BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE:**	**1/21/2016**
SECTION: DRUGS	**LAST REVIEW DATE:**	**2/17/2022**
	LAST CRITERIA REVISION DATE:	**2/17/2022**
	ARCHIVE DATE:	

COTELLIC™ (cobimetinib) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Cotellic (cobimetinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     a. Unresectable **OR** metastatic melanoma with a BRAF V600E **OR** V600K mutation, used in combination with Zelboraf (vemurafenib)

     b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

  4. Cotellic (cobimetinib) is to be used in combination with Zelboraf (vemurafenib)

  5. **ALL** of the following baseline tests have been completed before initiation of treatment:
     a. Left ventricular ejection fraction (LVEF) is above institutional lower limit or ≥ 50%
     b. Liver function test
     c. Creatine phosphokinase (CPK)
     d. Serum creatinine
     e. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-1

  6. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Cotellic (cobimetinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

  2. Individual's condition responded while on therapy
     a. Response is defined as:
        i. Documented evidence of efficacy, disease stability and/or improvement
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

  3. Individual has been adherent with the medication

  4. The requested dose is at least 20 mg daily

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5. Individual has not developed any significant adverse drug effects that may exclude continued use
    a. Significant adverse effects include:
        i. Hemorrhage: First occurrence of life-threatening hemorrhage or severe hemorrhage that did not improve with dose interruption and dose reduction
        ii. Cardiomyopathy:
            1. Asymptomatic absolute decrease in LVEF of > 10% from baseline that is below the lower limit of normal and the LVEF does not recover after dose modification
            2. Symptomatic decrease in LVEF from baseline where symptoms persist or LVEF is less than lower limit of normal or absolute decrease from baseline LVEF is more than 10% after dose modification
        iii. Retinal vein occlusion (RVO) or serious retinopathy that does not improve after dose modification
        iv. Hepatotoxicity: First occurrence of life-threatening liver toxicity or liver toxicity that recurs or fails to improve after dose interruption and dose reduction
        v. Rhabdomyolysis: Life-threatening CPK elevation or any CPK elevation and myalgia that does not improve after dose modification
        vi. Photosensitivity: Moderate or severe or life-threatening reaction that does not improve after dose modification
        vii. Any moderate or severe reaction that does not improve after dose modification
        viii. Any first occurrence or recurrence of a life-threatening reaction

6. There are no significant interacting drugs

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

    1. **Off-Label Use of Non-cancer Medications**

    2. **Off-Label Use of Cancer Medications**

Description:

Cotellic (cobimetinib) is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with Zelboraf (vemurafenib). It is not indicated for treatment of patients with wild-type BRAF melanoma.

Cobimetinib is a reversible inhibitor of mitogen-activated protein kinase (MAPK)/extracellular signal regulated kinase 1 (MEK1) and MEK2. The MEK proteins are upstream regulators of the extracellular signal related kinase (ERK) pathway, which promotes cellular proliferation. BRAF V600E and V600K mutations result in constitutive activation of the BRAF pathway which includes MEK1 and MEK2.

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Cobimetinib and vemurafenib target two different kinases in the RAS/RAF/MEK/ERK pathway. Compared to either drug alone, co-administration results in increased apoptosis and reduced tumor growth in tumor cell lines harboring BRAF V600E mutations.

Cobimetinib is the second MEK inhibitor approved in the United States. The other available MEK inhibitor is Mekinist (trametinib), which is given simultaneously with Tafinlar (dabrafenib), a BRAF inhibitor. BRAF inhibitors [Tafinlar (dabrafenib), Zelboraf (vemurafenib)] or BRAF inhibitors combined with MEK inhibitors may be used as therapies for unresectable or metastatic melanoma when BRAF V600E or V600K mutations are present. These mutations appear in approximately half of malignant melanomas.

Resources:

Cotellic (cobimetinib) product information, revised by Genentech, Inc. 01-2018. Available, at DailyMed http://dailymed.nlm.nih.gov. Accessed December 01, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Melanoma: Cutaneous Version 2.2021 – Updated February 19, 2021. Available at https://www.nccn.org. Accessed November 29, 2021.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.