Drug Policy:

Braftovi™ (encorafenib)

POLICY NUMBER UM ONC_1335	**SUBJECT** Braftovi™ (encorafenib)		**DEPT/PROGRAM** UM Dept	**PAGE 1 of 4**
DATES COMMITTEE REVIEWED 07/19/18, 06/13/19, 10/09/19, 12/11/19, 05/13/20, 12/09/20, 05/12/21, 11/15/21, 05/11/22, 03/08/23, 04/12/23, 11/08/23, 11/13/24, 01/08/25	**APPROVAL DATE** January 08, 2025	**EFFECTIVE DATE** January 31, 2025	**COMMITTEE APPROVAL DATES** 07/19/18, 06/13/19, 10/09/19, 12/11/19, 05/13/20, 12/09/20, 05/12/21, 11/15/21, 05/11/22, 03/08/23, 04/12/23, 11/08/23, 11/13/24, 01/08/25	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Evolent Specialty Services Clinical Guideline Review Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses clinical guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. A list of codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this clinical guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their plan customer service representative for specific coverage information.

I. PURPOSE

To define and describe the accepted indications for Braftovi (encorafenib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. Colorectal Cancer

1. The member has BRAF V600E mutation positive unresectable or metastatic colorectal cancer, regardless of KRAS/NRAS status AND
2. Braftovi (encorafenib) will be used in combination with Erbitux (cetuximab) or Vectibix (panitumumab) after prior therapy with an oxaliplatin and/or irinotecan containing regimen.
3. Braftovi (encorafenib) may be used in combination with Erbitux (cetuximab) and FOLFOX in the initial line setting in members with stage IV, metastatic BRAF V600E mutation positive colorectal cancer, and KRAS/NRAS status is either Wild-Type or unknown.
    a. Members must also:
        i. Have not had prior treatment with any selective BRAF inhibitors or EGFR inhibitors
        ii. Have tumors that are not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) unless the member is ineligible to receive immune checkpoint inhibitors

C. Melanoma

1. Braftovi (encorafenib) may be used in combination with Mektovi (binimetinib) in BRAF V600E or V600K mutation positive unresectable/metastatic melanoma.

D. Non-Small Cell Lung Cancer (NSCLC)

1. Braftovi (encorafenib) may be used in combination with Mektovi (binimetinib) in BRAF V600E mutation positive metastatic non-small cell lung cancer (NSCLC).

III. EXCLUSION CRITERIA

A. Disease progression while receiving Braftovi or another BRAF inhibitor (either as a single agent or as part of a combination regimen).

B. Dosing exceeds single dose limit of Braftovi (encorafenib) 450 mg (melanoma and NSCLC)/300 mg (colorectal cancer).

C. Treatment exceeds the maximum limit of Braftovi 180 (75 mg) capsules per month.

D. Investigational use of Braftovi (encorafenib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.

4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. CODING INFORMATION

HCPCS Code	Description
J8999	encorafenib
C9399	encorafenib

V. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

VI. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VII. ATTACHMENTS

A. None

VIII. REFERENCES

A. Dummer R, et al. Encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with BRAF-mutant melanoma (COLUMBUS): a multicentre, open-label, randomised phase 3 trial. Lancet Oncol. 2018 May;19(5):603-615.

B. Kopetz S, et al. BREAKWATER: An open-label, multicenter, randomized, phase 3 study, with a safety lead-in (SLI), of first-line (1L) encorafenib (E) + cetuximab (C) ± chemotherapy (CT) vs standard-of-care (SOC) CT for BRAF V600E-mutant metastatic colorectal cancer (mCRC). Journal of Clinical Oncology. 2023 May 31; 41(16). https://doi.org/10.1200/JCO.2023.41.16_suppl.TPS3627

C. Kopetz S, et al. Encorafenib, Binimetinib, and Cetuximab in BRAF V600E-Mutated Colorectal Cancer. N Engl J Med. 2019 Oct 24;381(17):1632-1643.Braftovi prescribing information. Array BioPharma Inc. Boulder, Colorado 2022.

D. Riely G, et al. Phase II, Open-Label Study of Encorafenib Plus Binimetinib in Patients With BRAFV600-Mutant Metastatic Non-Small Cell Lung Cancer. Journal of Clinical Oncology 2023 July; 41 (21): 3700-3711. DOI: 10.1200/JCO.23.00774

E. Braftovi prescribing information 2024. Array BioPharma Inc., Boulder, CO

F. Clinical Pharmacology Elsevier Gold Standard 2025.

G. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.

H. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.

I. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.

J. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

K. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.