327	**SUBJECT** Aliqopa™ (copanlisib)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 3**
DATES COMMITTEE REVIEWED 10/11/17, 10/10/18, 10/09/19	**APPROVAL DATE** October 9, 2019	**EFFECTIVE DATE** October 9, 2019	**COMMITTEE APPROVAL DATES** (latest version listed last) 10/11/17, 10/10/18, 10/09/19	
PRIMARY BUSINESS OWNER: UM **APPROVED BY:** Dr. Andrew Hertler		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1		**NCQA STANDARDS**	**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Oncology	

I. PURPOSE

To define and describe the accepted indications for Aliqopa (copanlisib) usage in the treatment of cancer.

II. DEFINITIONS

Aliqopa (copanlisib): is a kinase inhibitor of phosphatidylinositol-3-kinase (PI3K) and works primarily through isoforms PI3K-alpha and PI3K-beta which are expressed in malignant B cells. The result may be tumor cell death via apoptosis and inhibition of proliferation of primary malignant B cell lines. Several important cell-signaling pathways are also inhibited by copanlisib, such as CXCR12 mediated chemotaxis of malignant B cells, B-cell receptor (BCR) signaling and NF-kappa-B signaling in lymphoma cell lines.

Aliqopa (copanlisib) is FDA approved for the treatment of adults with relapsed follicular lymphoma who have received at least 2 prior systemic treatments. It was granted an accelerated approval for use in these patients.

Aliqopa (copanlisib) is available in 60 mg single dose vial.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Aliqopa (copanlisib) may be considered medically necessary when any of the following selection criteria is met:

1. **Non-Hodgkin Lymphoma**
    a. Follicular Non-Hodgkin Lymphoma
        i. The member has a diagnosis of relapsed follicular NHL **AND**
        ii. Aliqopa (copanlisib) is being used as a single-agent **AND**
        iii. The member has failed at least two prior therapies, including alkylating agents (i.e., cyclophosphamide and rituximab).
    b. Aliqopa (copanlisib) is being used as a single-agent as subsequent therapy for relapsed/refractory disease after 2 prior therapies for one of the following:
        i. Nodal marginal zone lymphoma
        ii. Gastric MALT lymphoma
        iii. Non-gastric MALT lymphoma
        iv. Splenic marginal zone lymphoma

Exclusion Criteria: Aliqopa (copanlisib) is not considered medically necessary when any of the following selection criteria are met:

1. Aliqopa (copanlisib) is being used after disease progression with the same regimen or prior PI3K inhibitors (i.e. idelalisib).
2. Concurrent use with other chemotherapy, immunotherapy, or ongoing systemic corticosteroid.
3. Dosing exceeds single dose limit of Aliqopa (copanlisib) 60 mg.
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Aliqopa (copanlisib) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:** 60 mg IV over 1 hour on days 1, 8, and 15 repeated every 28 days until disease progression.
2. **Dosage Adjustments:**
    a. Concomitant use with strong CYP3A inhibitors: Reduce dose to 45 mg.
    b. Cutaneous reaction (Severe, grade 3): Withhold until resolved, then restart and reduce dose from 60 mg to 45 mg or from 45 mg to 30 mg.
    c. Cutaneous reaction (Life-threatening): Discontinue use.
    d. Geriatric: No adjustment necessary.
    e. Hyperglycemia (Pre-dose fasting blood glucose (FBG) 160 mg/dL or greater or non-fasting blood glucose 200 mg/dL or greater): Withhold until FBG is 160 mg/dL or less or non-fasting blood glucose is 200 mg/dL or less.
    f. Hyperglycemia (First occurrence of pre-dose or post dose blood glucose level 500 mg/dL or greater): Withhold until FBG is 160 mg/dL or less or until non-fasting blood glucose is 200 mg/dL or less, then restart and maintain at a dose of 45 mg.
    g. Hyperglycemia (Repeat occurrence of pre-dose or post dose blood glucose level 500 mg/dL or greater): Withhold until FBG is 160 mg/dL or less or until non-fasting blood glucose is 200 mg/dL or less, then restart and maintain at a dose of 30 mg. Upon recurrence at a dose of 30 mg, discontinue use.
    h. Hypertension (Pre-dose blood pressure 150/90 mmHg or greater): Withhold therapy until BP is less than 150/90 mmHg on 2 consecutive measurements at least 15 minutes apart.
    i. Hypertension (Post dose blood pressure 150/90 mmHg or greater): If antihypertensive therapy is not needed, continue at current dose; if antihypertensive therapy is necessary, consider reducing dose from 60 mg to 45 mg or from 45 mg to 30 mg. If blood pressure is uncontrolled despite antihypertensive therapy, discontinue use.
    j. Hypertension (Life-threatening post dose elevation): Discontinue use.
    k. Infection (Grade 3 or higher): Withhold until resolution.
    l. Infection (Suspected Pneumocystis jiroveci pneumonia (PJP), any grade): Withhold; if infection confirmed, withhold until infection resolves, then restart at previous dose with concomitant PJP prophylaxis.

m. Neutropenia (Absolute neutrophil count (ANC) 0.5 to 1 x 103cells/mm3): Continue at current dose and monitor ANC at least weekly.

n. Neutropenia (ANC less than 0.5 x 103 cells/mm3): Withhold and monitor ANC at least weekly until ANC is at least 0.5 x 103 cells/mm3, then resume at previous dose; upon recurrence, reduce dose to 45 mg.

o. Noninfectious pneumonitis (NIP; grade 2): Withhold during NIP treatment; upon recovery to grade 0 or 1 NIP, restart at a dose of 45 mg; if grade 2 NIP recurs, discontinue use.

p. Noninfectious pneumonitis (NIP; grade 3 or higher): Discontinue use.

q. Thrombocytopenia (Platelet count less than 25 x 109/L): Withhold; if platelet count recovers to 75 x 109/L or greater within 21 days, restart and reduce dose from 60 mg to 45 mg or from 45 mg to 30 mg; if platelet count does not recover to 75 x 109/L within 21 days, discontinue use.

r. Other severe, non-life-threatening toxicities (Grade 3): Withhold until resolved, then restart and reduce dose from 60 mg to 45 mg or from 45 mg to 30 mg.

s. Other life-threatening toxicities: Discontinue use.

3. **Monitoring:**

a. Tumor response may be indicative of efficacy.

b. CBC, including absolute neutrophil count, at least weekly during treatment

c. Signs or symptoms of infection

d. Hyperglycemia; closely in patients with diabetes mellitus

e. Blood pressure; pre- and post-infusion.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Aliqopa PI prescribing information. Bayer HealthCare Pharmaceuticals Inc., Whippany, NJ 2019.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.