POLICY NUMBER UM ONC_1279	SUBJECT Cotellic™ (cobimetinib)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATES COMMITTEE REVIEWED 03/23/16, 01/05/17, 01/02/18, 01/07/19, 12/11/19, 01/08/20	APPROVAL DATE January 8, 2020	EFFECTIVE DATE January 8, 2020	COMMITTEE APPROVAL DATES (latest version listed last) 03/23/16, 01/05/17, 01/02/18, 01/07/19, 12/11/19, 01/08/20	
PRIMARY BUSINESS OWNER: UM APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1		NCQA STANDARDS UM 2	ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS All	

I. PURPOSE

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

II. DEFINITIONS

Cotellic (cobimetinib): is a selective inhibitor of the mitogen-activated extracellular kinase (MEK) pathway reversibly inhibiting MEK1 and MEK2, which are upstream regulators of the extracellular signal-related kinase (ERK) pathway. The ERK pathway promotes cellular proliferation. MEK1 and MEK2 are part of the BRAF pathway, which is activated by BRAF V600E and K mutations. Cobimetinib and vemurafenib are used in combination, increased apoptosis and reduced tumor growth occurs. Vemurafenib targets a different kinase in the RAS/RAF/MEK/ERK pathway.

Cotellic (cobimetinib) is FDA approved to be used in combination with vemurafenib to treat advanced melanoma that has spread to other parts of the body or is unresectable in surgery, and that has a certain type of abnormal gene (BRAF V600E or V600K mutation).

Cotellic (cobimetinib) is available in 20 mg oral tablets.

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century 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: Cotellic (cobimetinib) may be considered medically necessary when any of the following selection criteria is met:

1. **PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:**
    a. When health plan Medicaid coverage provisions- including any applicable PDLs (Preferred Drug Lists)- conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the **Preferred Drug Guidelines OR**
    b. When health plan Exchange coverage provisions- including any applicable PDLs (Preferred Drug Lists)- conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the **Preferred Drug Guidelines OR**
    c. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the **Preferred Drug Guidelines shall follow NCH L1 Pathways** when applicable, otherwise shall follow NCH drug policies: http://pathways.newcenturyhealth.com **AND**

d. Continuation requests of previously approved non-preferred medication are not subject to this provision **AND**

e. When available, generic alternatives are preferred over brand-name drugs.

2. **Malignant Melanoma**

a. The member has BRAF V600 activating mutation, and Cotellic (cobimetinib) is being used in combination with vemurafenib for ONE of the following:

i. Metastatic or unresectable disease

A. First-line or reinduction therapy **OR**

B. Second-line or subsequent therapy for disease progression for patients with if targeted therapy not previously used.

ii. Adjuvant therapy in combination with vemurafenib in members who have unacceptable toxicities to dabrafenib/trametinib.

Exclusion Criteria: Cotellic (cobimetinib) is not considered medically necessary when any of the following selection criteria is met:

1. Cotellic (cobimetinib) is not indicated to treat patients with wild-type BRAF melanoma.
2. Concomitant use of another MEK or BRAF inhibitor such as Mekinist (trametinib) or Tafinlar (dabrafenib).
3. Disease progression while taking Cotellic (cobimetinib).
4. Dosing exceeds single dose limit of 60 mg.
5. Treatment exceeds the maximum limit of 63 (20 mg) tablets/month.

IV. PROCEDURE

Requests for Cotellic (cobimetinib) 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 (3 x 20 mg tablets) once daily for 21 out of 28-day cycle until the disease progresses or there is evidence of unacceptable toxicity.**
2. **Dosage Adjustments:**

a. First dose reduction is 40 mg orally once daily. The second dose reduction is 20 mg orally once daily. Discontinue Cotellic (cobimetinib) if 20mg/day is not tolerated.

b. Hepatic: First occurrence of Grade 4

i. Withhold therapy for up to 4 weeks and resume at a dose reduction after patient has improve to grade 0 or 1.

ii. Permanently discontinue medication if there is no improvement to grade 0 or 1 after 4 weeks or if there is a recurrent grade 4.

3. **Monitoring Parameters**

a. Monitor for signs of bleeding which may lead to a major hemorrhagic event

i. Withhold therapy for 4 weeks if member has a grade 3 hemorrhage.

A. If symptoms improve to grade 0 or 1 then resume at a dose reduction

B. If grade 3 hemorrhage does not improve after 4 weeks then discontinue Cotellic (cobimetinib).

ii. Permanently discontinue Cotellic (cobimetinib) if member has a grade 4 hermorrhage.

b. Check LVEF 1 month before treatment and every 3 months as there is an increased risk of cardiomyopathy when taking cobimetinib and vermurafenib.

i. In asymptomatic patients

A. If member has an absolute decrease by 10% or greater in LVEF and less than institutional lower limit of normal (LLN) then withhold Cotellic (cobimetinib) therapy for 2 weeks.

B. Resume therapy at a dose reduction if the LVEF is above the LLN and the absolute decrease of LVEF is 10% or less

C. Permanently discontinue Cotellic (cobimetinib) if the member has an absolute decrease by 10% or greater in LVEF or less than institutional lower limit of normal (LLN) after 2 weeks of withholding therapy.

ii. In symptomatic patients with a decrease of LVEF from basline

A. Cotellic (cobimetinib) therapy should be withheld for up to 4 weeks and resumed at a dose reduction if

1) The symptoms have resolved and

2) The LVEF is at or above LLN, and

3) The absolute decrease from baseline LVEF is 10% or less.

4) If all 3 of the above does not occur than Cotellic (cobimetinib) therapy must be permanently discontinued.

c. Monitor for severe dermatologic reactions such as skin rashes.

d. Monitor for serous retinopathy and retinal vein occlusion if there are any visual disturbances.

e. Monitor liver function with laboratory tests.

f. Monitor Creatinine phosphokinase for Rhabdomyolysis

i. If there is a grade 4 CPK elevation or any CPK elevation with myalgia

A. Withhold Cotellic (cobimetinib) for up to 4 weeks as resume therapy at a dose reduction if symptoms improve to grade 3

B. If there is not improvement after 4 weeks, then discontinue therapy permanently

g. Members may have severe photosensitivity and should avoid sun exposure

i. If there are any grade 2 intolerable occurrences or above

A. Withhold Cotellic (cobimetinib) therapy for up to 4 weeks until symptoms improve to grade 0 or 1 and resume at a dose reduction

B. If symptoms do not improve to a grade 0 or 1 after 4 weeks, then discontinue permanently.

V. APPROVAL AUTHORITY

1. Review – Utilization Management Department
2. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. PI prescribing information accessed on 1/9/19: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206192s000lbl.pdf.
2. Clinical Pharmacology Elsevier Gold Standard. 2020.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2020.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2020.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2020.