Cotellic® (cobimetinib)
(Oral)

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I. Length of Authorization [1,7]

Coverage is provided for six months and may be renewed (unless otherwise specified).

- Coverage for the adjuvant treatment of melanoma is up to a maximum of 1 year of therapy.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

– Cotellic 20 mg tablet: 63 tablets per 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 60 mg daily for 21 days in a 28 day cycle

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Patient has not received prior therapy with BRAF and/or MEK inhibitors (e.g., trametinib, encorafenib, dabrafenib, binimetinib, etc.) unless otherwise specified; **AND**

Universal Criteria [1]

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient will avoid coadministration with all of the following:
  - Strong CYP3A4 inhibitors (e.g., fluconazole, itraconazole, etc.)
  - Moderate CYP3A4 inhibitors (e.g., erythromycin, clarithromycin, etc.), if short-term therapy (≤14 days) is unavoidable, the patient will be monitored closely for adverse reactions and/or dose modifications will be implemented
  - Strong or moderate CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**

Cutaneous Melanoma † ‡ [1,3,4]

- Patient has BRAF V600 mutation-positive disease as detected by an FDA approved or CLIA compliant test*; **AND**
  - Patient has unresectable or metastatic** disease; **AND**
    - Used in combination with atezolizumab and vemurafenib as first-line therapy; **OR**
    - Used in combination with vemurafenib; **AND**
      - Used as initial therapy or subsequent therapy; **OR**
      - Used as re-induction therapy for patients who experience disease control *(i.e., complete response, partial response, or stable disease)* from prior MEK inhibitor therapy, but subsequently have disease progression/relapse >3 months after treatment discontinuation; **OR**
  - Used as adjuvant therapy in combination with vemurafenib in patients with unacceptable toxicities to dabrafenib/trametinib; **AND**
    - Patient has lymph node involvement following complete resection, complete lymph node dissection (CLND), therapeutic lymph node dissection (TLND), or nodal basin ultrasound surveillance; **OR**
    - Patient has clinical satellite/in-transit metastases or local satellite/in-transit recurrence with no evidence of disease (NED) after complete excision to clear margins

***Metastatic disease includes stage III clinical satellite/in transit metastases or local satellite/in-transit recurrence in patients with limited resectable and unresectable disease, unresectable nodal recurrence, and disseminated (unresectable) distant metastatic disease*

Central Nervous System (CNS) Cancers ‡ [3]

- Patient has BRAF V600E mutation-positive disease; **AND**
- Used in combination with vemurafenib; **AND**
  - Used as adjuvant treatment in a patient with incomplete resection, biopsy, or surgically inaccessible location; **AND**
    - Patient has pilocytic astrocytoma OR pleomorphic xanthoastrocytoma (PXA) OR ganglioglioma; **OR**
  - Used for treatment of recurrent or progressive low-grade glioma; **OR**
  - Used for treatment of recurrent anaplastic glioma or glioblastoma

Histiocytic Neoplasms ‡ [3]

- Used as a single agent; **AND**
- Patient has a MAP kinase pathway mutation, or no detectable mutation, or testing not available; **AND**
- Patient has one of the following:
  - Patient relapsed/refractory or symptomatic Erdheim-Chester Disease **OR**

- Rosai-Dorfman Disease; **AND**
  - Patient has symptomatic unifocal unresectable (bulky/site of disease) or symptomatic multifocal disease; **OR**
  - Relapsed or refractory disease; **OR**
- Langerhans Cell Histiocytosis (LCH) **AND**
  - Patient has multisystem disease with symptomatic or impending organ dysfunction; **OR**
  - Patient has pulmonary disease; **OR**
  - Patient has multifocal single system bone disease not responsive to treatment with a bisphosphonate and >2 lesions; **OR**
  - Patient has CNS lesions; **OR**
  - Patient has relapsed or refractory disease

** If confirmed using an immunotherapy assay-http://www.fda.gov/CompanionDiagnostics*

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s)

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment defined as stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: new malignancies, serous retinopathy and retinal vein occlusion, severe dermatologic reactions, severe photosensitivity reactions, severe hepatotoxicity, rhabdomyolysis, severe hemorrhagic events, cardiomyopathy, etc.
- Left ventricular ejection fraction (LVEF) has not had an absolute decrease of > 10% from baseline and is not below the lower limit of normal (LLN) *(LVEF results must be within the previous 3 months)*; **AND**

Adjuvant treatment of Melanoma [3]

- Treatment has not exceeded 1 year of therapy

Cutaneous Melanoma (re-induction therapy) [3]

- *Refer to Section III for criteria (see Cutaneous Melanoma – Used as re-induction therapy)*

V. Dosage/Administration [1,7]

Indication	Dose

All indications	60 mg (three 20 mg tablets) orally once daily for the first 21 days of each 28-day cycle until disease progression or unacceptable toxicity *(Note: for adjuvant treatment of melanoma, treat until disease recurrence or unacceptable toxicity for up to 1 year).*

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug, oral, chemotherapeutic, nos
- C9399 – Unclassified drugs or biologicals (Hospital Outpatient use only)

NDC:

- Cotellic 20 mg tablet: 50242-0717-xx

VII. References

1. Cotellic [package insert]. South San Francisco, CA; Genentech USA, Inc; January 2018. Accessed September 2021.
2. Zelboraf [package insert]. South San Francisco, CA; Genentech USA, Inc; May 2020. Accessed September 2021.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) cobimetinib. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2021.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Melanoma: Cutaneous. Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2021.
5. Larkin J, Ascierto PA, Dréno B, Atkinson V, Liszkay G, Maio M, Mandalà M, Demidov L, Stroyakovskiy D, Thomas L, de la Cruz-Merino L, Dutriaux C, Garbe C, Sovak MA, Chang I, Choong N, Hack SP, McArthur GA, Ribas A. Combined vemurafenib and cobimetinib in BRAF-mutated melanoma. N Engl J Med. 2014 Nov 13;371(20):1867-76. doi: 10.1056/NEJMoa1408868. Epub 2014.
6. Gutzmer R, Stroyakovskiy D, Gogas H, et al. Atezolizumab, vemurafenib, and cobimetinib as first-line treatment for unresectable advanced BRAFV600 mutation-positive melanoma

(IMspire150): primary analysis of the randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2020;395:1835-44.

7. Mekinist [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; May 2021. Accessed September 2021.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C43.0	Malignant melanoma of lip
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of left lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe

ICD-10	ICD-10 Description
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.0	Malignant neoplasm of spinal cord
C72.9	Malignant neoplasm of central nervous system, unspecified
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
C96.20	Malignant mast cell neoplasm unspecified
C96.5	Multifocal and unisystemic Langerhans-cell histiocytosis
C96.6	Unifocal Langerhans-cell histiocytosis
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D43.1	Neoplasm of uncertain behavior of brain, infratentorial
D43.2	Neoplasm of uncertain behavior of brain, unspecified
D43.4	Neoplasm of uncertain behavior of spinal cord
D43.9	Neoplasm of uncertain behavior of central nervous system, unspecified
D76.3	Other histiocytosis syndromes
Z85.841	Personal history of malignant neoplasm of brain

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC