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# 5.21.068

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| **Section:** | Prescription Drugs | **Effective Date:** | April 1, 2024 |
| **Subsection:** | Antineoplastic Agents | **Original Policy Date:** | December 11, 2015 |
| **Subject:** | Cotellic | **Page:** | 1 of 5 |

***Last Review Date:*** March 8, 2024

# Cotellic

## Description

### Cotellic (cobimetinib)

**Background**
Cotellic (cobimetinib) is an inhibitor of kinase proteins that are part of the regulation of cellular proliferation, including mitogen-activated protein kinase (MAPK) and extracellular signal regulated kinase 1 and 2 (MEK1 and MEK2). Dysfunction in these pathways has been found to be an important mechanism in cancer cell survival and proliferation (1).

**Regulatory Status**
FDA-approved indications: Cotellic is a kinase inhibitor indicated: (1)

- For the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib.
- As a single agent for the treatment of histiocytic neoplasms.

New primary malignancies, cutaneous and non-cutaneous can occur with Cotellic. Patients should be monitored for signs and symptoms of both cutaneous and non-cutaneous malignancies. Suspicious skin lesions should be managed by excision and dermopathologic evaluation. Dermatologic monitoring should occur for 6 months following the last dose of Cotellic when administered with vemurafenib (1).

Major hemorrhagic (bleeding) events, severe dermatologic reactions, hepatotoxicity, rhabdomyolysis and severe photosensitivity can occur with Cotellic. Patients should be monitored for hemorrhage, skin abnormalities, liver enzyme abnormalities, creatinine phosphokinase elevations periodically and as clinically indicated. Patients should be advised to

avoid sun exposure, wear protective clothing, and use a broad-spectrum UVA/UVB sunscreen (1).

The risk of cardiomyopathy is increased in patients receiving the combination of Cotellic with vemurafenib. The safety of Cotellic has not been established in patients with decreased left ventricular ejection fraction. Left ventricular ejection fraction (LVEF) should be evaluated before treatment, after one month of treatment then every 3 months thereafter during treatment with Cotellic (1).

Prescriber should perform an ophthalmological evaluation at regular intervals and for any visual disturbances. Permanently discontinue Cotellic for retinal vein occlusion (1).

Cotellic can cause fetal harm when administered to a pregnant woman. Females of reproductive potential are advised to use effective contraception during treatment and for 2 weeks following the final dose of Cotellic (1).

Safety and efficacy of Cotellic in patients less than 18 years of age have not been established (1).

**Related policies**
Braftovi, Mekinist, Mektovi, Tafinlar, Zelboraf

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Cotellic may be considered **medically necessary** if the conditions indicated below are met.

Cotellic may be considered **investigational** for all other indications.

## Prior-Approval Requirements

**Age** 18 years of age and older

**Diagnoses**

Patient must have **ONE** of the following:

1. Unresectable or metastatic melanoma
    a. Must be used in combination with vemurafenib (Zelboraf)
    b. Documented BRAF V600E or V600K mutation as detected by an FDA-approved test

2. Histiocytic neoplasms (Erdheim-Chester disease, Langerhans Cell histiocytosis, Rosai-Dorfman disease, Xanthogranuloma, etc.)
    a. Used as a single agent

**AND** the following for **ALL** indications:

1. Left ventricular ejection fraction (LVEF) > 50%

## Prior – Approval *Renewal* Requirements

**Age** 18 years of age and older

**Diagnoses**

Patient must have **ONE** of the following:

1. Unresectable or metastatic melanoma
    a. Must be used in combination with vemurafenib (Zelboraf)

2. Histiocytic neoplasms (Erdheim-Chester disease, Langerhans Cell histiocytosis, Rosai-Dorfman disease, Xanthogranuloma, etc.)
    a. Used as a single agent

**AND ALL** of the following for **ALL** indications:

1. **NO** disease progression or unacceptable toxicity
2. Left ventricular ejection fraction (LVEF) > 50%

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Quantity** 189 tablets per 84 days

**Duration** 12 months

## Prior – Approval *Renewal* Limits

Same as above

## Rationale

**Summary**

Cotellic (cobimetinib) is a kinase inhibitor targeting the MAPK and MEK proteins. Patients should be monitored for malignancies prior to treatment, during treatment and up to 6 months after final dose. Left ventricular ejection fraction should be monitored prior and during treatment. If the patient experiences severe dermatological reactions, the Cotellic dose should be interrupted, reduced, or discontinued. Cotellic should be permanently discontinued in the event of retinal vein occlusion occurring. Liver function should be monitored during treatment and as clinically indicated. Creatinine phosphokinase should be periodically monitored for signs and symptoms of rhabdomyolysis. The patient should be advised to avoid sun exposure. Female patients of reproductive potential are advised to use effective contraception during treatment and for 2 weeks following the final dose of Cotellic. Safety and efficacy of Cotellic in patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Cotellic while maintaining optimal therapeutic outcomes.

**References**

1. Cotellic [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2022.
2. NCCN Drugs & Biologics Compendium® Cobimetinib 2023. National Comprehensive Cancer Network, Inc. Accessed on January 29, 2024.

## Policy History

| Date | Action |
|---|---|
| December 2015 | Added to PA |
| March 2016 | Annual review<br>Changed qty limits from 63 tabs per 84days<br>Policy number change from 5.04.68 |
| June 2016 | Annual editorial review and reference update |

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| | Removal of no wild-type BRAF melanoma<br>Change of the assessment of left ventricular ejection fraction (LVEF) by echocardiogram or multigated acquisition (MUGA) scan before initiation and every 3 months to left ventricular ejection fraction (LVEF) is above 50% per SME |
| September 2016 | Annual review |
| June 2017 | Annual editorial review and reference update<br>Addition of age limit to renewal section |
| June 2018 | Annual editorial review and reference update |
| September 2018 | Annual editorial review |
| June 2019 | Annual review |
| June 2020 | Annual review |
| March 2021 | Annual editorial review |
| March 2022 | Annual review and reference update |
| November 2022 | Added indication of histiocytic neoplasms. Added severe dermatological reactions, rhabdomyolysis, severe photosensitivity, and embryo-fetal toxicity to regulatory status. Changed policy number to 5.21.068 |
| March 2023 | Annual review and reference update |
| June 2023 | Annual review and reference update |
| March 2024 | Annual review and reference update |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.**