Clinical Policy: Encorafenib (Braftovi)
Reference Number: CP.PHAR.127
Effective Date: 09.01.18
Last Review Date: 05.20
Line of Business: Commercial, HIM, Medicaid

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, 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, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, as detected by an FDA-approved test, after prior therapy

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

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 unresectable or metastatic;
      3. Prescribed by or in consultation with an oncologist;
      4. Age ≥ 18 years;
      5. Prescribed in combination with Mektovi®;
      6. Request meets one of the following (a or b):*
         a. Dose does not exceed 450 mg (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 – 6 months
Commercial – Length of Benefit
B. Colon Cancer, Rectal Cancer (must meet all):
   1. Diagnosis of colon cancer 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®;
   6. One of the following (a or b):
      a. Member previously received adjuvant therapy (e.g., FOLFOX, CapeOX);
      b. Request is for subsequent therapy following previous treatment (e.g., oxaliplatin or irinotecan based therapy);
   7. Request meets one of the following (a or b):*
      a. Dose does not exceed 300 mg (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 – 6 months
Commercial – Length of Benefit

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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 Braftovi for a covered indication and has received this medication for at least 30 days;
   2. Member is responding positively to therapy;
   3. If request is for a dose increase, request meets one of the following (a, b, or c):*
      a. Melanoma: New dose does not exceed 450 mg (6 capsules) per day;
      b. Colon or rectal cancer: New dose does not exceed 300 mg (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 – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is
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.PHAR.21 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

   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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>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</td>
<td>Colorectal cancer: Varies</td>
<td>Varies</td>
</tr>
</tbody>
</table>

   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
<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>450 mg PO QD in combination with Mektovi until disease progression or unacceptable toxicity</td>
<td>450 mg per day</td>
</tr>
<tr>
<td>Colon cancer, rectal cancer</td>
<td>300 mg PO QD with either Erbitux or Vectibix</td>
<td>300 mg per day</td>
</tr>
</tbody>
</table>

VI. Product Availability
   Capsules: 75 mg

VII. References

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created</td>
<td>07.24.18</td>
<td>08.18</td>
</tr>
<tr>
<td>No significant changes: added HIM line of business per SDC.</td>
<td>10.23.18</td>
<td></td>
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<tr>
<td>2Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>02.26.19</td>
<td>05.19</td>
</tr>
<tr>
<td>2Q 2020 annual review: RT4: added newly FDA-approved and NCCN compendium supported use in colon and rectal cancers in combination with either Erbitux or Vectibix; added maximum quantity for all indications; references reviewed and updated.</td>
<td>02.06.20</td>
<td>05.20</td>
</tr>
</tbody>
</table>

**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.

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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.

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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.

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