BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

COTELLIC™ (cobimetinib) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for COTELLIC (cobimetinib)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by an Oncologist or is in consultation with an Oncologist

Indication
- Unresectable or metastatic melanoma with BRAF V600E or V600K mutation, used in combination with Zelboraf (vemurafenib)
- Histiocytic neoplasm, used as a single agent

- Other oncologic direct treatment uses listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Presence of BRAF V600E or V600K mutation in melanoma tumor specimens
- Left ventricular ejection fraction (LVEF) is above institutional lower limit or greater than 50 percent
- Liver function test
- Creatine phosphokinase
- Serum creatinine
- Electrocardiogram (ECG) and electrolytes
- Eastern Cooperative Oncology Group Performance Status of 0 to 1

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- There is **NO** concurrent use with the following:
  - Moderate or strong CYP3A inhibitors (e.g., fluconazole, erythromycin, ketoconazole, itraconazole, clarithromycin)
  - Moderate or strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, dexamethasone, nafcillin)

Additional Requirements
- Does not have wild type BRAF melanoma
- No severe renal impairment

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (LVEF, liver function, creatine phosphokinase, serum creatinine)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualifications
- Continues to be seen by an Oncologist or is in consultation with an Oncologist

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Clinical Response
- No evidence of disease progression or unacceptable toxicity

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- There is **NO** concurrent use with the following:
  - Moderate or strong CYP3A inhibitors (e.g., fluconazole, erythromycin, ketoconazole, itraconazole, clarithromycin)
  - Moderate or strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, dexamethasone, nafcillin)
- There are **NONE** of the following significant adverse drug effects:
  - Hemorrhage not improved with dose modification
  - Persistent symptoms of cardiomyopathy or left ventricular ejection fraction decrease greater than 10 percent
  - Severe dermatologic reaction
  - Retinal vein occlusion or serious retinopathy not improved with dose modification
  - Hepatotoxicity not improved with dose modification
  - Rhabdomyolysis not improved with dose modification
  - Photosensitivity not improved with dose modification
  - Any moderate or severe reaction not improved with dose modification
  - Any first occurrence or recurrence of a life threatening reaction

Additional Requirements
- Does not have wild type BRAF melanoma
- No severe renal impairment
- Requested dose is at least 20 mg daily

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

ORIGINAL EFFECTIVE DATE: 01/21/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/19/2026

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Criteria for Off-Label Use Requests:

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. Cotellic (cobimetinib), as a single agent, is indicated for the treatment of adult patients with histiocytic neoplasms.

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.
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.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Eastern Co-operative Oncology Group (ECGO) Performance Status:

Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physical strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled, cannot carry on any self-care, totally confined to bed or chair

5	Dead
Oken, MM, Creech, RH, Tormey, DC, et al.: Toxicity and Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

Resources:

Cotellic (cobimetinib) product information, revised by Genentech, Inc. 05-2023. Available, at DailyMed http://dailymed.nlm.nih.gov. Accessed November 10, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Melanoma: Cutaneous Version 2.2025 – Updated January 28, 2025. Available at https://www.nccn.org. Accessed January 06, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Histiocytic Neoplasms Version 2.2025 – Updated November 21, 2025. Available at https://www.nccn.org. Accessed January 06, 2026.

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.