Mektovi® (binimetinib)
(Oral)

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I. Length of Authorization [1,12]

Coverage is provided for 6 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]:

- Mektovi 15 mg tablet: 6 tablets per day

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

- 90 mg daily

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., vemurafenib, dabrafenib, cobimetinib, trametinib, encorafenib, 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 2-3 months) during treatment; **AND**

Cutaneous Melanoma † ‡ Φ [1,5,8]

- 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 as in combination with encorafenib; **AND**
            - Used as first-line or subsequent therapy; **OR**

        - Used as re-induction therapy for patients who experience disease control *(i.e., complete response, partial response, or stable disease and no residual toxicity)* from prior MEK inhibitor therapy, but subsequently have disease progression/relapse >3 months after treatment discontinuation; **OR**
    - Patient has limited resectable disease; **AND**
        - Used as initial treatment in combination with encorafenib; **AND**
        - Patient has unacceptable toxicities to dabrafenib/trametinib or on the basis of agent side effect profiles; **AND**
            - Patient has stage III disease with clinical satellite/in-transit metastases; **OR**
            - Patient has local satellite/in-transit recurrence; **OR**
    - Used as adjuvant therapy in combination with encorafenib in patients with unacceptable toxicities to dabrafenib/trametinib or on the basis of agent side-effect profiles; **AND**
        - Patient has stage III disease; **AND**
            - Patient has resected sentinel node positive disease either during observation without additional nodal surgery and with mandatory radiographic nodal surveillance OR after complete lymph node dissection (CLND); **OR**
            - Patient has clinically positive node(s) following wide excision of the primary tumor and therapeutic lymph node dissection (TLND) OR following neoadjuvant therapy; **OR**
            - Patient has clinical satellite/in-transit metastases and no evidence of disease (NED) after complete excision to clear margins; **OR**
        - Patient has local satellite/in-transit recurrence with NED after complete excision to clear margins; **OR**
        - Patient has resectable disease limited to nodal recurrence following excision and complete TLND OR following neoadjuvant therapy

***Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in transit metastases, as well as unresectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.*

Non-Small Cell Lung Cancer (NSCLC) † ‡ [1,5]

- Patient has BRAF V600E mutation-positive disease as detected by an FDA-approved or CLIA-compliant test*; **AND**
- Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
- Used in combination with encorafenib

Histiocytic Neoplasms ‡ [5]

- Used as single agent therapy; **AND**
- Patient has a mitogen-activated protein (MAP) kinase pathway mutation, or no detectable mutation, or testing not available; **AND**
- Patient has Langerhans Cell Histiocytosis (LCH); **AND**
    - Patient has multisystem disease with symptomatic or impending organ dysfunction or critical organ involvement; **OR**
    - Patient has single-system lung disease; **OR**
    - Patient has multifocal single system bone disease not responsive to treatment with a bisphosphonate; **OR**
    - Patient has CNS lesions; **OR**
    - Patient has relapsed or refractory disease

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

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s); Φ Orphan Drug

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 as defined by 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: new primary malignancies, interstitial lung disease/pneumonitis, cardiomyopathy, severe hemorrhagic events, venous thromboembolism, ocular toxicities (e.g., serous retinopathy, retinal vein occlusion [RVO], uveitis), rhabdomyolysis, hepatotoxicity, etc.; **AND**
- 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 Cutaneous Melanoma [5,12]

- Treatment has not exceeded 1 year of therapy

Cutaneous Melanoma (re-induction therapy) [5]

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

V. Dosage/Administration [1,5,12]

Indication	Dose
Cutaneous Melanoma and NSCLC	Administer 45 mg (three 15 mg tablets) orally twice daily, in combination with encorafenib, until disease progression or unacceptable toxicity *Note: for adjuvant treatment of melanoma, treat until disease recurrence or unacceptable toxicity for up to 1 year.*
Histiocytic Neoplasms	Administer 45 mg (three 15 mg tablets) orally twice daily until disease progression or unacceptable toxicity

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug oral, chemotherapeutic, Not Otherwise Specified
- C9399 – Unclassified drugs or biologics

NDC:

- Mektovi 15 mg tablet: 70255-0010-xx

VII. References

1. Mektovi [package insert]. Boulder, CO; Array BioPharma; October 2023. Accessed October 2023.
2. Flaherty KT, Robert C, Hersey P, et al. Improved survival with MEK inhibition in BRAF-mutated melanoma. N Engl J Med. 2012 Jul 12; 367(2):107-14.
3. Flaherty KT, Infante JR, Daud A, at al. Combined BRAF and MEK inhibition in melanoma with BRAF V600 mutations. N Engl J Med. 2012 Nov; 367(18):1694-703. doi: 10.1056/NEJMoa1210093. Epub 2012 Sep 29.
4. Long GV, Stroyakovksy D, Gogas H, et al. Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma. N Eng J Med 2014 Sep 29, {Epub ahead of print]
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) binimetinib. National Comprehensive Cancer Network, 2023. 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 October 2023.
6. Dummer R, Asciedrto PA, Gogas H, et al. Overall survival in COLUMBUS: A phase 3 trial of encorafenib (ENCO) plus binimetinib (BINI) vs vemurafenib (VEM) or enco in BRAF-mutant melanoma (Abstract 9504). American Society of Clinical Oncology 2018 annual meeting.

7. Van Cutsem E, Huijberts S, Grothey A, et al. Binimetinib, Encorafenib, and Cetuximab Triplet Therapy for Patients With BRAF V600E-Mutant Metastatic Colorectal Cancer: Safety Lead-In Results From the Phase III BEACON Colorectal Cancer Study. J Clin Oncol. 2019 Jun 10;37(17):1460-1469.
8. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Melanoma: Cutaneous. Version 2.2023. National Comprehensive Cancer Network, 2023. 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 October 2023.
9. Braftovi [package insert]. Boulder, CO; Array BioPharma, Inc.; October 2023. Accessed October 2023.
10. Awada G, Seremet T, Fostier K, et al. Long-term disease control of Langerhans cell histiocytosis using combined BRAF and MEK inhibition. Blood Adv. 2018 Aug 28; 2(16): 2156–2158. Published online 2018 Aug 28. doi: 10.1182/bloodadvances.2018021782.
11. Riely G, Smit E, Ahn M, et al. Phase II, Open-Label Study of Encorafenib Plus Binimetinib in Patients With BRAFV600-Mutant Metastatic Non-Small-Cell Lung Cancer. J Clin Oncol 2023 Jul 20;41(21):3700-3711. doi: 10.1200/JCO.23.00774. Epub 2023 Jun 4.
12. Mekinist [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; August 2023. Accessed October 2023.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung

ICD-10	ICD-10 Description
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right 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
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
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
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.820	Personal history of malignant melanoma of skin

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.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)
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