BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 1/21/16**
SECTION: DRUGS	**LAST REVIEW DATE: 1/18/18**
	LAST CRITERIA REVISION DATE: 1/18/18
	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.**

COTELLIC™ (cobimetinib) oral tablet (cont.)

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.

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.

National Comprehensive Cancer Network (NCCN) Melanoma: version 1.2018 (Oct 11, 2017)
Metastatic or un-resectable melanoma:

- First-line therapy: (choice is based on evaluation of the individual patient)
  - Immunotherapy:
    - Anti-PD-1 monotherapy:
      - Nivolumab (category 1)
      - Pembrolizumab (category 1)
    - Nivolumab/ipilimumab
  - Targeted therapy if BRAF V600 activating mutation: (preferred if clinically needed for early response)
    - Dabrafenib/trametinib (category 1)
    - Vemurafenib/cobimetinib (category 1)

Disease progression or Maximal clinical benefit from BRAF targeted therapy:

- Second-line or subsequent therapy:
  - Anti-PD-1 monotherapy:
    - Nivolumab
    - Pembrolizumab
  - Nivolumab/ipilimumab
  - Targeted therapy if BRAF V600 activating mutation:
    - Dabrafenib/trametinib
    - Vemurafenib/cobimetinib
  - Ipilimumab
  - High dose IL-2
  - Cytotoxic agents: dacarbazine, temozolomide, paclitaxel, albumin-bound paclitaxel, carboplatin/paclitaxel

- Imatinib for tumor with activating mutations of KIT
- Consider best supportive care for poor performance status

Cotellic (cobimetinib)

Medication class:
Antineoplastic Agent, Mitogen-activated Extracellular Kinase (MEK) Inhibitor

FDA-approved indication(s):
- Treatment of unresectable or metastatic melanoma in patients with a BRAF V600E or V600K mutation (in combination with vemurafenib)

Limitations of use:
- Cotellic is not indicated for the treatment of patients with wild-type BRAF melanoma

Recommended Dose:
- 60 mg once daily days 1-21 of each 28-day treatment cycle (in combination with vemurafenib)

Maximum dosage
- Not stated

Available Dosage Forms:
- 20 mg tablets

Warnings and Precautions:
- Permanently discontinue Cotellic in an individual who cannot tolerate a dose of 20 mg daily
- Permanently discontinue Cotellic in an individual who develops major hemorrhage or symptomatic bleeding in a critical area or organ that cannot be controlled
- The safety of Cotellic has not been established in patients with a baseline LVEF that is either below the institutional limit of normal or below 50%
- Permanently discontinue Cotellic in an individual who develops asymptomatic cardiomyopathy if the LVEF is less than the institutional lower limit of normal or has an absolute decrease in LVEF of more than 10% from baseline
- Permanently discontinue Cotellic in an individual who develops symptomatic cardiomyopathy if symptoms persist, the LVEF is less than the institutional lower limit of normal or has an absolute decrease in LVEF of more than 10% from baseline
- Permanently discontinue Cotellic in an individual who develops serious retinopathy such as chorioretinopathy or retinal detachment
- Permanently discontinue Cotellic in an individual who develops retinal vein occlusion
- Cotellic pharmacokinetics has not been studied in patients with moderate to severe hepatic impairment
- Permanently discontinue Cotellic in an individual who develops significant hepatotoxicity
- Permanently discontinue Cotellic in an individual who develops rhabdomyolysis or myalgia and any elevation of CPK that does not improve within 4 weeks
- Permanently discontinue Cotellic in an individual who develops photosensitivity that does not improve within 4 weeks

COTELLIC™ (cobimetinib) oral tablet (cont.)

- Patients should avoid sun exposure, wear protective clothing, and use broad spectrum UVA/UVB sunscreen and lip balm (SPF >30) when outdoors
- Permanently discontinue Cotellic in an individual who develops a serious adverse reaction that does not improve within 4 weeks or in an individual who has a recurrence of a life-threatening adverse reaction
- A dose recommendation has not been established for patients with severe renal impairment (Creatinine clearance < 30 mL/min)
- Do not use with strong or moderate CYP3A inhibitors
- Temporarily reduce Cotellic dose to 20 mg daily if need to use short term (< 14 days) moderate CYP3A inhibitors
- Avoid use with use with strong or moderate CYP3A inducers (such as Carbamazepine, Efavirenz, Phenytoin, Rifampin, St. John's Wort)
- Woman of child bearing potential should be warned against becoming pregnant
- Woman of child bearing potential should use effective contraceptive therapy
- Woman who is breast feeding an infant or child should stop breast feeding
- The absolute bioavailability of Cotellic is 46%

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 an Oncologist
  2. Individual is 18 years of age or older
  3. A confirmed diagnosis of unresectable **OR** metastatic melanoma with a BRAF V600E **OR** V600K mutation
  4. Cotellic is to be used in combination with Zelboraf (vemurafenib)
  5. **ALL** of the following baseline tests have been completed before initiation of treatment:
     - Left ventricular ejection fraction (LVEF) is above institutional lower limit or ≥ 50%
     - Liver function test
     - Creatine phosphokinase (CPK)
     - Serum creatinine

  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 an Oncologist
  2. Individual's condition has not worsened while on therapy
     - Worsening is defined as:
       - Cancer progression

COTELLIC™ (cobimetinib) oral tablet (cont.)

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
   - Significant adverse effects include:
     - Hemorrhage
       - Signs and symptoms may include: blood in stool, dark red or tar-like stools, coughing up blood, vomiting blood, or unusual bleeding, easy bruising, blood in urine, dizziness or feeling faint
     - Cardiomyopathy
       - Signs and symptoms may include: edema of ankles or feet, shortness of breath, weight gain, chest pain, shortness of breath, fatigue
     - Retinopathy or RVO
       - Signs and symptoms may include: blurred vision, distorted vision, partial missing vision, halos, or other vision changes
     - Hepatotoxicity
       - Signs and symptoms may include: right sided abdominal pain, bruising, yellow skin or eyes, dark brown urine, severe nausea or vomiting, fatigue, light colored pale stools, itching, confusion
     - Rhabdomyolysis
       - Signs and symptoms may include: muscle aches or pains, muscle spasm or weakness, dark red urine
     - Photosensitivity
       - Signs and symptoms may include: severe exaggerated skin rash or sunburn, rashes may or may not itch, severe blistering

5. There are no significant interacting drugs

Renewal duration: 12 months

Resources:

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.

Cotellic. Package Insert. Revised by manufacturer 11/2015. Accessed 01-26-2016.

Cotellic. Package Insert. Revised by manufacturer 05/2016. Accessed 11-29-2016, 12-26-2017.

NCCN Clinical Practice Guidelines in Oncology: Melanoma. Version 1.2018, Oct 11, 2017. https://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.