Clinical Policy: Encorafenib (Braftovi)

Reference Number: CP.PHAR.127
Effective Date: 09.01.18
Last Review Date: 05.26
Line of Business: Commercial, HIM/ICHRA, Medicaid Revision Log

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

Description

Encorafenib (Braftovi®) is a kinase inhibitor.

FDA Approved Indication(s)

Braftovi is indicated:

- In combination with binimetinib (Mektovi®), for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.
- In combination with cetuximab and fluorouracil-based chemotherapy, for the treatment of adult patients with metastatic colorectal cancer (mCRC) with a BRAF V600E mutation, as detected by an FDA-approved test.
- In combination with cetuximab, for the treatment of adult patients with mCRC with a BRAF V600E mutation, as detected by an FDA-approved test, after prior therapy.
- In combination with binimetinib (Mektovi), for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600E mutation, as detected by an FDA-approved test.

Limitation(s) of use: Braftovi is not indicated for treatment of patients with wild-type BRAF melanoma, wild-type BRAF CRC, or wild-type BRAF NSCLC.

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 Braftovi 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, or c):
   a. Unresectable or metastatic melanoma;
   b. Stage III melanoma as adjuvant or neoadjuvant therapy;
   c. Limited resectable melanoma;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;

5. For unresectable or metastatic melanoma: Prescribed in combination with Mektovi, unless Braftovi/Mektovi combination therapy is contraindicated;
6. For adjuvant therapy or limited resectable melanoma: Both of the following (a and b):
   a. Prescribed in combination with Mektovi;
   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 Mekotvi*
7. For Braftovi requests, member must use generic encorafenib, 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. 450 mg per day;
      ii. 6 capsules 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/ICHRA– 12 months
Commercial – 12 months or duration of request, whichever is less

B. Colon Cancer, Rectal Cancer (must meet all)**:**
1. Diagnosis of colon or rectal cancer with BRAF V600E mutation;
2. Disease is unresectable, advanced, or metastatic;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Prescribed in combination with either Erbitux® or Vectibix®, with or without chemotherapy (e.g. FOLFOX, FOLFIRI, CapeOX);
   **Prior authorization may be required for Erbitux and Vectibix*
6. For Braftovi requests, member must use generic encorafenib, 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. 300 mg per day;
      ii. 4 capsules 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/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Non-Small Cell Lung Cancer (must meet all)**:**
1. Diagnosis of advanced, metastatic, or recurrent NSCLC with BRAF V600E mutation-positive;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with Mektovi*;

**Prior authorization may be required for Mekotvi*

5. For Braftovi requests, member must use generic encorafenib, 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. 450 mg per day;
      ii. 6 capsules 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/ICHRA– 12 months
Commercial – 12 months or duration of request, whichever is less

D. NCCN Recommended Uses (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Appendiceal neoplasms and cancers;
   b. Advanced or metastatic small bowel adenocarcinoma;
2. Disease is BRAF V600E mutation positive;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Prescribed in combination with Erbitux or Vectibix*;
   **Prior authorization may be required for Erbitux and Vectibix*
6. For Braftovi requests, member must use generic encorafenib, 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. 300 mg per day;
      ii. 4 capsules 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/ICHRA– 12 months
Commercial – 12 months or duration of request, whichever is less

E. 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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, 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 Braftovi for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Braftovi requests, member must use generic encorafenib, 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, b, or c):*
   a. Melanoma or non-small cell lung cancer: New dose does not exceed both of the following (i and ii):
      i. 450 mg per day;
      ii. 6 capsules per day;
   b. Colon or rectal cancer, small bowel adenocarcinoma, or appendiceal neoplasms and cancers: New dose does not exceed both of the following (i and ii):
      i. 300 mg per day;
      ii. 4 capsules per day;
   c. 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/ICHRA– 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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, 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/ICHRA, 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
CRC: colorectal cancer
FDA: Food and Drug Administration
mCRC: metastatic colorectal cancer
NCCN: National Comprehensive Cancer Network
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
Colorectal Cancer		
Examples of previous therapy: • FOLFOX (fluorouracil, leucovorin, and oxaliplatin) • CapeOX (capecitabine and oxaliplatin) • FOLFIRI (irinotecan, leucovorin, 5-FU) • FOLFOXIRI (irinotecan, oxaliplatin, leucovorin, fluorouracil) • IROX (oxaliplatin, irinotecan); oxaliplatin and irinotecan	Varies	Varies
Opdivo (nivolumab)	Monotherapy: 240 mg IV every 2 weeks or 480 mg IV every 4 weeks With ipilimumab: 240 mg IV, followed by ipilimumab 1 mg/kg IV on the same day every 3 weeks for 4 doses, then nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks	Monotherapy: 480 mg/dose With ipilimumab: See regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Keytruda (pembrolizumab)	200 mg IV every 3 weeks OR 400 mg every 6 weeks up to 24 months	200 mg every 3 weeks OR 400 mg every 6 weeks
Melanoma		
Tafinlar® and Mekinist®	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	450 mg PO QD in combination with Mektovi until disease progression or unacceptable toxicity	450 mg/day
Colon cancer, rectal cancer	300 mg PO QD with Erbitux ± fluorouracil-based chemotherapy (mFOLFOX6 or FOLFIRI)	300 mg/day

VI. Product Availability

Capsule: 75 mg

VII. References

1. Braftovi Prescribing Information. Boulder, CO: Array BioPharma Inc.; February 2026. Available at: https://braftovi.pfizerpro.com/.Accessed March 6, 2026
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 4, 2026.
3. National Comprehensive Cancer Network. Cutaneous Melanoma Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed February 4, 2026.
4. National Comprehensive Cancer Network. Colon Cancer Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed March 6, 2026.
5. National Comprehensive Cancer Network. Rectal Cancer Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed March 6, 2026.
6. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 3.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 4, 2026.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2022 annual review: for melanoma, added option for Braftovi monotherapy in melanoma if Mektovi is contraindicated and 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.	02.12.22	05.22
Template changes applied to other diagnoses/indications.	09.30.22	
2Q 2023 annual review: for melanoma criteria added limited resectable melanoma, and for colon and rectal cancer added appendiceal adenocarcinoma 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: removed appendiceal adenocarcinoma per NCCN compendium removal; removed redundant criteria for treatment naïve or subsequent therapy, removed criteria for prior BRAF therapy; references reviewed and updated.	02.07.24	05.24
RT4: added newly FDA-approved use in mCRC in combination with cetuximab and mFOLFOX6.	01.02.25	
2Q 2025 annual review: for colorectal cancer, clarified combination use with Vectibix is off-label per NCCN; references reviewed and updated.	02.13.25	05.25
2Q 2026 annual review: for melanoma, added option for use in stage III melanoma as neoadjuvant therapy; for colon and rectal cancer, simplified to combination use with or without chemotherapy (capecitabine- or fluorouracil-based) per NCCN; RT4: updated FDA Approved Indication(s) section for mCRC from accelerated approval to full approval per PI; added off-label criteria for small bowel adenocarcinoma and appendiceal neoplasms and cancer per NCCN compendium; for all indications, extended Medicaid and HIM initial approval duration from 6 months to 12 months for this maintenance medication for a chronic condition; references reviewed and updated. Added ICHRA line of business.	03.31.26	05.26

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.