Clinical Policy: Binimetinib (Mektovi)

Reference Number: CP.PHAR.50
Effective Date: 09.01.18
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Binimetinib (Mektovi®) is a kinase inhibitor.

FDA Approved Indication(s)

Mektovi is indicated, in combination with encorafenib (Braftovi®) for the treatment of:

- Patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test;
- Adult patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600E mutation, as detected by an FDA-approved test.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Mektovi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Melanoma (must meet all)**:**

1. Diagnosis of melanoma with BRAF V600E or V600K mutation;
2. Disease is for treatment of one of the following (a, b, c, or d):
   a. Unresectable or metastatic melanoma;
   b. Stage III melanoma as adjuvant therapy or neoadjuvant;
   c. Limited resectable melanoma;
   d. Re-induction therapy for disease progression or relapse;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. For unresectable or metastatic melanoma: Prescribed in combination with Braftovi™; unless Braftovi/Mektovi combination is contraindicated;
6. For stage III melanoma or limited resectable melanoma: Both of the following (a and b):
   a. Prescribed in combination with Braftovi;
   b. Member has unacceptable toxicities to Tafinlar®/Mekinist®, or Tafinlar/Mekinist are not appropriate for the member on the basis of agent side-effect profiles;
   **Prior authorization may be required for Braftovi*
7. For Mektovi requests, member must use generic binimetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;

8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 90 mg per day;
      ii. 6 tablets per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Non-Small Cell Lung Cancer (must meet all):
1. Diagnosis of advanced, metastatic, or recurrent NSCLC with BRAF V600E mutation;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with Braftovi*;
   **Prior authorization may be required for Braftovi*
5. For Mektovi requests, member must use generic binimetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 90 mg per day;
      ii. 6 tablets per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Histiocytic Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of Langerhans cell histiocytosis;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease meets one of the following (a, b, or c):
   a. Positive for mitogen-activated protein (MAP) kinase pathway mutation,
   b. No detectable mutation;
   c. Mutation testing not available;
5. Prescribed as a single agent;
6. For Mektovi requests, member must use generic binimetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 90 mg per day;
      ii. 6 tablets per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Mektovi for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Mektovi requests, member must use generic binimetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed both of the following (i and ii)
      i. 90 mg per day;
      ii. 6 tablets per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
BRAF: B-Raf proto-oncogene, serine/threonine kinase
FDA: Food and Drug Administration
NSCLC: non-small cell lung cancer

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Melanoma		
Tafinlar® (dabrafenib) and Mekinist® (trametinib)	Tafinlar 150 mg PO BID with Mekinist 2 mg PO QD	Tafinlar: 300 mg/day Mekinist: 2 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Melanoma, NSCLC	45 mg PO BID, approximately 12 hours apart, in combination with Braftovi until disease progression or unacceptable toxicity	90 mg/day

VI. Product Availability

Tablet: 15 mg

VII. References

1. Mektovi Prescribing Information. Boulder, CO: Array BioPharma Inc.; October 2023. Available at: https://labeling.pfizer.com/ShowLabeling.aspx?id=12988. Accessed February 22, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 22, 2024.
3. National Comprehensive Cancer Network. Melanoma: Cutaneous Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed February 22, 2024.
4. National Comprehensive Cancer Network. Histiocytic Neoplasms Version 1.2023. Available at: ttps://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf. Accessed February 6, 2024.
5. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 9, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: removed colorectal cancer off-label use as it is no longer included in the NCCN Compendium; oral oncology generic redirection language added; revised reference to HIM off-label use policy from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	01.13.21	05.21
2Q 2022 annual review: for melanoma, added adjuvant therapy category 2A indication per NCCN; Commercial approval durations revised from “Length of Benefit” to “12 months or duration of request, whichever is less”; references reviewed and updated.	02.13.22	05.22
Template changes applied to other diagnoses/indications.	11.23.22	
2Q 2023 annual review: for melanoma added limited resectable melanoma and added off-label criteria for histiocytic neoplasms per NCCN category 2A recommendation; references reviewed and updated.	02.21.23	05.23
RT4: added newly FDA-approved and NCCN compendium supported use in non-small cell lung cancer in combination with Mektovi.	11.02.23	
2Q 2024 annual review: for melanoma, added criteria for neoadjuvant therapy and re-induction therapy for disease progression/relapse; for NSCLC, removed redundant criteria for treatment naïve or subsequent therapy, removed criteria for prior BRAF therapy, revised capsules to tablets; references reviewed and updated.	02.06.24	05.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members

and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.